# Potential Triggers of Lichen Planus: A Review

**E.P. Sridevi Anjuga[1], N. Aravindha Babu[2]**

*[1]Post Graduate Student, [2]Professor, Department of Oral Pathology & Microbiology, Sree Balaji Dental College & Hospital, Chennai, BIHER*

## Abstract

Oral lichen planus (OLP) is mucocutaneous and chronic inflammatory disease of unclear pathogenesis. OLP usually affects the mucous membrane of oral cavity. It is an autoimmune disorder araising from several etiological factors like genetics, stress, virus, dental restorative materials, drugs and systemic diseases. It is a T-cell mediated autoimmune disease usually encountered by dentists and dermatologists. Although much work is being done on this disorder, there is still uncertainty over the specific etiopathogenesis and treatment. Because there is a risk of reported malignant potential with this disease, the patient needs early diagnosis and proper management. This article reviews mainly the etiology, pathogenetic mechanisms through which this unique disorder occurs along with the aspects of clinical, histopathological and treatment.

***Key Words:*** *Lichen planus. Pathogenesis, T-cell mediated, Autoimmune disorder,*

## Introduction

Lichen planus is a mucocutaneous condition involving different mucosal surfaces, either alone or in combination with skin involvement[1]. Similar to other mucosal areas, it most often includes the oral mucosa[1]. Oral lichen planus (OLP) is an unidentified etiology disease that affects stratified epithelial squamous[1]. More generally, this disorder affects 30-60-year-old middle-aged patients and females are more vulnerable than males with a 1.4:1 ratio[1]. Children and young adults rarely see OLP[1]. OLP should be considered a potentially malignant condition because there is a link between oral cancer and OLP although there is a variable degree of risk involved[1].The incidence of OLP varies from 1-2 percent in the general population.

Clinically, OLP has six forms: reticular(Figure 1), papular, plaque-like, atrophic(Figure 2), erosive and bullous(Figure 3)[3]. Oral lichen planus has been noted to occur independently of the skin form and tends to be constant and treatment-resistant.[4] Lateral border, tongue dorsum, gingiva, hard palate and vermilion border are common sites of involvement and occur as reticular, plaque-like or papular intraoral lesions[4]. However, Buccal mucosa remains the most frequent site of involvement[4].

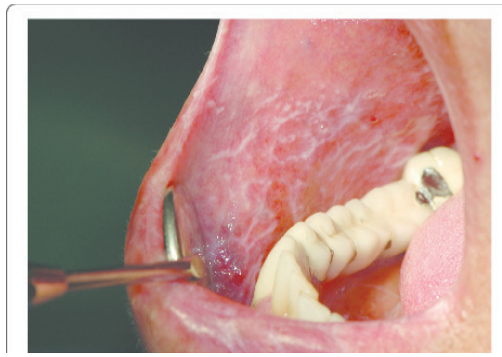
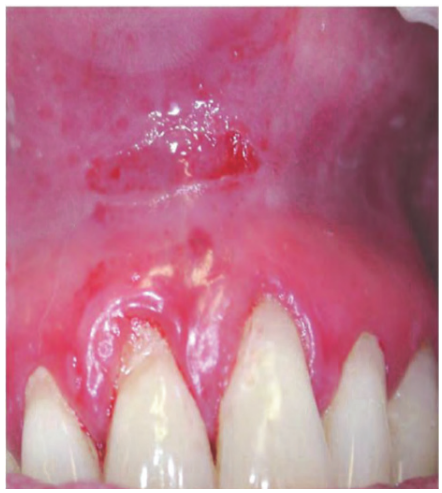


**Fig 1: Reticular lichen planus in right buccal mucosa**



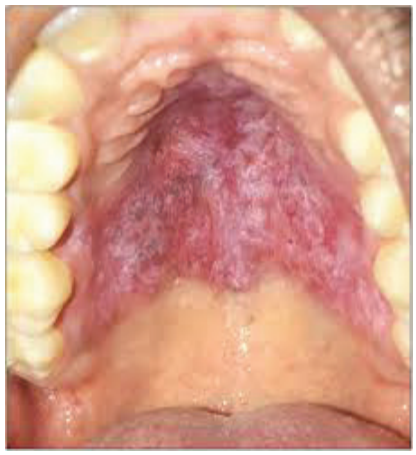
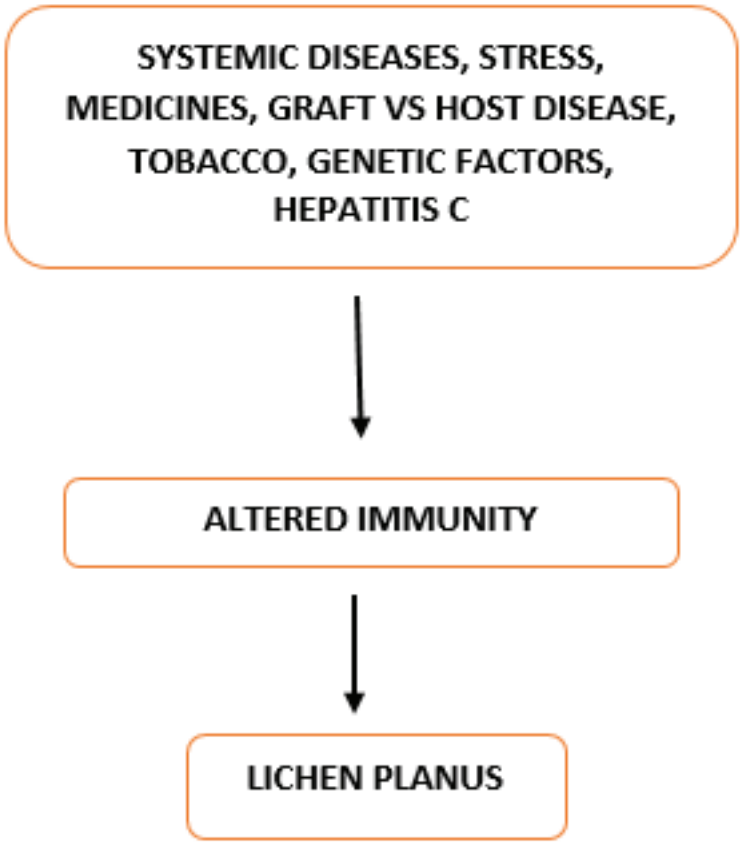


**Figure 2: Atrophic lichen planus**

**Figure 3: Bullous lichen planus**

**Etiological Factors:**




**Women:**

It is also generally accepted that OLP mainly affects females, indicating probably a genetic predisposition to OLP development[2]. This has given rise to the possibility that the consumption of drugs in women is associated with an increased susceptibility to OLP lesions[2].It is also generally accepted that OLP mainly affects females, indicating probably a genetic predisposition to OLP development[2].Drug history was found to be substaintially more prevalent in females patients with oral lichen planus[2] .

**Systemic Diseases:**

This correlation may be attributed to endocrine dysfunction in DM that may be associated with an immunological deficiency and may lead to OLP production[3]. Antidiabetic drugs and certain antidiabetic drugs in DM patients can cause an allergic reaction to lichenoid reaction[3]. Higher prevalence of oral mucosal lesions in DM patients may be due to lower healing levels in these patients, leading to longer duration of the lesion and not to increased incidence3. Therefore, if a lesion in a DM patient takes two months to heal and one month in the subject of control the incidence would increase in DM patients at a given time point[3].

A number of studies suggested that OLP in DM patients may be associated with a compromised immune system in these patients or may be associated with a number of oral hypoglycemic medicines taken by older people in particular[3].

In insulin-dependent diabetics as well as patients with NIDDM but with a higher frequency compared to normal subjects, oral LP has been reported A great deal of work is being conducted on the relationship between diabetes mellitus and oral LP[4].Autoimmune history of LP and diabetes mellitus further support the association relationship between oral LP and diabetes mellitus[4].

In relation with healthy subjects, oral lichen planus has a large association with noninsulin-dependent diabetes mellitus. Other reports also suggest a similar association with insulin-dependent diabetes mellitus

**HCV:**

HCV induced OLP pathogenesis is uncertain, but two hypotheses were raised to explain the mechanism of HCV-induced OLP triggering[5].

The first hypothesis indicates that replication of the virus is associated with the oral epithelium, thus directly contributing to lesion growth[5]. The second hypothesis suggests that the virus‘ high rate of mutation results in repeated immune cell activation, increasing the possibility of cross-reaction with its own tissue and consequently, the risk of autoimmune disease[5] .

HCV infection is pervasive, with an approximately 3% of the world’s population infected and involved as an etiological factor in lichen planus occurrence[6]. It is a single stranded RNA virus that is mainly spread through blood or blood products transfusion[6]. The mechanisms suggested for the cause of lichen planus are:

1) HCV is susceptible of cytopathic replication in cell types outside the liver[6].

2) It may activate an autoimmune process directed at antigens expressed in extra-hepatic cells[6].

3) 3) Persistent infection, followed by deposition on small blood vessels, can lead to immune complex formation with antibodies[6].

4) The activated CD8 T cells, cytokines and the expansion of certain B cell clones are the triggers of immunological processes leading to dermatological manifestations[6].

In OLP, HCV replication was reported by reverse transcription / polymerase chain reaction or in-situ hybridization in the epithelial cells of LP lesions in the mucosa; in the subepithelial group, HCV-specific CD4 and CD8 lymphocytes were also identified[7]. This probably suggest that lymphocytes with HCV-specific T may play a role in OLP’s pathogenesis[7].

**Medicines:**

Even though many drugs have been reported as possibility LDR inducers, non-steroidal anti-inflammatory drugs (NSAIDs) and antihypertensives, principally angiotensin-converting enzyme inhibitors (ACE inhibitors) are the most frequently involved drugs in LDRs[2] .

Two studies have shown that NSAIDs are clearly established as LDR inducers, with case history strongly indicating a correlation between NSAID consumption and the initiation of OLP, complete resolution or marked improvement of lesions when these medications are removed, and recurrence if patients are given the offending drug again[2].

Systemic drugs like anti-malarial drugs, non-steroidal anti-inflammatory drugs (NSAIDs), anti-hypertensive drugs and enzyme-converting angiotensin have been strongly linked with oral lichenoid reactions[8]. Diuretics, oral hypoglycaemic agents, gold salts, penicillin are other drugs reported to cause oral lichenoid

reactions[8].

**Tress:**

OLP's acerbations are associated with periods of emotional stress and anxiety. Ivonavaski et al., proposed that excessive emotional stress in OLP patients lead to psychosomatization, which may in turn contribute to OLP's initiation and clinical expression, and also indicated that psychosocial and emotional stress may be a possible factor that may precipitate reticular stress[10].

**Genetics:**

Genetic background seems to play a role in pathogenesis of OLP as there have been records of several family cases [9]. In a study of British patients with cutaneous lichen planus, Lowe et al., first reported a massively increased level of HLA-A3[9]. {8}

**Tobacco:**

This OLP-like lesion consisted of white, linear, wavy, parallel, non-elevated streaks which could not be scraped off[9].The lesions radiated in some instances from a central erythematous region. However as in classical OLP, the fine white lines did not intersect or criss-cross[9]. The lesion usually viewed at the site of placement of the betel quid[9]. In order to describe this OLP-like lesion, Zain et al. (63) coined the word ' betel-quid lichenoid' lesion[9]. There was no indication of a causal effect for betel quid in OLP[9].

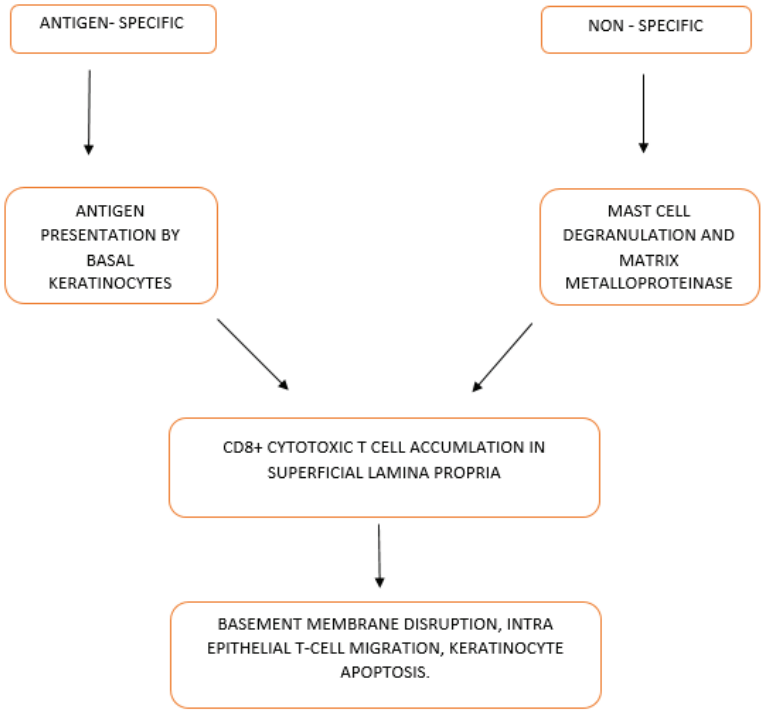
**Graft Vs Host Disease:**

Oral lichenoid lesions are part of the spectrum of chronic graft-versus-host disease following allogeneic transplantation of the bone marrow [9]. While the etiology of oral lichenoid lesions and chronic graft-versus-host disease 92 is different, there are quite similar clinical and histological appearances[9].

LP is identified as a disease of adults. The average presentation age ranges from 30 to 60 years.

Exact etiology of the LP is unclear, but it has been shown that degeneration of the basal epithelial layer, resulting from a switch in the cell-mediated immune response, plays an important role in the pathogenicity of the lesion.

**Pathogenesis:**



**Diagnosis:**

Based on the history, medical and histopathological examination, the diagnosis can be made[1]. Nevertheless, the diagnosis can only be made in classical lesions based on clinical appearances[1]. If skin lesions also occur, diagnostic reliability is reinforced[1].Biopsy is mandatory for to diagnose OLP[1]. Biopsy should include marginal tissue comprising areas that are both lesion and normal areas[1]. Direct and indirect immunofluorescent tests, ELISA can be helpful in diagnosing troublesome cases and preventing malignancy[1].

| POTENTIAL BIOMARKER: | LEVEL IN OLP PATIENTS: |
|---|---|
| Peroxidation products | Increase |
| Antioxidants ( Vit C and E) | Decrease |
| GPCA | Increase |
| Cortisol | Decrease |
| Immunoglobulin | Increase |

Potential biomarkers for to diagnose OLP[10]:

**Differential Diagnosis:**

For reticular OLP[1]:

- Leukoplakia,
- Lichenoid reaction,
- Graft vs host disease,
- Lupus erythematosus.

For erosive OLP[1]:

- Chronic cheek chewing,
- Hypersensitivity mucositis,
- Chronic candidiasis,
- Discoid lupus erythematosus,
- Squamous cell carcinoma,
- Benign mucous membrane pemphigoid,
- Pemphigus vulgaris,
- Erythema multiforme.

## Conclusion

Lichen planus is a chronic mucocutaneous disease with a malignant transformation of 0.4-5% affecting the oral mucosa and skin. The presence of different factors is likely to be responsible for initiating, aggravating and persisting OLP. Not only are the current treatment strategies not only ineffective for treating all patients and avoiding recurrences, but they also have serious adverse effects. More clarification on pathogenesis can help to adjust therapeutic interventions, increasing the morbidity of OLP patients dramatically.

## References

1. Gangesheety N, Kumar B P., Oral lichen planus: Etiology, Pathogenesis, Diagnosis and Management. World journal of stomatology2015;4(1):12-21. ISSN:2218-6263.
2. Hirota S K, Moreno R A, Seo J et al., Analysis of a possible association between oral lichen planus and drug intake. A controlled study. Med Oral Pathol Oral Cir Bucal 2011; 16(6):e750-6
3. Mozaffari H R, Sharif R, Sadeghi M., Prevalence of Oral lichen Planus in diabetes mellitus: A meta - analysis study. ACTA INFORM MED 2016; 24(6):390-393.
4. Ahmed I, Nasreen S, Jehangir U, Wahid Z. Frequency of Oral lichen planus in patients with non – insulin dependent diabetes mellitus. Journal of Pakistan association of Dermatologist 2012; 22:30-34.
5. Donempudi P, Bhayya H, Meduri V, Paramkusam G et al., Association of Oral lichen planus with hepatitis C virus, surface antigen of hepatitis B virus and diabetes: A clinical and biochemical study. Journal of Indian Academy of Oral medicine and radiology. 2016;28(3)
6. Prabhu S, Pavithran K, Sobhanaden G., Lichen Planus and hepatitis C virus (HCV) – is there an association? A serological study of 65 cases. Indian Journal of Dermatology, venerelogy and leprology 2002; 68(5): 273-274.
7. Lavanya N, Jayanthi P, Rao U K et al., Oral lichen planus: An update on pathogenesis and treatment. Journal of oral and maxillofacial pathology 2015; 15(2).

8. Ismail S B, Zain R. Oral lichen planus and Lichenoid reaction: Etiopathogenesis, Diagnosis , Management and Malignant transformation. Journal of oral science 2007;49(2): 89-106.

9. Kalkur C, Sattur A P, Guttal K S., Role of depression, anxiety and stress in patients with oral lichen planus: A pilot study. Indian Journal of Dermatology 2015;60(5):445-9

Type of article : Review