Prevalence of Oral Lichen Planus in Diabetes Mellitus: a Meta-Analysis Study

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ABSTRACT

Background: Oral lichen planus (OLP) is associated with various other systemic conditions such as hypertension, diabetes mellitus (DM). This study evaluated the prevalence of OLP in DM patients compared with non-diabetic control subjects in a meta-analysis study. **Methods**: In this study from January 1973 to August 2016, we searched the studies in Web of Science, Medline/PubMed, Scopus, Science direct, SID (Scientific Information Database), Cochrane and Embase databases. Strategy search was the Medical Subject Heading (MeSH) term oral lichen planus or oral mucosa combined with diabetes in PubMed and this search in other databases. Heterogeneity between estimates was evaluated by the Q and I^2 statistic. Also, publication bias was assessed through funnel plot analysis with the Kendall's and Egger's tests. **Results**: From 831 studies were identified with different search strategies, 11 studies met the criteria to be included in meta-analysis (11 case-control studies). The overall prevalence of OLP in 11 studies with 4937 DM patients and 3698 control subjectswas 1.5% and 0.75%, respectively. In this meta-analysis, the OR in prevalence of OLP in DM patients compared with control subjects was 1.584 (95%CI1.013-2.477; P=0.044) with a low level of heterogeneity (I^2 = 0%) that the result showed the prevalence of OLP in DM patients is significantly more than control subjects. **Conclusions**: This meta-analysis study showed an association between OLP with DM, whereas this association was no significant in previous studies, it was probably because different selecting of age, sex, type of DM, medications and criteria. Totally, the meta-analysis showed the risk of OLP in DM was higher compared with control subjects.

Keywords: Oral lichen planus, Diabetes mellitus, Meta-analysis study.

1. INTRODUCTION

Oral lichen planus (OLP) is a chronic inflammatory disease that its incidence is more in women than men with different age range in around the world (1). The prevalence of OLP in the general population varies from 1-2% (2). Clinically OLP is divided into six forms: reticular, papular, plaque like, atrophic, erosive and bullous types (3). Smokers and/or patients with alcohol abuse show a higher prevalence of OLP lesions (4). Numerous different topical and general treatments have been suggested for OLP such as corticosteroids, immunosuppressants such as cyclosporin, tacrolimusand retinoids (5). Diabetes mellitus (DM) is a chronic disease with serious long-term, debilitating complications and no known cure (6) that is characterized by disturbances in carbohydrate, fat and protein metabolism (7). There are two types of diabetes: type I (insulin-dependent) and type II (non-insulin-dependent) (8). Nowadays, there are different treatments; oral and injectable, available for the treatment of type II diabetes (9), but insulin is the only antihyperglycemic therapy for type I diabetes. Because of varied clinical forms of OLP, it is associated with various other systemic conditions such as diabetes mellitus (10). This association can be due to the endocrine dysfunction in DM that may be related to an immunological defect and contribution to the development of OLP (11).Antidiabetic drugs and certain antidiabetic drugs in DM patients can be caused an allergic manifestation to produce lichenoid reaction (12). Consideration to the incidence and characteristics of oral mucosal lesions among DM patients can be useful for the planning, prevention and reducing the incidence of these lesions. The aim of this study was to evaluate

the prevalence of OLP in DMpatients compared with control subjects in a meta-analysis study.

2. PATIENTS AND METHODS

Eligibility criteria

The studies were searched for the finding of the prevalence of OLP in DM compared with non-DM group (control subjects). We selected full text articles based on following inclusion criteria: a) only original articles of case-control studies in English's abstract; b) it must evaluate the prevalence of OLP in DM patients; c) for meta-analysis, the results must be compared with control subjects; d) OLP must be in DM and non-DM. After that, the criteria for eligible studies were:

- Diagnosis of OLP was based on clinical, histological methods or both;
- The classification of DM was made according to WHO (World Health Organization);
- Diagnosis of DM patients and control subjects was based on FBS, HbA1c or both;
- The control subjects did not have DM or OLP and any cutaneous dermatological or systematic disease;
- The DM patients had no any systematic disease.

Search Strategy

We searched the articles in Web of Science, Medline/PubMed, Scopus, Science direct, SID (Scientific Information Database), Cochrane and Embase databases from January 1973 to August 2016, using the Medical Subject Heading (MeSH) term oral lichen planus or oral mucosa combined with diabetes in PubMed and this strategy in other databases.

Data Extraction

The relevant data extracted from every study wasthe name of author, year of publication, type of study, number of DM patients, number of control subjects, number of OLP patients, percentage of sex, the mean age, type of DM and duration of DM. One reviewer (M.S) searched the articles and then the second reviewer (H.R.M) blinded to the first reviewer. If there was any disagreement between two reviewers, third reviewer (R.S) resolved the problem.

Analysis

The odds ratios (ORs) of the studies were calculated in comparison of the risk estimate of OLP in DM patients compared with control subjects by using meta-analysis. Heterogeneity between estimates was evaluated by the Q and I^2 statistic and for the Q statistic, heterogeneity was considered for P<0.1. In this study, confidence interval (CI) was 95% and 2-sided P<0.05 was considered to be statistically significant. Publication bias was assessed through funnel plot analysis with the Kendall's and Egger's tests.

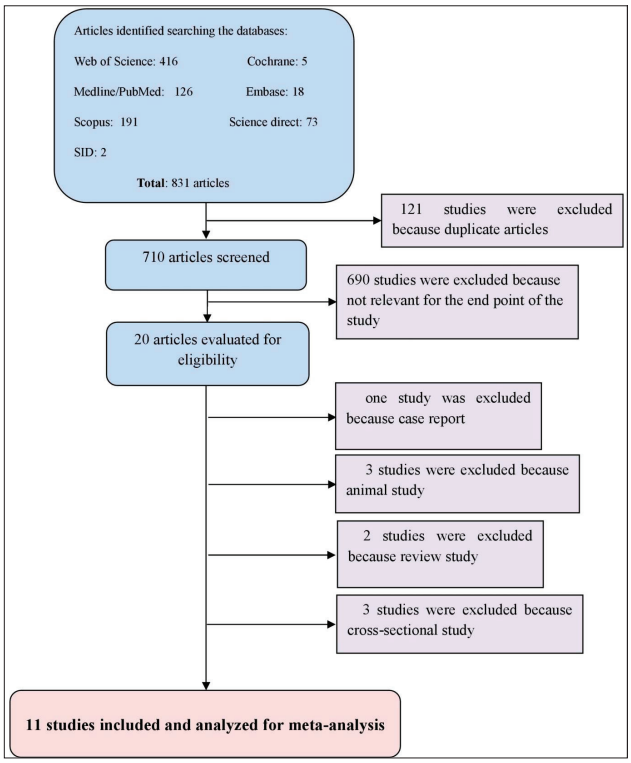

Figure 1. Flow diagram of study

3. RESULTS

From 831studies identified with different search strategies, 20 eligible studies were found. Out of 20studies, one study was case report, 3 studies of animal, 3 studies of review and 3 studies of cross-sectional that were excluded (Figure 1). Therefore, 11studies met the criteria to be included in meta-analysis (11 case-control studies) (Table 1).

Study	No. of DM patients	No. of controls	No. of OLP (DM patients /controls)	Male (DM patients /controls)	Mean age (DM patients /controls)	Type of DM	Duration of DM
Al-Maweri,2013	391	391	2/0	170/152	54.71/53.04	Type 2	Mean: 8.26 years
Petro-Amerikanou,1998	353	274	10/5	127/110	60.4/51.7	Type 2	-
Mohsin,2014	395	405	7/4	212/270	53/46	Type 2	-
Bastos,2011	146	111	9/0	56/53	53.10/51.4	Type 2	<10 years: 24.7% ≥10 years: 75.3%
Van Dis,1995	273	273	11/8	161/161	48.4/50.8	Type 2	-
Albrecht,1992	1600	621	17/0	980/163	-	Type 1:815 Type 2:761	-
Guggenheimer, 2000	405	268	2/2	201/160	33/31.8	Type 2	Mean: 24.6 years
Saini,2010	420	420	2/0	185/167	52.96/51.80	Type 1:29 Type 2:309	Mean: 8.36 years
Borghelli,1993	729	676	4/6	350/326	52.5/51.2	Type 1 and type 2	-
Borhan Mojabi,2009	124	156	5/3	59/72	50.83/41.31	Type 2	
Zareei,2000	101	103	5/2	Sex-matched	Age-matched	Type 1 and type 2	-

Table 1. Characteristics of the analyzed studies in the review investigating the prevalence of lichen planus patients in diabetes mellitus patient
Abbreviation: OLP, oral lichen planus; DM, diabetes mellitus.

The age, sex and prevalence of OLP of the included studies in meta-analysis

In previous studies in this review, the prevalence rate of OLP was reported 0.5 to 9.3% in DM patients and 0 to 1.8% in control subjects. The overall prevalence of OLP in 11 studies (13, 11, 14-18, 19, 20-22) with 4937 DM patients and 3698 control subjectswas 74 (1.5%) and 28 (0.75%), respectively (Table 1). The percentage of males in these studies was between 36 to 61.2% in DM patients and 26.2 to 59.7% in control subjects. Overall, the minimum age was 8 years. Seven studies (13, 14, 16, 17, 19, 20, 22) were age-matched. The mean age of DM patients and control subjects was 51 and 47.7 years, respectively. Out of 11 studies, type II diabetes alone was reported in 7 studies and other four studies were included both type I and type II. The duration of DM has been shown in Table 1.

Treatment and duration of DM in the review

In study of Al-Maweri (13), 261 DM patients were not treated medications, 91 cardiovascular agents, 10 antibiotics, 14 non-steroidal anti-inflammatory drugs (NSAIDs), 6 antiasthmatic and 9 others. Also, 327 control subjects were not treated medications, 42 cardiovascular agents, 4 antibiotics, 6 NSAIDs, 7 antiasthmatics and 5 others. In study of Bastos, 67.1% patients took hypoglacemic, 19.8% insulin and 19% both (14). In study of Van Dis, 65% DM patients and 75% control subjects were not taking medications, 21% and 8% had angiotensin-converting enzyme inhibitors, 7% and 8% NSAIDs, 5% and 4% furosemide, 9% and 8% thiazide derivatives, 0.3% and 0.3% sulfonamide, 1% and 1% propranolol, 0.3% and 0% levamisole and also 0% and 0.3% tetracycline (17). In the study of Saini (19), 68.1% DM patients and 84.3% control subjects were not taking medications, 22.4% and 10%

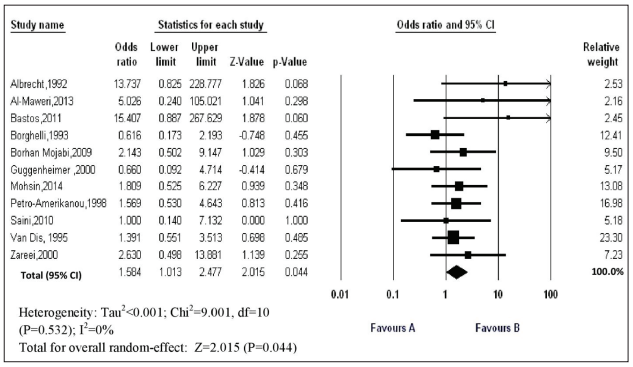

Figure 2. Forest plot of odds ratio of prevalence of oral lichen planus (95% confidence intervals) in diabetes mellitus patients compared with control subjects (Favours A: Patients; Favours B: Controls)

cardiovascular agents, 2.4% and 1% antibiotics, 3.3% and 4.1% NSAIDs, 1.4% and 1.7% antiasthmatics, and also 2.4% and 1.7% others. Other studies didn't report any drugs for the groups.

Meta-analysis

Eleven case-control studies were included in meta-analysis (Figure 2). The OR in prevalence of OLP in DM patients compared with control subjects was 1.584 (95% CI 1.013-2.477; P=0.044) with a low level of heterogeneity (I^2=0%). Therefore, the prevalence of OLP in DM patients is significantly more than control subjects.

Bias indicators

For the risk of bias, we used below two tests (Figure 3):

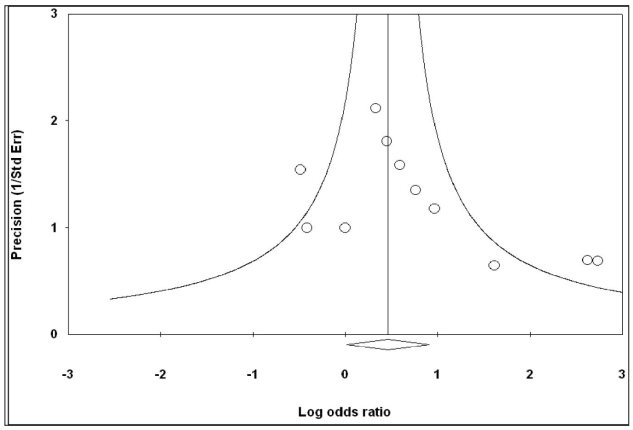

Figure 3. Funnel plot of the included studies in the meta-analysis investigating the prevalence of lichen planus in diabetes mellitus patients

Kendall's test; tau =0.418, z-value of 1.79 and p-value of 0.073 and Egger's test as 1.42 (95% CI=-0.18 to 3.03), standard error 0.7114,t=2.00,p=0.076. Therefore, there was no evidence for the risk of bias.

4. DISCUSSION

A number of studies reported the prevalence of OLP in DM patients with different percentages. The studies showed that the prevalence rate of OLP was 0.5 to 9.3% in DM patients and 0 to 1.8% in control subjects.Van Dis et al., (17) Potts et al. (23) and Robertson & Wray (24), concluded that the type of medication was associated with the presence of OLP lesions. Age is a risk factor for OLP. Ara et al. (25) and Bastos et al. (14) reported the correlation between age and OLP that majority of OLP patients had age 40-50 years. Also, the report of Bastos et al. (14) showed that more OLP patients had DM for a period more than 5 years. The OLP was estimated to affect 0.5% to 2.0% of the general population. This disease has most often been reported in middle-aged patients with 30-60 years of age and is more common in women than in men (26). The relative risk of OLP is 3.7% in people with mixed oral habits, lowest (0.3%) in non-users of tobacco and highest (13.7%) among those who smoked and chewed tobacco (27). Al-Maweri et al. (13) reported that in DM patients and control subjects with no oral habits such as smoking, alcohol consumption or tobacco or betel nut chewing, the prevalence rate of OLP was 0.5 and 0%, respectively, and Ahmed et al. (28) showed this rate in DM patients without a history of addiction was 9.3%.Two studies (14, 15), checked the prevalence rate of OLP in DM patients/control subjects with smoking that concluded the rate was 6.2%/0% and 1.06%/0%, respectively, and this rate in study of Guggenheimer et al. (16) with smoking and alcohol consumption was 0.5%/0.74%. Therefore, the results showed that alcohol consumption, smoking or tobacco or chewing betel nutcan increase risk of OLP in DM patients compared with control subjects. One study (13), reported that this higher prevalence rate of oral mucosa lesions in DM patients may be due to slower healing rates in these patients that leads to a longer duration of a given lesion and not be due to an increase in the incidence. Therefore, if a lesion takes two months to cure in a DM patient and one month in control subject, the prevalence will be more in DM patients at a given point of time. Poor metabolic control can correlate with various diabetic complications (29) that this

control may lead to many pathological changes and increase the susceptibility of oral tissues to infection and local irritants (30). A number of researchers indicated that OLP in DM patients could be linked with compromised immune system in these patients (11) or may be connected to a number of oral hypoglycemic medications taken particularly by older people (31). This meta-analysis study evaluated the prevalence of OLP in a total of 14 studies and comparison of OLP rate in DM patients compared with control subjects that the results showed the prevalence of OLP was 1.37% in DM patients and 0.75% in control subjects. However, previous studies concluded that there was no significant difference between the prevalence of OLP and DM patients compared with control subjects, but the meta-analysis showed the difference was statistically significant($P<0.05$) and the prevalence of OLP was significantly higher in DM patients than control subjects that a very important factor can be type of medications and reducing of immune system in DM patients.To better and more understanding about the reason of increasing the OLP in DM patients should be done cross-sectional and clinical trials studies in DM patients in future, especially considering to the type and duration of treatment, changes in the immune system and also type of diabetes.

Limitations

There were several limitationsin this study. First, we could not evaluate some studies that published in other languages. Second, some studies in meta-analysis had added the patients with type I diabetes to study and therefore, we couldn't report the prevalence of OLP in type II diabetes alone. Third, treatment duration can be effective in incidence of OLP in DM patients, but a number of studies had not reported it. Forth, diagnosis of diabetes in some studies was just based on fasting blood sugar level, whereas HbA1c test is complementary test for more accurate diagnosis of diabetes and it can be because the price of the more that can't be check in all patients. At last, a number of effective factors on the incidence of OLP such as age, sex, oral habits, smoking and alcohol consumption had not been controlled in some studies and type of treatments were different.

5. CONCLUSIONS

This meta-analysis study showed an association between OLP with DM, whereas this association was no significant in previous studies, it was probably because different selecting of age, sex, type of DM, medications and criteria. Totally, the meta-analysis showed the risk of OLP in DM was more compared with control subjects (high prevalence 9.3% in DM patients compared with 1.8% in control subjects).

- Conflict of interest: none declared.

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