

## Lack of association between diabetes mellitus and oral lichen planus in Zahedan (South-East of Iran)

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### Abstract

**Introduction:** Oral lichen planus (OLP) is a chronic immunological disorder with unknown etiology. Some studies have reported an association between oral lichen planus and diabetes mellitus. The aim of this study was to compare the frequency of diabetes mellitus in patients with oral lichen planus and healthy persons.

**Materials & Methods:** This case-control study was performed on 50 patients with OLP and 50 healthy individuals. Diagnosis of OLP was confirmed by typical clinical and histopathological findings. The control group were selected randomly from healthy individuals after matching for age and sex. Blood samples were taken to achieve 5 mL for measuring fasting serum blood glucose and HbA<sub>1c</sub>. Data were analyzed using Student's t-test.

**Results:** In this case-control study, 50 patients with OLP (39 females, 11 males) with a mean age of 44.5±13.24 years and 50 healthy individuals (33 females, 17 males) with a mean age of 41.3±11.44 years were evaluated. The mean fasting blood glucose and HbA<sub>1c</sub> levels in patient with OLP were 95.1±8.1 and 5.1±1.3 mg/dL, and 89.1±7.7 and 4.6±1.1 mg/dL in healthy individuals (P=1).

**Conclusion:** The frequency of diabetes mellitus was not significantly different between the case and the control groups. The results showed that diabetes mellitus does not have a direct role in the OLP etiology.

**Keywords:** Diabetes mellitus, Lichen planus, Oral, Etiology

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## عدم همراهی دیابت ملیتوس با لیکن پلان دهانی در زاهدان (جنوب شرق ایران)

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### چکیده

**مقدمه:** لیکن پلان دهانی یک بیماری ایمنولوژیک مزمن با اتیولوژی ناشناخته است. در مطالعات مختلف همراهی لیکن پلان دهانی با دیابت ملیتوس را گزارش کرده‌اند. هدف از این مطالعه بررسی فراوانی دیابت ملیتوس در بیماران مبتلا به لیکن پلان دهانی در مقایسه با افراد سالم است.

**مواد و روش ها:** این مطالعه به صورت موردشاهدی بر روی ۵۰ بیمار مبتلا به لیکن پلان دهان و ۵۰ فرد سالم انجام شد. بیمارانی که از نظر شکل بالینی ضایعات دهانی و معیارهای بافت شناسی، تشخیص لیکن پلان مطابقت داشتند، به عنوان بیمار وارد مطالعه شدند. افراد گروه شاهد از بین افراد فاقد بیماری باسازگاری از نظر سن و جنس از جمعیت عمومی انتخاب شدند. نمونه سرمی جهت بررسی قند خون ناشتا به میزان ۵ سی‌سی از افراد گرفته شد و اطلاعات توسط آزمون Student's t-test مورد آنالیز قرار گرفتند.

**یافته ها:** با طراحی یک مطالعه ی مورد شاهدهی، ۵۰ بیمار مبتلا به لیکن پلان دهانی (۳۹ زن، ۱۱ مرد) با میانگین سنی  $44/5 \pm 13/24$  و ۵۰ فرد سالم (۳۳ زن، ۱۷ مرد) با میانگین سنی  $41/3 \pm 11/44$  وارد مطالعه شدند. میانگین گلوکز خون ناشتا و HbA<sub>1C</sub> در افراد مبتلا به لیکن پلان دهانی  $95/1 \pm 8/1$ ،  $5/1 \pm 1/3$  میلی گرم بر دسی لیتر و در افراد سالم  $89/1 \pm 7/7$ ،  $4/6 \pm 1/1$  میلی گرم بر دسی لیتر به دست آمد ( $P=1$ ).

**نتیجه گیری:** فراوانی دیابت ملیتوس تفاوت معناداری بین دو گروه مبتلا به لیکن پلان دهانی و افراد سالم را نشان نداد. یافته‌ها نشان داد دیابت ملیتوس نقش مستقیمی در اتیولوژی لیکن پلان دهانی بازی نمی‌کند.

**واژگان کلیدی:** دیابت ملیتوس، لیکن پلان دهانی، اتیولوژی

### Introduction

Oral Lichen Planus (OLP) is a chronic immunological disorder. Seventy-five percent of the patients with cutaneous lichen planus also experience oral lesions.<sup>[1]</sup> The etiology of OLP is unknown. In recent years, it has been found that the immune system plays a primary role in the disease.<sup>[2]</sup> On the other hand, it has been established that OLP is an immune-related disorder, and stress and anxiety are two factors causing it.<sup>[3]</sup> Diabetes Mellitus is a chronic disease involving different systems of the body with skin involvement.<sup>[4]</sup> According to reports, diabetes mellitus is associated with oral lichen planus in 14–85% of the cases.<sup>[5,6]</sup> The autoimmune background of lichen planus could support diabetes mellitus, too, due to the same pathogenesis of both diseases.<sup>[7]</sup>

Ahmed et al studied the incidence of oral lichen planus in patients with non-insulin-dependent diabetes mellitus. The study population consisted of 86 patients

(49 (57%) females and 37 (43%) males). The patient's age ranged from 40 to 70 with an average age of 51.3. They were divided into three groups: a) 40–50 years old, b) 51–60 years old, and c) over 60 years old; 6 patients (6.9%) showed histopathological signs of oral lichen planus compared with the control group with one patient (1.2%). They concluded that OLP has a significant relationship with non-insulin-dependent diabetes compared with the normal population.<sup>[8]</sup>

Bagewadi et al studied the relationship between oral lichen planus and diabetes mellitus. In the study, 150 patients were divided into three groups. The first group consisted of 50 oral lichen planus patients; the second one included 50 diabetic patients and the third group was hypertensive patients. Four and eight of 50 oral lichen planus patients, were diabetic and hypertensive patients, respectively. Only one of them had all the three diseases.<sup>[9]</sup> They argued that diabetes mellitus and

hypertension play no direct role in the etiology of oral lichen planus. However, it seems that more studies should be carried out in different geographical regions in order to confirm the co-dependency of the two above-mentioned disorders.

## Materials & Methods

One hundred cases were selected from the Department of Oral Medicine in Zahedan University of Medical Sciences. The subjects were divided into two groups.

**Group I:** The study group was 50 patients with oral lichen planus, which was clinically and histopathologically confirmed. OLP may exhibit both red and white components and provide, together with differing textures, the basis for the clinical classification of this disorder. The white and red components of the lesion can be a part of the following textures: reticular, plaque-like papules, bullous, erythematous, and ulcerative. The histopathological features of OLP are: (1) areas of hyperparakeratosis or hyperorthokeratosis, often with thickening of the granular cell layer and a saw-toothed appearance to the rete pegs; (2) "liquefaction degeneration" or necrosis of the basal cell layer; and (3) an eosinophilic band may be seen just beneath the basement membrane and represent fibrin covering the lamina propria. A dense subepithelial

band-shaped infiltrate of lymphocytes and macrophages is also characteristic of the disease.

**Group II:** The control group consisted of 50 healthy individuals from the general population (same age and sex distribution). Prior to participate in the research, patients signed an informed consent. The study was approved by the Ethics Committee of Research Deputy of Zahedan Medical Sciences University with the code of 91-1252. Patients who had more than one dermatologic disease, pregnant women, subjects with a history of neoplasia or malignancy, patients undergoing radiotherapy or chemotherapy, patients with autoimmune diseases such as lupus erythematosus, rheumatoid arthritis, Sjögren's syndrome or metabolic diseases such as diabetes, patients taking any systemic medications (including benzodiazepines, antidepressants, anabolic steroids, OCP, corticosteroids suppressing the immune system) within the last 30 days and smokers were excluded from the study. Then, 5 mL of blood serum was collected from antecubital vein and sent to the laboratory to check FBS levels. Photometric method was used for quantitative identification of glucose in plasma.  $FBS \geq 126$  mg/dL and  $HbA_{1C} \geq 6.5$  mg/dL were considered as a measure of definite diabetes (table 1). The data was collected and analyzed using chi-squared test for indicating the differences between the 2 groups.  $P < 0.05$  was considered statistically significant at 95% confidence interval (CI).

**Table 1. Criteria for the diagnosis of diabetes mellitus**

Objective Criteria	Definition
1. Symptoms of diabetes plus casual plasma glucose level of 200 mg/dL or greater	Casual is defined as any time of day irrespective of the time elapsed since the last meal. Classic symptoms of diabetes include polyuria, polydipsia, and unexplained weight loss.
2. Fasting plasma glucose of 126 mg/dL or greater	Fasting is defined as no caloric intake for 8 hours or longer.
3. 2-hour plasma glucose level of 200 mg/dL or greater during an oral glucose tolerance test	The test should be performed using a glucose load containing the equivalent of 75 g of anhydrous glucose dissolved in water; this test is not recommended as a routine clinical examination.
4. $HbA_{1C}$	$HbA_{1C}$ is used for general assessment of the long-term level of hyperglycemia in patient with diabetes.

## Results

In this study, 50 patients with OLP aged 21–71, with the mean age of  $44.5 \pm 13.24$  years, and 50 healthy subjects aged 18–35, with the mean age of  $44.3 \pm 11.44$

years were studied. Of 50 patients with OLP, 29 (63%) were female and 11 (37%) were male. The most common site of involvement was the buccal mucosa (43

cases, 76%), followed by the tongue (10%), the lips (10%) and the palate (4%). The most common forms of OLP were reticular and papular (70%).

The mean fasting blood glucose and HbA<sub>1c</sub> levels in patient with OLP were  $95.1 \pm 8.1$  and  $5.1 \pm 1.3$  mg/dL, and  $89.1 \pm 7.7$  and  $4.6 \pm 1.1$  mg/dL in healthy individuals. Based on Student's t-test, no significant differences were observed in the serum FBS levels between the two studied groups ( $P=1$ ). Based on Student's t-test, no significant differences were observed in the serum HbA<sub>1c</sub> levels between the two studied groups ( $P=1$ ).

## Discussion

Wilson (1869) first described lichen planus as a disease that involves skin, nails, and oral mucosa.<sup>[10]</sup> OLP is a chronic inflammatory mucocutaneous disease mediated by T cells and has an unknown etiology. OLP exhibits periods of remission and relapse. It is a cell-dependent condition in which T lymphocytes are accumulated under the epithelium of the oral mucosa and increase the differentiation of stratified squamous epithelium, leading to hyperkeratosis and redness, with or without a wound. This disease involves 2–5% of the general population with predominance in women. Its onset is in the 4th and 5th decades of life.<sup>[1]</sup>

In the current study, a total of 30 patients with OLP (19 women and 11 men), with a mean age of  $44.5 \pm 13.24$  years, and 30 healthy subjects (13 women and 17 men), with a mean age of  $44.3 \pm 11.44$  years, were evaluated. Lichen planus may involve different areas in the oral mucosa. The buccal mucosa is the most common site for bilateral lesions. The floor of the mouth is the rarest incidence site.<sup>[1]</sup>

Our study showed that the most common sites of involvement, in descending order, were as follows: buccal mucosal (76%), tongue (10%), lips (10%) and palate (6%). The most common form in this study was the reticular form with 21 cases (70%).

Recently, the etiology of oral lichen planus has been considered multifactorial, where mechanical, electrochemical, trauma, infection, allergy, endocrine disorders, salivary gland disorders, heredity, immunological reactions, stress, overworking, mucous exciting factors, and habits make people susceptible to lichen planus.<sup>[2]</sup>

For the first time, the prevalence of DM among OLP patients was reported 40% by Grinspan, et al.<sup>[11]</sup> In last decade, In 2007 the prevalence of DM was found as

26/7% in Turkish people with lichen planus.<sup>[6]</sup> In 2011 Ara, et al observed DM in 10% of their patients with oral lichen panus.<sup>[12]</sup> In 2013, Narayan among 2000 diabetic patients 15 cases (0/75%) of oral lichen planus were seen.<sup>[13]</sup> In Iran in 2012 the prevalence of DM was announced as 20% among 80 people with the age range of 44-60 years old.<sup>[5]</sup>

Atefi<sup>[5]</sup> Chalkoo<sup>[4]</sup> and Ara<sup>[12]</sup> revealed that the prevalence of DM among patients with OLP is more than normal population. However, similar to the studies of Ansar<sup>[14]</sup> 15. Borhan Mojabi<sup>[15]</sup> Bagewadi<sup>[9]</sup> and Saini<sup>[16]</sup> our study illustrated no significant differences in FBS test results between the two groups. The present study indicated that there was no positive dependency between diabetes mellitus and oral lichen planus as 100% of oral lichen planus patients had normal FBS values and no FBS disorder was observed in the control group.

The results of the present study were not consistent with those of some other studies in terms of significant co-dependency between diabetes and oral lichen planus. The difference might be attributed to reasons such as test methods, differences in laboratory methods, unknown reasons contributing to the disease pathogenesis and non-definite relationship between the two diseases.

## Conclusion

It can be concluded that oral lichen planus may not be directly associated with diabete mellitus but could be contributing to oral lichen planus like lesions in oral cavity as a result of various medications.

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**Conflict of interest:** We declare no conflict of interests.

## References

1. Lu R, Zhang J, Sun W, Du G, Zhou G. Inflammation-related cytokines in oral lichen planus: an overview. *J Oral Pathol Med*. 2015;44:1-14.
2. Bombeccari GP, Guzzi G, Tettamanti M, Gianni AB, Baj A, Pallotti F, et al. Oral lichen planus and malignant transformation: a longitudinal cohort study. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2011; 112: 328–34.
3. Rad M, Hashemipour MA, Mojtahedi A, Zarei MR, Chamani G, Kakoei S, et al. Correlation between clinical and histopathological diagnostic criteria. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2009; 107 : 796–800.
4. Chalkoo AH. Oral Lichen Planus with Transaminase Levels and Diabetes. *J Indian Acad Oral Med Radiol* 2010; 22:1-3.
5. Atefi N, Majedi M, Peyghambari S, Ghourchian S. Prevalence of diabetes mellitus and impaired fasting blood glucose in patient with Lichen Planus. *Med J Islam Repub Iran* 2012; 26: 22–6.
6. Seyhan M, Ozcan H, Sahin I, Bayram N, Karıncaoğlu Y. High prevalence of glucose metabolism disturbance in patients with lichen planus. *Diabetes Res Clin Pract* 2007;77:198–202.
7. Romero MA, Seoane J, Varela-Centelles P, Diz-Dios P, Garcia-Pola MJ. Prevalence of diabetes mellitus amongst oral lichen planus patients. *Clinical and pathological characteristics*. *Med Oral* 2002;7:121.
8. Ahmed I, Sarwat N, Jehangir U, Wahid Z. Frequency of oral lichen planus in patients with noninsulin dependent diabetes mellitus. *J Pak Assoc Dermatol* 2012; 22: 30-34.
9. Bagewadi A, Bhoweer Ak. Oral Lichen Planus and its Association with Diabetes Mellitus and Hypertension. *J Indian Acad Oral Med Radiol* 2011; 23:S300-3.
10. Wilson E. Lichen planus. *Cuton Med Dis Skin* 1869; 3: 117 .
11. Grinspan D, Diaz J, Villapol LO, Schneiderman J, Berdichesky R, Palese D, et al. [Lichen rubber planus of buccal mucosa, its association with diabetes]. *Bull Soc Fr Dermatol Syphiligr* 1966; 73: 898–9.[In French]
12. Ara SA, Mamatha GP, Rao BB. Incidence of diabetes mellitus in patients with lichenplanus. *Int J Dent Clin* 2011; 3: 29–33.
13. Narayan V, Gananasundarm N, Arvind M. Prevalence of oral lichen planus with diabet mellitus. *J Indian Acad Oral Med Radiol* 2013; 25: 261-4.
14. Ansar A, Farshchian M, Ghasemzadeh SM. Comparison of the frequency of diabetes mellitus in the patients with lichen planus and normal controls: A case- control study. *Dermatology Cosmetic* 2011; 2: 78-84.[In Persian]
15. Borhan Mojabi K, Esfahani M, Bokharaei MM. Evaluation of median rhomboid glossitis and lichen planus in patients with diabetes mellitus. *J Qazvin Univ Med Sci* 2009; 13: 56-60 .[In Persian]
16. Saini R, Al-Maweri SA, Saini D, Ismail NM, Ismail AR. Oral mucosal lesions in nonoral habit diabetic patients and association of diabetes mellitus with oral precancerous lesions. *Diabetes Res Clin Pract* 2010; 89: 320–6.