

Oral Lichen Planus and Thyroid Disease: A Case-Control Study

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Abstract

Background: Oral lichen planus (OLP) is a chronic inflammatory condition that primarily affects the oral mucosa. While the exact cause of OLP remains unclear, recently, there has been particular interest in researching the potential link between OLP and thyroid gland disorders.

Methods and Results: A total of 100 subjects participated in our research. Among them, 50 were patients (80% women and 20% men) diagnosed with OLP (the main group [MG]), and 50 subjects (60% women and 40% men) with various other oral mucosa concerns (aphthous stomatitis, burning mouth syndrome, herpetic stomatitis, and geographic tongue) comprised the comparison group [CG]. All participants underwent a comprehensive assessment of thyroid function, which included the measurement of free thyroxine (FT4), free triiodothyronine (FT3), thyroid-stimulating hormone (TSH), thyroid peroxidase antibodies (TPO-Ab), and an ultrasound examination of the thyroid gland performed by an endocrinologist.

Our results reveal a noteworthy gender-based difference in the occurrence of mucosal disorders, indicating a predominance of females. MG had a significantly higher prevalence of hypothyroidism, with 46% of patients affected. In contrast, in CG, the prevalence of hypothyroidism was lower, at 16%, and this difference was statistically significant ($P=0.0012$). In MG, 50% of cases were found to be in a euthyroid state. In contrast, in CG, a larger proportion (80%) of patients were in a euthyroid state, and this difference was statistically significant ($P=0.0017$).

Conclusion: Our study has identified a significant and positive association between hypothyroidism and OLP. We recommend that individuals diagnosed with OLP, especially women, consider undergoing routine screening for thyroid disease as part of their healthcare regimen. (International Journal of Biomedicine. 2023;13(4):312-316.)

Keywords: oral lichen planus • mucosa • hypothyroidism

For citation: Krasniqi MS, Dalipi ZS, Zhjeqi V. Oral Lichen Planus and Thyroid Disease: A Case-Control Study. International Journal of Biomedicine. 2023;13(4):312-316. doi:10.21103/Article13(4)_OA13

Abbreviations

FT3, free T3; **FT4**, free T4; **OLP**, oral lichen planus; **TSH**, thyroid-stimulating hormone; **T4**, thyroxine; **T3**, triiodothyronine; **TSHR**, thyroid-stimulating hormone receptor.

Introduction

Oral lichen planus (OLP) is a persistent, non-malignant condition affecting oral mucosa.⁽¹⁾ This condition is relatively rare, accounting for less than 1% of oral cavity disorders.⁽²⁾ While its exact cause remains unknown, there is evidence suggesting a potential genetic predisposition, as well as associations with

certain medications, including NSAIDs, oral hypoglycemics, antimalarials, and psychotropic drugs. The use of tobacco has also been considered a potential contributing factor.^(3,4) OLP predominantly affects females. Additionally, numerous studies have explored the possible link between thyroid disorders and the development of lichenoid changes in the oral mucosa, although the nature of this relationship remains unclear.⁽⁵⁻⁷⁾

Thyroid-stimulating hormone (TSH) is a hormone produced by the pituitary gland. It stimulates the thyroid gland to produce thyroxine (T4) and triiodothyronine (T3) through a negative feedback mechanism involving free T3 (FT3) and T4 (FT4).^(6,8) The thyroid-stimulating hormone receptor (TSHR) presented in thyroid follicular cells is a key regulator of thyroid hormone synthesis and secretion.⁽⁹⁾ Thyroid hormones are crucial for governing the body's growth, development, and metabolic processes. Thyroid disorders can disrupt the body's homeostasis and impact tissue healing capabilities.^(10,11) Active TSHR has been identified in various tissues, such as osteoblasts, osteoclasts, bone marrow cells, cardiomyocytes, adipocytes, fibroblasts, and skin keratinocytes. However, the available information on thyroid protein expression in the oral mucosa is limited.^(12,13)

Materials and Methods

A total of 100 subjects participated in our research. Among them, 50 were patients diagnosed with OLP (the main group [MG]), and they were assessed at the University Dental Clinical Center of Kosovo, having been referred by primary or secondary medical centers in Kosovo. To establish a basis for comparison, we also evaluated a comparison group [CG] of 50 subjects who presented with various other oral mucosa concerns, including conditions like aphthous stomatitis, burning mouth syndrome, herpetic stomatitis, and geographic tongue.

Inclusion Criteria: Participants in the study were required to be at least 18 years of age and should not have any pre-existing chronic illnesses. They were examined after providing written informed consent, and the examination findings were duly recorded.

Exclusion Criteria: Individuals with chronic coexisting medical conditions or autoimmune disorders, and pregnant women were not considered for inclusion in this research.

The diagnosis of OLP was based on both clinical and histological criteria. The clinical criteria involved the identification of specific features, including bilateral and symmetrical lesions. These lesions could manifest as net-like patterns with gray-white lines, in the form of white plates, or exhibit characteristics such as atrophy, blistering, or erosions.

Histological criteria were equally important and encompassed the presence of a well-defined band-like area of cellular infiltration restricted to the superficial layer of the connective tissue. Additionally, liquefaction degeneration in the basal cell layer was considered a significant histological marker. Importantly, the absence of epithelial dysplasia was also a crucial factor in diagnosing OLP.

In cases where the disease did not display typical clinical manifestations, tissue samples were sent for histopathological examination. All collected samples were fixed in a 10% formalin solution.

The WHO criteria were employed as the standard for clinical and histopathological assessments in diagnosing OLP.

Clinical Criteria

Presence of bilateral and symmetrical lesions.

Clinical manifestations may include reticular, erosive,

atrophic, bullous, and plaque-type lesions.

Histological Criteria

Identification of a band-like area of lymphocytic infiltration within the superficial connective tissue.

Observance of signs of degeneration in the basal cell layer.

Absence of epithelial dysplasia.

Thyroid Gland Examination

All participants underwent a comprehensive assessment of thyroid function, which included the measurement of FT4, FT3, TSH, thyroid peroxidase antibodies (TPO-Ab), and an ultrasound examination of the thyroid gland performed by an endocrinologist.

Statistical analysis was performed using statistical software package SPSS version 21.0 (SPSS Inc, Armonk, NY: IBM Corp). Baseline characteristics were summarized as frequencies and percentages. Group comparisons were performed using chi-square tests or, alternatively, Fisher's exact test when expected cell counts were less than 5. A probability value of $P < 0.05$ was considered statistically significant.

Results

Our results reveal a noteworthy gender-based difference in the occurrence of lichenoid changes, indicating a predominance of females (Table 1). This gender-based distinction was also observed in CG, where a significant difference was noted (Table 2). Table 3 summarizes the study's findings, indicating that 80% of cases exhibited manifestations of reticular lichen, primarily localized in the buccal mucosa, gingiva, tongue, and lip. Additionally, 74% of patients reported subjective symptoms, including burning sensations and oral mucosal discomfort. The thyroid gland function analysis in the study groups is presented in Table 4.

Table 1.

Distribution of the main group by age and gender.

| Age | Gender* | | | | Total | |
|-------|---------|-------|------|-------|-------|-------|
| | Female | | Male | | | |
| | n | % | n | % | n | % |
| 25-39 | 10 | 22.7 | - | 0.0 | 10 | 20.0 |
| 40-49 | 16 | 36.4 | 2 | 33.3 | 18 | 36.0 |
| 50-65 | 18 | 40.9 | 4 | 66.7 | 22 | 44.0 |
| Total | 44 | 100.0 | 6 | 100.0 | 50 | 100.0 |

* - $P < 0.0001$ for Female versus Male.

Prevalence of Hypothyroidism

MG had a significantly higher prevalence of hypothyroidism, with 46% of patients affected. In contrast, in CG, the prevalence of hypothyroidism was lower, at 16%, and this difference was statistically significant.

Table 2.
Distribution of the comparison group according to age and gender.

| Age | Gender* | | | | Total | |
|-------|---------|-------|------|-------|-------|-------|
| | Female | | Male | | | |
| | n | % | n | % | n | % |
| 25-39 | 7 | 23.3 | 10 | 50.0 | 17 | 34.0 |
| 40-49 | 11 | 36.7 | 6 | 30.0 | 17 | 34.0 |
| 50-65 | 12 | 40.0 | 4 | 20.0 | 16 | 32.0 |
| Total | 30 | 100.0 | 20 | 100.0 | 50 | 100.0 |

*- $P=0.0466$ for Female versus Male.

Table 3.
Characteristics of OLP lesions in the main group.

| Variable | | n | % | Statistic |
|---------------|----------------------|----|------|------------------------------------|
| Clinical type | Reticular | 40 | 80.0 | $\chi^2=49.12$ DF=2, $P<0.0001$ |
| | Ulcerative & Erosive | 6 | 12.0 | |
| | Plaque like | 4 | 8.0 | |
| Location | Buccal zone | 46 | 92.0 | $\chi^2=82.80$ DF=3, $P<0.0001$ |
| | Gingiva | 6 | 12.0 | |
| | Lip | 4 | 8.0 | |
| | Tongue | 5 | 10.0 | |
| Symptoms | Yes | 37 | 74.0 | $\chi^2=11.52$ DF=1, $P=0.0007$ |
| | No | 13 | 26.0 | |
| Gender | Female | 44 | 88.0 | $\chi^2=28.88$ DF=1, $P<0.0001$ |
| | Male | 6 | 12.0 | |

Table 4.
The thyroid gland function analysis in the study groups.

| Morbidity | MG | | CG | | Statistic |
|-----------------------|----|-------|----|-------|--------------------------------|
| | n | % | n | % | |
| Hypothyroidism | 23 | 46.0 | 8 | 16.0 | $\chi^2=10.519$ $P=0.0012$ |
| Hashimoto Thyroiditis | 2 | 4.0 | 2 | 4.0 | Fisher's Exact Test, $P=0.140$ |
| Euthyroid State | 25 | 50.0 | 40 | 80.0 | $\chi^2=9.89$ $P=0.0017$ |
| Total | 50 | 100.0 | 50 | 100.0 | |

Hashimoto Thyroiditis

A small proportion (4%) of patients in MG had Hashimoto thyroiditis. This prevalence did not differ significantly from CG, where 4% of patients had Hashimoto thyroiditis.

Euthyroid State

In MG, 50% of cases were found to be in a euthyroid state. In contrast, in CG, a larger proportion (80%) of patients were in a euthyroid state, and this difference was statistically significant.

These findings highlight a higher prevalence of hypothyroidism in OLP patients than in CG, as well as differences in the euthyroid state between the two groups.

Discussion

OLP is a chronic inflammatory condition that primarily affects the oral mucosa, although, in some instances, it can also manifest as red papules on the skin.⁽¹⁴⁾ Clinically, OLP is categorized into six forms: reticular, papular, plaque, erosive, atrophic, and bullous, with the reticular form being commonly observed within the oral cavity.⁽¹⁵⁾

While the exact cause of OLP remains unclear, it is known to be associated with several systemic disorders. Recently, there has been particular interest in researching the potential link between OLP and thyroid gland disorders.

Our study observed a higher prevalence of lichenoid lesions among female subjects, with 44 (88%) females affected compared to 6 (12%) males. These findings suggest a greater predilection for OLP among females with lichenoid lesions.

The findings of our study are consistent with previous research conducted by Tang et al.⁽¹⁶⁾ and Xue et al.,⁽¹⁷⁾ which also observed a higher prevalence of lichenoid lesions among female subjects.

Our study showed that the most common type of OLP was the reticular form, accounting for 80% of cases. This was followed by the erosive ulcerative form, present in 12% of cases, and the plaque form, observed in 8% of cases. These results align with a study by Baharvand et al.,⁽¹⁸⁾ which also found a predominance of the reticular type of lichen.

Regarding the distribution of OLP lesions, our study showed that 92% of patients exhibited buccal mucosal involvement, followed by gingiva (12%), tongue (10%), and lip (8%). These findings align with the research conducted by Maddheshiya et al.,⁽¹⁹⁾ which reported similar distribution patterns.

Additionally, our study revealed that 74% of patients with lichenoid lesions reported experiencing subjective symptoms, such as burning, discomfort, and sensation.

In our study, we observed a notable prevalence of hypothyroidism, characterized by low values of FT3 and FT4, in 23 out of 50 patients diagnosed with OLP, which accounts for 46% of this group. Additionally, two out of 50 OLP patients were found to have elevated TPO-Ab values, while the remaining 25 were in a euthyroid state. Importantly, when comparing these results to CG, we discovered that the prevalence of thyroid disorders, particularly hypothyroidism,

was significantly higher in patients with OLP, demonstrating a statistically significant difference (46% versus 16%).

Our findings align with the research conducted by Zhou et al.,⁽²⁰⁾ Robledo-Sierra et al.,⁽²¹⁾ and Garcia-Pola et al.,⁽²²⁾ who also reported a strong correlation between OLP and hypothyroidism.

While our study did not identify a significant difference in the prevalence of Hashimoto's disease between the two groups, it is noteworthy that Alikhani et al.⁽²³⁾ reported that the severity of clinical expression of OLP lesions was directly linked to the levels of IL-8 in the serum, as well as the levels of TPO-Ab. This suggests that the severity of OLP symptoms in patients may be influenced by certain immune and inflammatory markers in the bloodstream, which could vary independently of Hashimoto's disease status.

We observed that 50% of MG patients were in a euthyroid state. In contrast, CG exhibited a higher proportion of patients (80%) in a euthyroid state. This difference suggests that thyroid function may impact the development or clinical expression of OLP. However, further research is needed to understand the relationship between thyroid function and OLP severity fully.

Conclusion

The relationship between OLP and thyroid diseases warrants further investigation and clarification. Our study has identified a significant and positive correlation between hypothyroidism and OLP, suggesting that thyroid disorders may potentially play a role in the development of OLP. However, it's important to acknowledge that our study has limitations due to the relatively small sample size.

Based on our findings, we recommend that individuals diagnosed with OLP, especially women, consider undergoing routine screening for thyroid disease as part of their healthcare regimen. Nevertheless, it is essential to emphasize that additional clinical research with larger sample sizes and more comprehensive evaluations is necessary to confirm and expand upon these conclusions. This will contribute to a better understanding of the complex relationship between OLP and thyroid disorders.

Ethical Approval

The study was conducted following the Declaration of Helsinki and approved by the Ethics Committee at the University of Prishtina "Hasan Prishtina," Prishtina, Kosovo. All participants provided written informed consent.

Competing Interests

The authors declare that they have no competing interests.

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