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Oral Lichen Planus And Thyroid Disease: Is There A Possible Connection?.

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ABSTRACT

Some results in the literature point out at the possible connection of oral lichen planus and thyroid gland disease. The aim of our case-control pilot study was to determine the prevalence of thyroid gland diseases and hormone levels in female patients with oral lichen planus and age and gender matched control group of patients. Activity of oral lichen planus was also noted. Significant difference between oral lichen planus and control group was observed only in values of free triiodothyronine. Our results have not shown a relationship between oral lichen planus and thyroid gland disorders. Future well-designed studies with larger number of patients are needed.

Keywords: oral lichen planus; thyroid gland disease; association; thyroid hormone levels

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INTRODUCTION

Oral lichen planus (OLP) is a chronic autoimmune inflammatory disease affecting oral mucosa with a prevalence of 1-2% in the general population. Middle-aged and elderly female are most commonly affected, generally between 30 and 60 years old [1-3]. According to World Health Organization (WHO), OLP is defined as an oral potentially malignant disorder (OPMD) with estimated malignant transformation rate of 1.09 to 1.14 % [2]. Clinical signs of OLP include plaque-like, reticular, papular, atrophic or erosive lesion which predominantly affects buccal mucosa, gingiva, lips and tongue [2]. Diagnosis is established based on clinical and/or histopathological examination [4, 5]. To date, etiology of OLP remains unknown, however, it is believed that various factors such as genetic predisposition, immune dysregulation and psychological conditions may be involved in the development of the disease. According to the literature data, systemic diseases such as diabetes, hypertension and thyroid disorders may increase the risk of OLP [6, 7].

According to the WHO, there are two billion people in the world suffering from a thyroid disorder, and 20% of them are residents of Europe. Women are more likely to suffer from thyroid disease. Data show that every third woman has a thyroid nodule and every tenth has some of the thyroid dysfunction [8]. The prevalence of thyroid hypofunction in Croatian population is 7,5% in women and 2,5% in men, and 15-18% of population has autoimmune thyroid disease [9]. Regarding the incidence of thyroid cancer, Croatia ranks fifth in Europe and 13th in the world, while mortality in Croatia from this type of cancer is among the lowest in the world [10].

There are some results in the literature that point out at the possible connection of OLP and thyroid disease [1-3, 6]. Some authors have reported that thyroid diseases are more frequent in OLP patients, compared to controls [2, 6, 11]. Significantly higher values of anti-thyroglobulin antibodies (anti-TGA) and anti-thyroid microsomal autoantibodies (anti-TMA) have been detected in OLP patients, compared to healthy controls [6, 12, 13]. It is also known that these autoantibodies, as well as anti-thyroid peroxidase (anti-TPO) can induce epithelial cell damage and are related to Hashimoto's thyroiditis and Graves' disease [14, 15]. Furthermore, available literature data suggests that patients with hypothyroidism are more likely diagnosed with OLP than healthy subjects [16, 17]. Some authors have found that erosive forms of OLP are more likely to be associated with anti-TPO autoantibodies in thyroid patients [1]. Authors have suggested to determine anti-TPO autoantibodies levels in these patients to diagnose a potential thyroid disorder and follow-up for malignancy [1]. However, we have not managed to find data regarding the association of OLP and thyroid disease for the Croatian population. Therefore, the aim of our case–control study was to evaluate possible relationship between OLP and thyroid diseases in the population of our oral medicine patients.

MATERIALS AND METHODS

This study was approved by the ethical committee of the University Hospital Center Zagreb (N0 17/20, 10/11/2019). Our research was registered at the U.S. National Institutes of Health (clinicaltrials.gov) (trial identifier: NCT04523077). Each participant signed informed consent according to the Declaration of Helsinki.

This was a case-control pilot study which included a total of 50 patients; 25 women with clinically and histopathologically confirmed oral lichen planus and a control group of 25 women without oral lichen planus. All patients included in the study were patients of the Department of Oral Medicine, School of Dental Medicine in Zagreb. Both oral lichen planus and thyroid disease are more frequent in females, so we included only female patients in the study, in order to have a more homogeneous groups. Excluding criteria were male gender and female patients which were not age-matched to study group.

All patients which gave their consent to participate in the study had their oral mucosa examined. In patients with OLP disease activity was also noted. The patients were then referred to a private laboratory for blood sampling. The levels of thyroid stimulating hormone (TSH), free triiodothyronine (FT3), free thyroxine (FT4), anti-thyroid peroxidase antibody (anti-TPO) and anti thyroglobulin antibody (anti-Tg) were determined. Statistical analysis was performed by the MedCalc statistical software version 18.10.2 (MedCalc Software, Belgium). The level of significance was set at 5%, where P values of 0.05 were considered to be significant.

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RESULTS

All patients in the present study were women (n=50). The mean age of the patients in OLP group and in control group were 55.8 and 51.96, respectively. Hypothyroidism was found in 24% patients of the OLP group compared to 28% of those in control group (P > 0.05). Demographic features and clinical characteristics of the patients are presented in Table 1.

Table 1. Demographic features and clinical characteristics of the patients included in the study.

	OLP group	Control group	P value
Gender (M/F)	0/25	0/25	
Age	55.8±10.26	51.96±11.13	0.247
Hypothyroidism	6 (24%)	7 (28%)	p>0.05
Clinical type of OLP -erosive -non-erosive	 2/25 23/25	 - -	 - -

Mean levels of thyroid gland function tests were within normal values in both groups. Significant difference between OLP and control group was observed only in values of free triiodothyronine (FT3) (P = 0.022). Results are presented in Table 2.

Table 2. Mean level (±SD) of thyroid gland function tests in OLP and control groups.

	Normal level	OLP group (n=25)	Control group (n=25)	P value
FT3 (pmol/L)	3.95-6.80	4.40±0.49	4.85±0.96	0.022*
FT4 (pmol/L)	12.00-22.00	15.39±2.05	15.53±2.07	0.734
TSH (mU/L)	0.27-4.20	2.71±1.32	2.75±1.26	0.892

We have not found significant difference between the groups regarding TSH, FT4, anti-TPO and anti-Tg levels (P > 0.05). Results are presented in Table 3.

Table 3. Number of serum positive anti-TPO and anti-Tg patients in OLP and control groups.

		OLP group (n=25)	Control group (n=25)	P value
Anti-TPO (<34 kIU/L)	Positive	5	2	p>0.05
	Normal value	20	23	p>0.05
Anti-Tg (<115.0 kIU/L)	Positive	7	2	p>0.05
	Normal value	18	23	p>0.05

DISCUSSION

To date, despite numerous research studies, etiopathogenesis of OLP remains unclear. There are literature data which suggested association between OLP and several systemic disorders such as metabolic syndrome, mental health disorders and autoimmune diseases [18, 19].

In the recent years, researchers have shown a great interest for the relationship between thyroid disease and OLP [11, 20]. It is hypothesised that thyroid auto-antibodies may be included in the pathogenesis of oral lesions, and that hypothyreosis probably develops before oral lichen planus [21, 22]. Some results have shown that thyroid gland diseases are more frequent in OLP patients [1, 2, 3, 6, 20, 22]. The present study failed

to assess the possible relationship between OLP and thyroid disease in female patients who are treated at the Department of Oral Medicine, University of Zagreb. This is in accordance with some results from the literature [23] and partially in accordance with results of Robledo-Sierra et al.[24] who also have not found significant difference in levels of thyroid antibodies between OLP and control group, although they have found higher levels of TSH and lower levels of FT4 in OLP group, which was not the case in our study.

Some authors have found that patients with OLP and hypothyreosis more frequently have asymptomatic OLP [20]. This is in accordance with our results because all but two patients had asymptomatic OLP lesions.

A few studies that investigated the association between OLP and TGDs also referred to the levels of thyroid gland hormones or thyroid auto-autoantibodies. In part of these studies, it was found that 84 to 95% of OLP patients had normal TSH levels [11, 16], with no difference when compared to control patients [11]. Our results have shown that all patients in study group and control group has levels of TSH within normal range, although some of them had a history of hypothyreosis.

Some authors have found that OLP patients with positive anti-TPO antibodies are significantly more affected with erosive OLP [1]. We could not evaluate this finding in our study because the number of OLP patients with positive (increased) anti-TPO antibodies was too small (five), and all but two patients had asymptomatic OLP lesions.

The only difference we found between OLP and control group was the one in mean levels of FT3. Mean levels of FT4 and TSH were also lower in OLP group, but the difference was not significant. This is partially in accordance with some results in the literature [24] where the authors have also found lower levels of FT3 and FT4 in OLP group, but higher levels of TSH, which was not the case in our study. In our study, the number of positive findings of anti-TPO and anti-Tg antibodies was greater in OLP group than in the control group. We assume that these findings are related because positive finding of anti-TPO and anti-TG antibodies is found in Hashimoto disease, where the levels of FT3 and FT4 are lower because the thyroid gland works with a lower intensity. Further research should clarify this connection.

CONCLUSION

Our results have not shown a relationship between OLP and thyroid gland disorders. This is in accordance with some of the previously published results, but in disagreement with others. Future well-designed studies with larger number of patients are needed to determine whether there is an association between these two diseases.

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