

# Analysis of Association of Systemic Drugs in Oral Lichen Planus Lesions

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## ABSTRACT

**Background:** Lichen planus is a relatively common mucocutaneous disorder that affects approximately 0.1% to 2.0% of the population. Etiology of lichen planus involves cell mediated immunologically induced degeneration of basal cell layer of the epithelium. Stress, diabetes, drugs, and graft versus host reactions are the other factors in the development of lichen planus. Studies have showed a relationship between Oral Lichen Planus (OLP) and daily intake of medicine.

Oral Lichenoid reactions related to long-term drug intake are referred to as lichenoid drug reactions (LDR). Drugs like anti-malarial, Non-steroidal anti-inflammatory [NSAIDs], antihypertensive agents, angiotensin enzyme inhibitors and diuretics cause lichenoid reactions. Since drugs have got role in affecting the oral mucosa either directly or indirectly, the present study was designed to investigate whether systemic medication contributes to the development of oral lichen planus (OLP) lesions.

**Objective:** To evaluate whether systemic medication contribute to the development of oral lichen planus lesions.

**Materials and Methods:** The study group comprised of 50 patients including 40 females and ten males with oral lichen planus reporting to the Department of Oral Medicine and Radiology, Karad (Western Maharashtra). Complete medical and drug history of the patients were recorded. Clinical examination of oral cavity was done, type and site of lichen planus was noted. The data obtained was statistically analyzed using SPSS software version 15.

**Results:** In our study group 80% of patients were females, with an age group between 31-50 years. The common site was buccal mucosa with reticular pattern as predominant type. Only ten patients were having history of intake of antihypertensive, hypoglycemic, drugs for thyroid disorders. There was no statistical significant association between systemic usage of drugs and occurrence of oral lichen planus

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lesions.

**Conclusion:** The use of systemic medication does not lead to significant increase in the incidence of oral lichen planus lesions in the study group.

**Keywords:** Oral lichen planus lesions, Drug intake, Buccal mucosa, Reticular lichen planus.

## INTRODUCTION

Lichen planus is a relatively common mucocutaneous disorder that affects approximately 0.1% to 2.0% of the population. The prevalence rate varies among races and geographic areas.<sup>1,2</sup> It affects both gender, but few studies have reported a slight female predilection.<sup>1,3,4</sup> Other studies had showed male predominance.<sup>5</sup> Lichen planus affects oral mucosa as well as skin. The skin lesions will appear as popular, purple, pruritic and polygonal areas. It primarily affects adults, with the mean age of onset in the fourth to fifth decades of life.<sup>4</sup> Oral Lichen planus (OLP) lesions are frequently found on the buccal mucosa, tongue, soft palate, gingiva and lips with a variety of clinical appearances.

Etiology of lichen planus involves cell mediated immunologically induced degeneration of basal cell layer of the epithelium. Stress, diabetes, drugs, and graft versus host reactions can also play a role in etiology of lichen planus. Various studies have suggested a possible relationship between OLP and daily intake of medicine.<sup>6-9</sup>

Long term intake of drugs can lead to changes in oral mucosa, these type of OLP lesions are termed as lichenoid drug reactions (LDR). The diagnosis of LDR usually relies on subjective criteria. Clinically and histopathologically the features of LDR lesions are indistinguishable to those of idiopathic OLP lesions. LDR usually remits with withdrawal

of drug and returns to normal with continuation of drugs.<sup>8-11</sup>

Systemic medications like anti-malarial drugs,<sup>12,13</sup> Non-steroidal anti-inflammatory drugs [NSAIDs],<sup>11,14</sup> antihypertensive agents<sup>15,16</sup> and angiotensin enzyme inhibitors,<sup>17</sup> diuretics,<sup>18</sup> oral hypoglycemic drugs,<sup>19</sup> penicillamine<sup>20</sup> and beta blockers<sup>21,22</sup> are implicated as a causative factor for LDR. Among the hypoglycemic drugs sulfonylurea have been reported in association with lichen planus. Cases of skin lichen planus have been reported with drugs like metformin therapy.<sup>23</sup>

Early and accurate diagnosis of lichen planus plays an important role on patient's health, since lichen planus lesions may undergo malignant transformation. Since drugs have got a role in affecting oral mucosa directly or indirectly, the present study was designed to evaluate the association of daily use of systemic medicines in the development of OLP lesions.

## MATERIAL AND METHODS

The present study was conducted at School of Dental Sciences, Karad, India. The study subjects were selected from the Department of Oral Diagnosis & Radiology, School of Dental Sciences Karad. The research protocol was initially submitted to the institutional ethical committee and review board of Krishna Institute of Medical

Sciences Deemed University (KIMSDU). The ethical clearance was obtained from KIMSDU before commencing the study. The study was conducted during the period from August 2012 to October 2014. Patients with habits of tobacco and pan chewing, amalgam restorations and metal crowns in the oral cavity were excluded from the study. Patients undergoing radiotherapy in head and neck regions and with history of organ transplantation recently were also excluded from the study. After considering the exclusion criteria, total 50 patients were enrolled in the study. All the participants were briefed about the purpose of the study. Complete medical and drug history of patients along with duration were recorded with their due consent. Clinical examination of oral cavity was conducted by two senior examiners (with double blind technique) using an artificial light, a mouth mirror, gauze, and wooden tongue blade. The diagnosis of lichen planus was based on the clinical criteria as based by Neville<sup>4</sup> and confirmed by histopathological examination.

Clinical features of the OLP lesions were analyzed, including the clinical forms and sites. The types were categorized in to annular, reticular, atrophic, erosive, bulous and plaque types. The reticular variety was characterized by the presence of white lace like striae, (Figure 1-3) the atrophic form by an erythematous lesion associated with reticular features. The annular type appears as white radiating oval areas. (Figure 4) The erosive form appears with combined features of ulceration and features of the atrophic form. The plaque-like form appears as a raised, flat white lesion with a smooth or rough surface with the presence of reticular features either at the periphery of the plaque or elsewhere in the oral mucosa.

#### Statistical analysis

The raw data was entered in MS Excel and analyzed into descriptive statistics.

Fisher exact test was applied to see the significant association between oral *lichen planus lesions and medication usage* and *P* value less than 0.05 was considered significant. Statistical calculations were performed using Statistical Package for the Social Sciences (SPSS) software version 15 (Armonk, New York: IBM. Corporation).

## RESULTS

#### Distribution of patients with age and gender: (Table 1)

In our study group out of 50 patients, 40 were females and 10 were males with a majority of age group between 31-50 years.

#### Distribution of patients with or without medication: (Table 2)

10 patients were under medication including eight females and two males. There was no statistical significant association between usage of medications and oral lichen planus lesions.

#### Type and site of OLP lesions: (Table 3)

In our study group most of the lesions were on buccal mucosa with reticular pattern as predominant type followed by erosive, atrophic and annular types.

#### Association of systemic diseases with OLP lesions: (Table 4)

10 patients were having systemic conditions, which includes three hypertensive, two diabetic, one with hyperthyroidism and four with combined hypertension and diabetes (Grinspan syndrome).

## DISCUSSION

Lichen planus (LP) is a chronic autoimmune disease with an unknown etiology that is marked by the invasion of lymphocytic infiltrate within the epithelial tissue inducing epithelial cell apoptosis and chronic inflammation.

The majority of the patients, around 80% in our study were females and rest 20% were males. The age group between 35 and 50 years were more affected, with a mean age of 41.2 years, which is in accordance with previous studies.<sup>1-4</sup>

There are six types of OLP lesions, which includes reticular, popular, plaque-like, erosive, atrophic and bullous. The most common pattern is reticular pattern, which presents as whitish striae known as Wickams striae.<sup>1</sup> The reticular type is asymptomatic in patients, but erosive and atrophic OLP are frequently associated with pain and burning sensations. Most common type of OLP observed in our study was reticular variety with bilateral distribution which is in consistent with other studies.<sup>24-26</sup> The common site for OLP was buccal mucosa followed by vestibule, gingiva, hard palate, retromolar area. The results were in accordance with previous studies.<sup>26</sup>

The precise etiology of OLP and LDR is unknown, but in the review of literature list of causative and exacerbating factors reported are drugs (anti-malarial, diuretics, gold salts, antiretroviral), dental materials (dental amalgam, composite and resin-based materials, metals), chronic liver disease and hepatitis C virus, genetics and tobacco chewing. Stress was identified as one of the most frequent causes of acute exacerbation of the disease.<sup>12-23</sup>

Studies had showed an association between diabetes, hypertension and lichen planus (Grinspan syndrome). Endocrine dysfunction in diabetes mellitus may be related to immunologic defect that may also contribute to the development of Lichen planus.<sup>19,27</sup> Borghelli *et al.*<sup>28</sup> reported prevalence rates of 0.55% in diabetic patients and 0.74% in their control group. Albercht *et al.* reported a 1% prevalence rate of lichen planus in the diabetic patients and no cases in their control group.<sup>27</sup> Most of the associations between lichen planus and systemic diseases

remain controversial. In our study, we found only four patients with Grinspan syndrome.

Previous studies have shown that the use of systemic medication does not lead to a significant increase in the incidence of OLP lesions which is in accordance with our study.<sup>22</sup> The studies done by Robertson and Wray found no association between OLP and antihypertensive drugs.<sup>16</sup> whereas the results of our study were contradictory to Robertson and Wray<sup>16</sup> and Potts *et al.*,<sup>29</sup> studies, where they found statistically significant association between angiotensin converting enzyme inhibitors and OLP.

An undesirable complication of OLP is the development of squamous cell carcinoma (SCC). Many studies have been focused on this potential malignant transformation of OLP,<sup>26</sup> but the potential for malignancy of these lesions is still controversial. The frequency of malignant transformation ranges from 0.4 to 5%, with the highest rates in the erosive lesions.<sup>25</sup> Early diagnosis of lesions, associated etiological factors and treatment help the patients to lead a normal life for longer duration.

## CONCLUSION

Lichen planus is a chronic mucocutaneous disease affecting oral mucosa and skin with a malignant transformation of 0.4-5%. In the present study OLP was more in females with a age group between 31-50 years. Buccal mucosa was the most common site observed in all cases with reticular pattern as predominant type. The present study showed no association between intake of antihypertensive, antidiabetic and thyroid drugs with OLP lesions. Further studies with larger sample size and association of both topical and systemic drugs with OLP and skin lesions were recommended.

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**Table 1.** Distribution of patients with age and gender

Age	Sex		Total
	Female	Male	
20-30	9	3	12
31-40	13	1	14
41-50	12	2	14
51-60	5	1	6
61-70	0	1	1
Above 70	1	2	3
Total	40	10	50

**Table 2.** Distribution of patients with/without medications

Category	Male	Female	Total
Patient with medication	2	8	10
Patient without Medication	8	32	40

Fisher exact test: - 95%confidence interval IP value =0.6157 (not-significant)

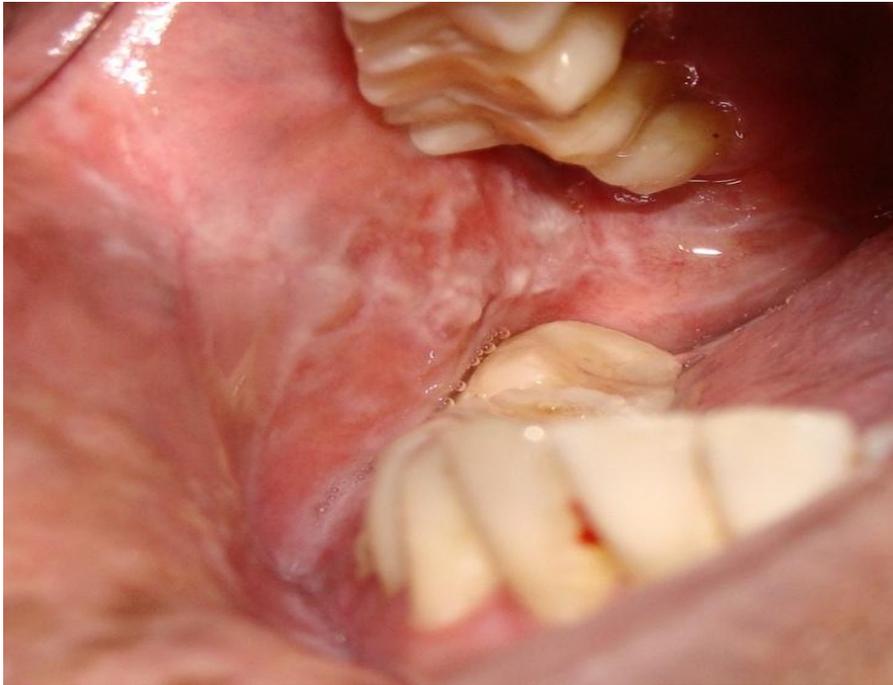
**Table 3.** Distribution of type of lesion with sites

Type	Buccal mucosa	Gingiva	Vestibule	Hard palate	Retromolar area	Combined	Total
Reticular	33	0	0	0	0	3	36
Erosive	5	0	0	0	1	3	9
Atrophic	3	0	0	0	0	1	4
Annular	0	0	0	0	1	0	1
Total	41	0	0	0	2	7	50

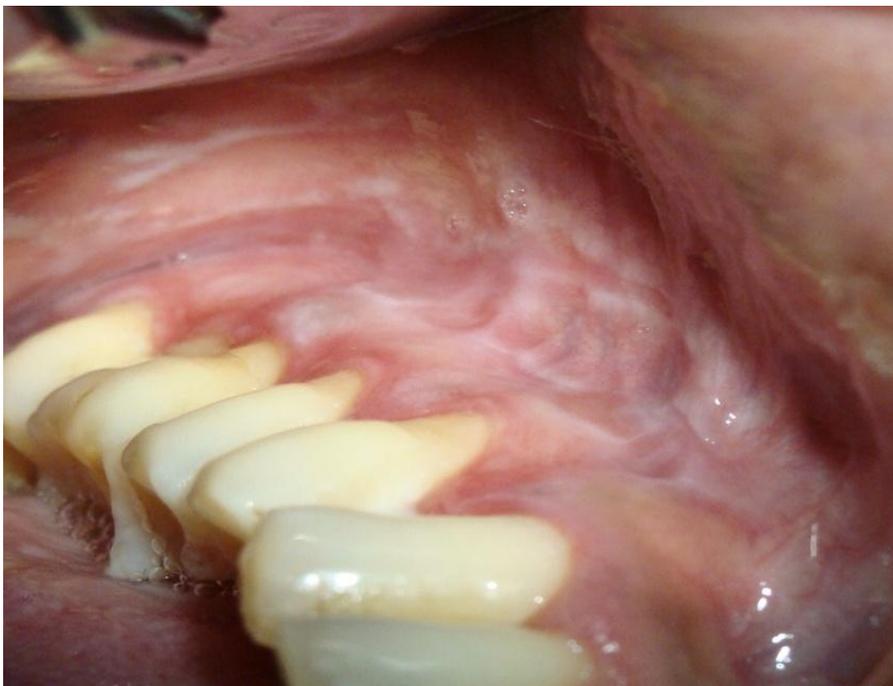
**Table 4.** Distribution of association of systemic condition with lesions

Systemic Condition	No. of patients
Hypertension	3
Diabetes	2
Thyroid Disorder	1
Combined Hypertension and diabetes	4

**Figure 1.** Reticular type OLP on left buccal mucosa



**Figure 2.** Reticular type OLP on right buccal mucosa



**Figure 3.** Reticular type OLP involving vestibule and Gingiva



**Figure 4.** Annular type of OLP on left buccal mucosa