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Short Communication

Possible interplay of diabetes mellitus and thyroid diseases in oral lichen planus: A pooled prevalence analysis

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Abstract The existence of a comorbidity between diabetes mellitus (DM) as well as between thyroid diseases (TD) and oral lichen planus (OLP), respectively, was substantially demonstrated. However, there is not enough attention to the concurrent status of both TD and DM in OLP patients. Herein, this short communication aimed to compare 1) the prevalence of DM when TD was concurrently investigated and that of DM when TD status was ignored; 2) the prevalence of TD when DM was concurrently investigated and that of TD when DM status was ignored in the studies. The pooled prevalence (9.86 %; 95 % confidence intervals [CI], 9.22–10.53 %) of DM when TD was concurrently investigated was significantly higher than that (8.13 %; 95%CI, 8.03–9.12 %) when TD status was not investigated in OLP patients. The pooled prevalence (12.48 %; 95%CI, 11.77–13.22 %) of TD when DM was concurrently investigated was significantly higher than that (10.45 %; 95%CI, 9.52–11.46 %) when DM status was not investigated in OLP patients. Thus, it is logical to presume for the first time that there is possible

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interplay of DM and TD in OLP occurrence. TD and DM should serve as important confounding factors each other in clinical investigation on OLP and associated comorbidities.

Introduction

Oral lichen planus (OLP) is a relatively common chronic inflammatory mucocutaneous disease mainly affecting oral mucosa.[1,2] Although the etiology and pathogenesis of OLP remain unclear, it has been reported to be of an autoimmune nature associated with several systemic comorbidities.[3–5] It's worth noting that a systematic review and meta-analysis of autoimmune disorders in OLP recently published by De Porras-Carrique et al.[6] They systematically evaluated the evidence on the prevalence of autoimmune disorders in 23,327 patients with OLP extracted from 153 studies and their magnitude of association, and demonstrated the existence of high prevalence and a significant association between OLP and diabetes mellitus (pooled prevalence, 9.41 %; 95 % confidence intervals [CI], 8.16–10.74; odds ratio (OR), 1.64; $P < 0.001$) and thyroid diseases (pooled prevalence, 7.96 %; 95%CI, 6.32–9.75; OR, 1.99; $P < 0.001$), respectively; while the results of association between OLP and other disorders (fibromyalgia, gastrointestinal disorders, rheumatic diseases, Sjogren's syndrome, lupus erythematosus, and dermatological diseases) were not robust and of little evidence based on a limited number of studies and patients.[6]

Since the existence of a comorbidity between diabetes mellitus (DM) as well as between thyroid diseases (TD) and OLP, respectively, was substantially demonstrated,[6,7] DM and TD as the most common comorbidities are also suggested to be the most important confounding factors in clinical investigation on OLP and associated comorbidities. This allows us to hypothesize that perhaps, there may be different prevalence of DM and TD when it is adjusted for confounding factor each other, and prevalence of only 1 comorbidity DM or TD when the other confounding factor is not considered to be adjusted in clinical investigation. In this short communication, we thus aimed to compare 1) the prevalence of DM when TD was concurrently investigated and that of DM when TD status was not reported; 2) the prevalence of TD when DM was concurrently investigated and that of TD when DM status was not reported in the studies. This hypothesis, if it is provided by evidence-based information that can be translated to clinical investigation, implies that there might be synergistic effect of DM concomitant with TD on OLP occurrence. The considerations made here could serve as recommendations to improve and standardize future research.

Materials and methods

In the context mentioned above, we further refined the relevant data on DM or TD in OLP from supplementary materials (Table S1) of the systematic review and meta-analysis by De Porras-Carrique et al. 6 As per the search strategy described previously,[6] we updated a systematic literature search regarding the relevant articles on Sep 30, 2023 from PubMed, Embase, Web of Science, and Scopus databases. The inclusion and exclusion criteria of analyzed studies were also according to the criteria described previously.[6] There was no restriction to language and year of publication, and an additional query was identified from cross-referencing. Titles and abstracts or full texts of the articles were screened and re-evaluated to confirm the eligible papers. Data search and extraction were undertaken independently by two investigators (W.L. and X.H.), and any disagreement was resolved in a consensus symposium. The management of each reference, as well as the elimination of duplicated records, was carried out using Mendeley v.1.19.8 (Elsevier, Amsterdam, The Netherlands). Descriptive statistics and associations were calculated for the bibliographical characteristics. The confidence intervals of the prevalence were calculated by GraphPad website (https://www.graphpad.com/quickcalcs/; GraphPad Software; Boston, MA, USA). It is considered statistically significant that the high and low values of 95%CI do not coincide.

Results

Prevalence of DM when TD was concurrently investigated was higher than that when TD status was ignored

As presented in Table 1, there were 44 studies on both DM and TD investigated concurrently in patients with OLP, and 783 DM and 991 TD were diagnosed among 7943 OLP patients. On the other side, there were 76 studies on only DM investigated in OLP patients and 856 DM were diagnosed among 10,405 OLP patients. As presented in Table 2, the pooled prevalence (9.86 %; 95%CI, 9.22–10.53 %) of DM when TD was concurrently investigated was significantly ($P < 0.05$) higher than that (8.13 %; 95%CI, 8.03–9.12 %) of DM when TD status was not investigated in OLP patients. As for subgroup distributions, the prevalence of DM when TD was concurrently investigated in the source of patients for clinics, retrospective type of study, longitudinal study design, self-reported method of DM, and subjects from North and South America was also significantly ($P < 0.05$) higher than that when TD status was ignored in OLP patients, respectively.

Table 1 Summary of previous epidemiological studies on diabetes mellitus (DM) and/or thyroid disease (TD) in oral lichen planus (OLP).

Variables	Both DM and TD investigated concurrently in OLP patients				Only DM investigated in OLP patients			Only TD investigated in OLP patients		
N	No. of studies	No. of DM patients	No. of TD patients	No. of OLP patients	No. of studies	No. of DM patients	No. of OLP patients	No. of studies	No. of TD patients	No. of OLP patients
Total	44	783	991	7943	76	856	10,405	18	400	3829
Source of patients										
Clinic	38	680	881	6735	67	621	8429	17	385	3139
Population	6	103	110	1208	9	235	1976	NA	NA	NA
Type of study										
Retrospective	24	497	484	5030	47	535	7195	11	187	2712
Prospective	20	286	507	2913	29	321	3210	7	213	1117
Study design										
Cross-sectional	32	607	842	6401	44	510	5186	10	340	3184
Longitudinal	12	176	149	1542	31	337	5152	8	60	645
Evaluation method of DM/TD										
Self-reported	20	367	442	3468	26	228	3676	6	257	2205
Medical assessment	21	371	506	4055	39	559	5931	9	135	1587
Subjects from continents										
Asia	13	143	327	2182	32	236	3424	5	212	1492
Europe	20	346	409	3778	29	434	4494	10	159	2268
North America	5	137	146	668	5	72	1360	2	24	55
South America	2	30	26	201	7	90	743	1	5	14

NA, not available.

Table 2 Pooled prevalence analysis of diabetes mellitus (DM) and/or thyroid disease (TD) in oral lichen planus (OLP).

Variables	Prevalence of DM when TD was concurrently investigated	Prevalence of DM when TD status was not investigated	Prevalence of TD when DM was concurrently investigated	Prevalence of TD when DM status was not investigated
% (95 % confidence intervals)	9.86 (9.22—10.53)	8.13 (8.03—9.12)	12.48 (11.77—13.22)	10.45 (9.52—11.46)
Source of patients				
Clinic	10.10 (9.40—10.84)	7.37 (6.83—7.95)	13.08 (12.30—13.91)	12.27 (11.16—13.46)
Population	8.53 (7.07—10.24)	11.89 (10.54—13.40)	9.11 (7.61—10.87)	NA
Type of study				
Retrospective	9.88 (9.09—10.74)	7.44 (6.85—8.07)	9.62 (8.84—10.47)	6.90 (6.00—7.91)
Prospective	9.82 (8.79—10.95)	10.0 (9.01—11.09)	17.40 (16.07—18.82)	19.07 (16.87—21.48)
Study design				
Cross-sectional	9.48 (8.79—10.23)	9.83 (9.05—10.68)	13.15 (12.35—14.00)	10.68 (9.65—11.80)
Longitudinal	11.41 (9.92—13.10)	6.54 (5.90—7.25)	9.66 (8.28—11.24)	9.30 (7.28—11.80)
Evaluation method of DM/TD				
Self-reported	10.58 (9.60—11.65)	6.20 (5.47—7.03)	12.75 (11.68—13.90)	11.66 (10.38—13.06)
Medical assessment	9.15 (8.30—10.08)	9.43 (8.71—10.20)	12.48 (11.50—13.53)	8.51 (7.23—9.99)
Subjects from continents				
Asia	6.55 (5.59—7.67)	6.89 (6.09—7.79)	14.99 (13.55—16.55)	14.21 (12.53—16.08)
Europe	9.16 (8.28—10.12)	9.66 (8.83—10.56)	10.83 (9.87—11.86)	7.01 (6.03—8.14)
North America	20.51 (17.62—23.74)	5.29 (4.22—6.62)	21.86 (18.88—25.15)	43.64 (31.37—56.74)
South America	14.93 (10.62—20.55)	12.11 (9.95—14.66)	12.94 (8.93—18.33)	35.71 (16.18—61.40)

NA, not available.

Prevalence of TD when DM was concurrently investigated was higher than that when DM status was ignored

There were 18 studies on only TD investigated in patients with OLP, and 400 TD were diagnosed among 3829 OLP patients (Table 1). The pooled prevalence (12.48 %; 95%CI, 11.77–13.22 %) of TD when DM was concurrently investigated was significantly ($P < 0.05$) higher than that (10.45 %; 95%CI, 9.52–11.46 %) of TD when DM status was not investigated in OLP patients (Table 2). As for subgroup distributions, the prevalence of TD when DM was concurrently investigated in the retrospective type of study, cross-sectional study design, medical assessment method of TD, and subjects from Europe was also significantly ($P < 0.05$) higher than that when TD status was ignored in OLP patients, respectively. Nevertheless, the prevalence of TD when DM was concurrently investigated in the subjects from North and South America was significantly ($P < 0.05$) lower than that when TD status was ignored in OLP patients, respectively.

Discussion

According to the results of our analysis, it is logical to presume for the first time that there is possible interplay of DM and TD in OLP occurrence. These 2 comorbidities should serve as important confounding factors each other in clinical investigation on OLP and associated comorbidities.[6,7] For this reason, it highlights that future studies should focus on communicating more data, in a better way, not forgetting to report and investigate both DM and TD that can occur in a patient with OLP. Also, DM and TD status as confounding factors should be further adjusted in the analysis of OLP associated comorbidities. Consequently, the role of the dentists and oral health providers who care for patients with OLP when suspecting these possible comorbidities in order to refer patients for a definitive diagnosis of these disorders. As mentioned previously, 6 dentists and other clinicians involved in the diagnosis and management of OLP should be aware of the frequent association of DM and TD with OLP, and explore the patient's medical history about the possible presentation of the most characteristic symptoms (xerostomia, tiredness, mood swings, nervousness, insomnia, gland enlargement, among others). It is expected that the alarming nature of the symptoms related to DM/TD makes the diagnosis of the disease possible; while it could happen that the progressive onset of the disorder or those cases with less apparent symptoms may go unnoticed for some time.

There are certain limitations in this analysis. This preliminary analysis cannot provide evidence-based scientific information on possible synergistic effect of DM concomitant with TD on OLP occurrence. The relative OR and the correlation coefficient were not analyzed due to lack of detailed data. The subgroup analyses indicate that there were the positive findings in retrospective but not prospective studies; and there was higher prevalence of DM by self-reported evaluation whereas higher prevalence of TD by laboratory test. The differences of the pooled prevalence were observed in the subjects from various continents, probably due to the ethnic population and geographic differences in Asian, European and American countries (Table 2). Also, the stratified analyses by subtypes of TD, such as Hashimoto's thyroiditis, hyperthyroidism, and hypothyroidism,[8,9] were not performed partly due to not available data. Another limitation is heterogeneity that given the methodological variabilities in the OLP studies.[6] Well-designed investigations are warranted to address these limitations.

Conclusively, it is important to increase knowledge about patients with OLP should periodically have venous blood glucose determination to rule out DM and periodically have thyroid stimulating hormone (TSH), T3 and/or T4 determinations to rule out TD, although there is insufficient scientific evidence to determine how often this test should be performed. In contrast, patients with DM and/or TD should undergo periodic oral mucosa examinations to rule out OLP.[10–12] Cross-referral of OLP patients seen in oral medicine to endocrine department for investigation and management of comorbidities. The impact that these proposals could have on health outcomes both in one group and another of patients should be analyzed in new specific studies designed for it, which could serve as recommendations to improve and standardize future research.

Declaration of competing interest

The authors have no conflicts of interest relevant to this article.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jds.2023.11.004.

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