



## Patient Characteristics Associated with the Development of Oral Lichen Planus in Two Provinces in Canada A Phenomenological Study

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### ABSTRACT

**Objectives:** To understand the risk factors that may be associated with the development of oral lichen planus (OLP) and its progression.

**Study Design:** We conducted retrospective chart reviews of adult patients with OLP who presented to oral medicine and oral pathology clinics in 2 provinces between September 2016 and January 2020. Data regarding age, sex, disease duration, sites of involvement, comorbidities, medications, allergies, smoking, alcohol use, treatment and follow up were collected. Descriptive statistics were assessed.

**Results:** Among the 94 patients with OLP, mean age was 62 years and most were female (73%). Mean disease duration was 3.1 years. Hypertension, thyroid disorders and diabetes were present in 32%, 28% and 17% of patients, respectively. A significant proportion of patients reported a major surgical procedure (47%) as a preceding event and an additional 7% reported a preceding stressful life event. Three OLP patients (3%) developed squamous cell carcinoma or dysplasia. The mean disease duration for these patients was 4.06 years and the frequency of biopsy in our study was approximately 14%.

**Conclusions:** Female sex, endocrine and immunological comorbidities, such as thyroid disease and diabetes, and psychological stress may play a role in the development of OLP in the Canadian population. A small percentage of patients may develop malignant transformation and, thus, require long-term monitoring.

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Oral lichen planus (OLP) is a common, chronic inflammatory dermatologic condition that often involves the skin, oral mucosa and/or genital mucosa. It is considered to be a dysregulated T-cell-mediated disorder that occurs in response to exogenous triggers.<sup>1</sup> Worldwide, the prevalence of OLP is estimated to be 0.22% to 5%, and the incidence is up to 2.2%.<sup>2</sup> Of those who develop OLP, a subset of patients (0–37%, mean 4.59%) may develop oral squamous cell carcinoma.<sup>3–11</sup> However, there is still controversy regarding the rate of malignant transformation of OLP and the need for and frequency of monitoring. This highlights the need for better understanding of the factors related to the development of this condition and its malignant transformation.<sup>8,12–14</sup>

The etiology of OLP is poorly understood. It is thought that genetic factors, environmental triggers and the immune system play an important role.<sup>15–18</sup> Several factors are considered to be associated with the development of OLP including psychological stress, drug intake and anxiety, as well as comorbidities such as hepatitis C (HCV) infection, hypertension, diabetes and thyroid disease.<sup>15,19,20</sup> Geographic differences exist in the prevalence, presentation and risk factors associated with development of OLP.<sup>4,15</sup> Currently, there is a lack of evidence on the risk factors that may be associated with the development of OLP in Canada. The main objective of this study was to characterize such factors and the malignant transformation of OLP in 2 Canadian provinces.

## Materials and Methods

### Study Design and Study Sample

To answer the clinical question, we conducted a retrospective, observational study. We reviewed the dental charts of patients who presented to oral medicine and oral pathology at the Montreal General Hospital (MGH) in Montréal, Quebec, and to a private oral and maxillofacial pathology clinic, the Atlantic Oral Surgery & Dental Implant Centre in St. John's, Newfoundland. All adult patients (≥18 years of age) who presented to the MGH clinic or the Atlantic Oral Surgery & Dental Implant Centre between 1 Sept. 2016 and 31 Jan. 2020 for an oral pathology appointment were screened for eligibility.

The patients were seen by a specialist in oral medicine and oral pathology for diagnosis and management. The visit was documented in their dental charts, and patients with a clinical diagnosis of OLP were included in the study. OLP diagnosis was based on the American Academy of Oral and Maxillofacial Pathology position paper.<sup>2</sup> Lesions were considered to be OLP if the presentation was symmetric, with well-defined white reticular lines or striae on an erythematous base with any 1 of the recognized patterns (reticular, atrophic, erosive, papular, plaque or bullous).<sup>2</sup> Two oral pathology specialists were involved in the diagnosis of patients. When a

diagnosis was difficult to ascertain clinically at the initial visit, a biopsy was performed and histology conducted to confirm the diagnosis. Patients were excluded if they did not have a diagnosis of OLP, if a drug- or dental-restoration related lichenoid reaction diagnosis was made and/or they had unilateral lesions.

The study protocol was reviewed and approved by the McGill University Health Centre Research Ethics Board and the Newfoundland and Labrador Health Research Ethics Board. We followed the Helsinki Declaration guidelines in this investigation.

### Study Variables

From patient charts, we recorded age, sex, medical history including comorbid conditions and previous surgeries, medications, allergies, tobacco and alcohol consumption, site of OLP lesion(s), disease duration, OLP-associated symptoms, treatments prescribed and investigations performed. Where follow up was available, the response to the treatment was recorded.

### Data Analysis

Data were entered into an electronic data collection document and descriptive statistical data (mean, frequency, range) were computed, using Excel, v. 16.38 (Microsoft Corp., Redmond, Wash., USA), for each study variable when appropriate.

## Results

### Demographic Characteristics

Among those who presented to the clinics in Montréal and St. John's during the study period, 94 OLP patients were identified. Their mean age was 62.2 years (range 35–92 years); 73% of the patients with OLP were female.

### Medical History

The most frequent comorbidities were hypertension (32%); thyroid disorders (28%), most frequently hypothyroidism; and diabetes (17%), with 6 patients with type II diabetes mellitus and 1 with a history of gestational diabetes. A significant proportion of patients (47%) noted that they had had a major surgical procedure, such as a mastectomy, hysterectomy, oophorectomy with or without salpingectomy, cholecystectomy, thyroidectomy, cardiac bypass surgery, hip and/or knee replacement or other types of musculoskeletal surgeries including knee replacement and back surgeries. Most of these surgeries were among women.

In the study group, 69 patients (73%) had had at least 1 surgery. In the general Canadian population, approximately, 1.8% of adults

over the age of 18 years have had at least 1 surgery.<sup>21,22</sup> Among the patients in this study who had a surgical procedure, the mean number of surgeries per person was 1.57. An additional 7% of patients self-reported that they had undergone a major stressful life event before development and diagnosis of OLP. Only 4 patients in our study reported a history of hepatitis, whether treated or active, and only 1 of these had HCV; 2 had autoimmune hepatitis and 1 had a history of hepatitis A.

The mean number of medications per patient was 3.62 (assessed in 93 of 94 patients as 1 patient's file did not include specific medications). The most frequent types of medications were antihypertensives (32%), statins (30%), proton-pump inhibitors (29%), levothyroxine (22%) and antihyperglycemic agents (14%). The antihypertensive medications, taken by 32% of patients, consisted of angiotensin II receptor blockers (24%), beta-blockers (22%), calcium-channel blockers (22%), angiotensin-converting enzyme inhibitors (18%), diuretics (14%); 2% could not remember the specific medication names. Of the 14% of patients on antidiabetic medications, most were taking metformin (32%), dipeptidyl peptidase 4 inhibitors (27%), sulfonylurea (18%), sodium-glucose cotransporter-2 inhibitors (18%) and insulin (5%). Most patients (63%) indicated that they did not have a history of allergies to medication.

### Social History

Smoking and alcohol use data were available for 64 patients. Approximately 25% of these patients (16) had a positive smoking history as current or previous smokers. Pack history was available for 10 of these 16 patients, and the mean was 14.6 pack years. Details on the relation between smoking history and OLP onset was not available. One patient reported marijuana use; however, the frequency of use was not specified.

Approximately 53% (34 of 64 patients) reported that they did not consume alcohol, while 27% (17) reported social alcohol use. For patients who reported regular alcohol consumption, 19% (12) indicated moderate alcohol use, defined as up to 1 drink/day for women or 2 drinks/day for men. Only 1 patient had a history of high alcohol use, defined as alcohol consumption greater than the threshold defining moderate use. **Table 1** summarizes medical and social history.

### OLP Lesions and Symptoms

A significant proportion of patients (78%) was affected by OLP at  $\geq 2$  sites, with gingivae and buccal mucosa being the most common sites (46% of patients each; **Figure 1**). The lesions were bilateral and symmetric in distribution. Other areas that were involved included the dorsum of the tongue (21%), lateral tongue (12%), ventral tongue (11%), lips (6%), hard palate (4%) and soft palate (1%). No differences in lesion location were based on

sex or disease duration. A small proportion of patients also had skin (5%) and genital (4%) involvement. Approximately 6% of patients had erosive OLP, and most patients (94%) had lesions that were described as white reticular lines on an erythematous base.

Mean disease duration, as assessed in the 85 (of 94) patients for whom this was recorded in their dental chart, was 3.06 years at the time the patient presented for an oral pathology consultation. The other 9 patients had indicated that they had OLP for "many years."

Of the patients, 73% presented with symptoms, such as sensitivity to hot and spicy foods, and an additional 7% indicated that they had sensitivity to toothpaste, particularly Sensodyne (GlaxoSmithKline Inc., Mississauga, Ont.), mouthwash or fluoride rinse. One fifth (20%) of patients indicated that they were asymptomatic and that their OLP lesions had been noticed by their dental professional during a routine check-up.

### OLP Management

All symptomatic patients were treated with topical corticosteroids, and all patients, regardless of symptoms, were provided with information on optimal mouth care for OLP lesions. In addition, 1 patient (1%) was given a corticosteroid injection for severe presentation of erosive OLP at the initial appointment, and 10 patients (11%) had incisional punch biopsies taken of their lesions. These lesions were bilateral and symmetric, and solitary lesions were excluded to reduce the risk of inadvertent inclusion of lichenoid lesions. The patients who had incisional biopsies to rule out dysplasia tended to present with suspicious lesions and/or had a history of smoking and/or ethanol use and/or long-standing OLP. Finally, 4 patients (4%) had lesions that were excised at the initial presentation and sent for pathology. As these lesions were OLP, the entire lesion was not excised, only the suspicious erythematous portions that were isolated and  $<1$  mm in size.

### Follow Up

For 65 patients (69%), follow-up information was available over an average duration of 5.10 months. For 8 patients (9%) follow up was still pending at the time of the data analysis, and 2 patients (2%) refused follow up. The remaining 19 patients (20%) were asymptomatic, with non-suspicious lesions at the initial presentation, and short-term follow up was deemed not required.

For patients with follow-up data available, 68% (44 of 65) had no symptoms, were stable or experienced improvement in their symptoms after topical corticosteroid use. Only 5 (8%) still had active OLP requiring corticosteroid injection or systemic treatment. Finally, 2 patients (3%) had suspicious lesions requiring incisional biopsy.

### Squamous Cell Carcinoma and Dysplasia

In our cohort of 94 OLP patients, 13 had either incisional or excisional biopsies taken during the course of their treatment. Of these, 3 resulted in a diagnosis of squamous cell carcinoma or dysplasia; 2 of these patients were female and 1 was male and their average age was 63.7 years. These 3 patients had a prior history of OLP with a mean disease duration of 4.06 years (range 2 months to 10 years). Two were previous smokers, although they had quit at the

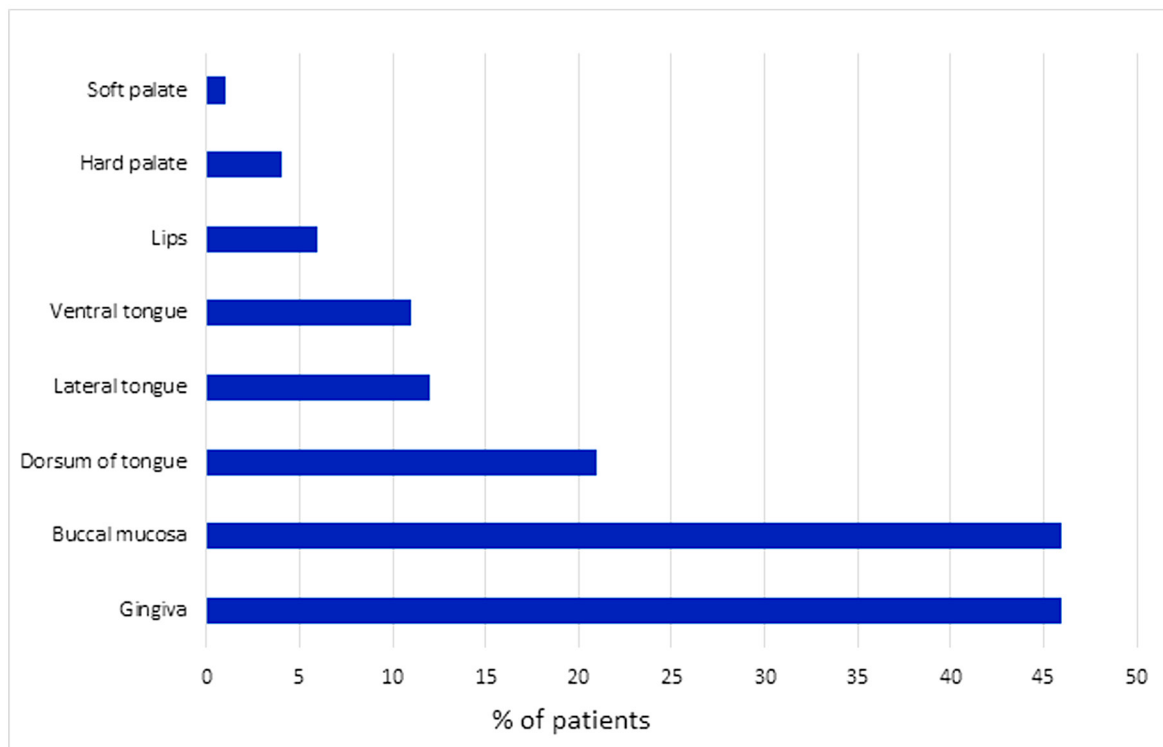
time of the biopsies. Two patients stated that they consumed alcohol socially, and the third reported zero alcohol consumption. The lesions were located on the lateral tongue in 2 patients and the third patient's lesion was on the hard palate. One patient did not have any concomitant medications or comorbidities, and the other 2 had multiple medical conditions, including diabetes, hypertension and a history of myocardial infarction, and were taking antihypertensives, antihyperglycemics, a statin and aspirin to treat these conditions.

**Table 1:** Demographic data for study population.\*

Characteristic	No. (%) of patients (n = 94)
<b>Sex</b>	
Male	24 (22)
Female	68 (73)
<b>Medical history</b>	
<b>Medical conditions</b>	
Hypertension	30 (32)
Thyroid disorders	26 (28)
Diabetes	16 (17)
<b>History of surgery</b>	44 (47)
<b>Stress</b>	7 (7)
<b>Medications</b>	
Antihypertensives	30 (32)
Statins	28 (30)
Proton pump inhibitors	27 (29)
Levothyroxine	21 (22)
Antihyperglycemic agents	13 (14)
<b>No known drug allergies</b>	59 (63)
<b>Social history</b>	
<b>Smoking</b>	
Cigarettes	16 (25)
Cannabis	1 (2)
<b>Alcohol</b>	
None	34 (53)
Moderate†	12 (19)
High use‡	1 (2)

\*Note: mean age, years: 62.2 (range 35–92).  
†Moderate alcohol use is defined as up to 1 drink/day for women and 2 drinks/day for men. High use is defined as >1 drink/day for women and >2 drinks/day for men.

Figure 1: Site of oral lichen planus lesions in our study population.



## Discussion

In this study, we aimed to describe the characteristics of patients with OLP in 2 provinces, as there is a lack of Canadian-specific data. Most of the OLP patients in our study were female (73%), which is consistent with the proportion observed in other geographic areas.<sup>15,24</sup> In our cohort, the mean age was 62 years, representing a slightly older patient population than previously described, which typically ranged from 30 to 60 years.<sup>23,24</sup> Race and ethnicity were not documented in the charts.

In terms of comorbid medical conditions, most patients in our cohort had hypertension, thyroid disease, specifically hypothyroidism, and diabetes. This is consistent with what has been observed in other populations.<sup>15,19,25</sup> Some antihypertensive medications, such as methyl dopa; beta-blockers, such as propranolol; amlodipine; and antihyperglycemics, such as metformin and sulfonylureas, have been associated with lichenoid drug reactions.<sup>26,27</sup> Given that such reactions may be difficult to differentiate clinically and histologically from OLP, they may have been inadvertently included in our study, although every attempt was made to identify them. Because of the retrospective nature of our study, a temporal relationship is also difficult to establish. However, an association for patients with

a history of HCV and OLP, as seen in some Japanese and Italian studies,<sup>28,29</sup> was not observed in our Canadian cohort. This may be a result of the treatment options for HCV that have been adopted in the last 5–10 years, thus reducing the number of active HCV infections in our cohort. Another possible explanation is an epidemiological difference between HCV and OLP in the Canadian population, as only 4 patients in our study reported a history of hepatitis whether treated or active, and only 1 of these was HCV.

A significant proportion of patients (47%) noted that they had had a major surgical procedure, such as a mastectomy, hysterectomy, oophorectomy with or without salpingectomy, cholecystectomy, thyroidectomy, cardiac bypass surgery, hip and/or knee replacement and other types of musculoskeletal surgeries. A possible explanation is that medical conditions requiring these surgeries may be correlated with the characteristics associated with development of OLP, such as female sex and older age. Among the patients who had had a surgical procedure, the mean number of surgeries per person was 1.57. However, a temporal association between the surgeries and the onset of OLP is difficult to establish in this retrospective study and may be an area of future investigation.

An additional 7% of patients noted that they had undergone a major stressful life event before their development of OLP. Stress may be a triggering factor for OLP flares.<sup>15,30</sup> In fact, in one study, 77% of patients reported that emotional stress was a trigger for OLP.<sup>30</sup> Furthermore, a recent systematic review found evidence that psychological disorders, specifically stress, anxiety and depression, were associated with the development of OLP.<sup>31</sup>

It would be of interest to investigate whether the physical, mental and emotional stress of serious medical conditions and their associated major surgical procedures have an impact on the development of OLP in susceptible patients. Because of the retrospective nature of this study, it was not feasible to evaluate whether surgical procedures and their associated stress also preceded the development of OLP. Also, although OLP patients were typically asked about their surgical history and stressful life events at the initial visit in both study sites, this information was not always documented in the charts, making it difficult to ascertain whether such lack of information indicated a negative response from the patient or a failure of the clinician to record it. Overall, the charts of about 65% of patients from the St. John's study site and 54% of the MGH patients documented a response to the question relating to stressful life events.

In terms of the association of previous or current smoking history with OLP, 75% of the patients (48 of 64 patients) indicated that they did not currently or previously smoke. This result was limited by the fact that 30 patients did not have smoking data available. To account for this, as a sensitivity analysis, we assumed that the patients with data missing were either all non-smokers or all smokers. Thus, the range of patients in our cohort with a current or previous smoking history would be 17% (16 smokers out of 94 patients) to 49% (46 smokers out of 94 patients). Therefore, as a conservative measurement, we can assume that at least 51% of our patients with OLP are non-smokers, and this value can go up to a maximum of 83% of the study population. Based on these calculations, it appears that most of the patients who developed OLP are non-smokers. Another study conducted in patients in Israel reported similar results, suggesting that OLP development was independent of smoking history.<sup>32</sup>

In contrast, there may be a correlation with malignant transformation of OLP lesions in smokers, as 2 of 3 of our patients who had positive biopsies for squamous cell carcinoma and/or dysplasia had previous smoking history. Of interest, the 2 patients had both quit smoking several years before their development of the dysplasia and/or carcinoma. However, these numbers are too small to conclude that smoking history is associated with malignant transformation, and additional studies are required to evaluate the role of smoking in such transformation in Canadian patients.

The duration of disease in patients who had malignant transformation ranged from 2 months to 10 years from the time of the diagnosis of OLP to the time of positive biopsy results, suggesting that malignant transformation can occur rapidly. This could be because many patients are asymptomatic; so, the lesions may be present for some time before they are diagnosed by a health care professional. At this time, in the Canadian setting, it may be prudent to evaluate all patients, smokers and non-smokers alike, for the development of OLP and to screen patients, including non-smokers, current smokers and those who have previously quit smoking, for the risk of malignant transformation of OLP regardless of disease duration.

Alcohol consumption did not appear to be correlated with OLP in our study as most patients (80%) indicated no or infrequent alcohol consumption. However, these findings are limited by the fact that the social history in the dental charts was collected from patient self-reports and, thus, may be prone to an under-reporting bias. Other studies conducted in the elderly and/or in women have noted that some patients may under-report their drinking habits to be perceived as socially acceptable.<sup>33,34</sup> Thus, additional studies are required to investigate the association of alcohol and OLP in Canada.

In our study, 3 patients (3.2%) developed malignant transformation of OLP lesions. This rate is consistent with the range of values quoted in other studies.<sup>8</sup> In contrast, in a recent publication,<sup>9</sup> the rate of malignant transformation of OLP was reduced from 1.2% to 0.44% when stricter criteria were applied to the definition of lesion that could lead to malignant transformation. This could also be the case in our study and, thus, a limitation: if stricter criteria were applied, the rate of malignant transformation observed may be reduced.

On follow up, most patients in our study demonstrated significant improvement in their symptoms after use of topical corticosteroids. A small percentage of patients required corticosteroid injections. Follow up was also important to assess suspicious lesions and conduct incisional biopsies to assess malignant transformation of these lesions in some patients.

## Conclusion

Our study is 1 of the first assessments of the characteristics of patients with OLP in Canada. It suggests that Canadian patients with OLP tend to be older females, and hypertension, thyroid disorders and diabetes were common in these patients. Malignant transformation was observed in 3% of patients and, thus, these lesions should be followed for changes. This study serves as an important preliminary analysis and suggests areas for future investigation.

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