



DEMOGRAPHIC PROFILE OF ORAL LICHEN PLANUS PATIENTS IN THE BULGARIAN POPULATION. CLINICOPATHOLOGICAL CORRELATION IN THE DIAGNOSIS OF THE DISEASE

Maria Mutafchieva

Department of Periodontology and Oral Mucosa Diseases, Faculty of Dental Medicine, Medical University of Plovdiv, Bulgaria.

ABSTRACT:

Oral lichen planus (OLP) is a relatively common mucosal disease that mainly affects middle-aged women, yet the epidemiological characteristics of this condition in the Bulgarian population are poorly studied. OLP is considered a clinic-pathological diagnosis that is sometimes challenging to make.

Aim. The aim of the present study was to determine the prevalence of OLP among the Bulgarian population and to evaluate the clinico-pathological correlation in the diagnosis of the disease.

Materials and Methods. The files of the patients with diseases of the oral mucosa consulted in the Department of Periodontology and Oral Mucosa Diseases, Medical University of Plovdiv, between 2012-2016, were retrospectively reviewed. A comparison was also made of the clinical and histopathological diagnoses retrieved from the archived pathohistological records for the same cohort of patients.

Results. Out of a total of 714 patients with mucosal diseases, 141 have been diagnosed with OLP, with the disease accounting for the largest proportion (20%) among the analyzed group. Male to female ratio was 1:4, and most patients were over 51 years of age. Histological confirmation of the clinical diagnosis OLP has been obtained in 84.1%, and there were additional 10.84% cases with a histological diagnosis of OLP that were clinically misdiagnosed.

Conclusion. OLP seems to be of great clinical importance in our country. There is a clinic-pathological discrepancy in the diagnostic evaluation of the disease in a relatively high percentage of cases. Therefore, stricter diagnostic criteria need to be introduced and followed to obtain a more reproducible diagnosis of OLP.

Keywords: OLP, demographic characteristics, diagnosis,

INTRODUCTION

Oral lichen planus (OLP) is a chronic inflammatory disease that can occur alone or as part of classic lichen planus (LP) with concomitant lesions of the skin, scalp, nails, genitals, and/or other mucous membranes. The exact etiology is uncertain, but it is considered an autoimmune disorder in which epithelial cells are recognized as foreign, secondary to changes in the antigenicity of the cell surface. This leads to sensitization of T-Ly, which ultimately destroy basal keratinocytes by activating the process of programmed cell death (apoptosis) [1]. OLP is included in the group of oral potentially malignant disorders (OPMDs) [2].

The total estimated global prevalence of OLP is 1.01%, but it seems to demonstrate geographic predominance [3]. India has the lowest reported prevalence of 0.49%, whereas the disease is relatively more common in Europe - 1.43% [3]. However, no racial distinctions are seen [4]. Oral lichen planus is almost exclusively a condition of adults, with most patients being between 30 and 60 years of age [4, 5]. Occurrence in childhood is casuistic [3, 5]. OLP is more common in women, with a male to female ratio varying between 1:2 [6, 7] to 1:4 among different studies [3]. Although there are no data to support a genetic basis for the disease, familial cases with two or three affected members have been reported in the literature [5]. The demographic characteristics of OLP have been well described in large series from developed countries; however, reports concerning the incidence rate and the epidemiological profile of the disease in the Bulgarian population are insufficient.

Six clinical forms of OLP have been described [8]. The classic manifestation of the disease includes white hyperkeratotic striae (Wickham striae) in a lace-like configuration (reticular form). Keratotic changes can also appear as papules (papular form) or a homogeneous white plaque (plaque form). Atrophic areas (atrophic form), erosions (erosive form) and even blisters (bullous form) can also be part of the clinical finding. This classification has been simplified by other authors who consider only reticular, atrophic and erosive clinical presentation [9]. The six clinical forms of OLP can be grouped into white lichen - in the presence of reticular, papular, or plaque-like lesions and red lichen -

in the presence of atrophic, erosive or bullous lesions, regardless of whether or not these coincide with white lichen at the periphery or in other sites [5]. Similarly, another otherclassification distinguishes keratotic (reticular, papular, plaque-like) and non-keratotic forms (atrophic, bullous, and erosive forms) [3, 6]. The latter are associated with more intense pain. Multiple lesions with bilateral and symmetrical distribution are characteristic of the disease.

Due to the great diversity in the clinical presentation, a wide range of diseases enter into the differential diagnostic consideration when making the diagnosis of OLP. Although the so-called Wickham striae are considered a pathognomonic sign of OLP, confirmation of the clinical diagnosis by means of histopathological study of a biopsy specimen is generally advised [10]. Histological criteria for OLP were first proposed by the World Health Organization (WHO) in 1978 [11] and then modified by Van der Meij in 2003 to include a well-defined band-like inflammatory infiltrate consisting mainly of lymphocytes and confined to the superficial part of the connective tissue; basal cell liquefactive (hydropic) degeneration and absence of epithelial dysplasia [10]. In the latest criteria update proposed by the American Academy of Oral and Maxillofacial Pathology in 2016, two more criteria were added - lymphocyte exocytosis and absence of verrucous epithelial architectural change [12]. However, the listed microscopic features are not pathognomonic of OLP. There are conditions, such as oral lichenoid contact hypersensitivity reaction (OLCHR) and oral lichenoid drug reaction (OLDR), which are clinically and histologically indistinguishable from idiopathic OLP, but in contrast, they have an identifiable causative factor, the removal of which leads to regression of the lesions [6, 12]. Additionally, chronic ulcerative stomatitis (CUS), lichen planus pemphigoides, proliferative verrucous leukoplakia, etc., also share histological features of OLP [12]. Therefore, OLP often presents a diagnostic challenge. A discrepancy between clinical and histological diagnosis is commonly observed [4]. The aim of the present investigation was to study the epidemiological characteristics of OLP in the Bulgarian population and to evaluate the clinico-pathological correlation in the diagnosis of the disease.

MATERIALS AND METHODS

Research Focused Questions

- What is the frequency distribution of OLP among the other oral mucosa diseases
- What is the clinicians-pathologists agreement rate in the diagnosis of OLP

Research materials

- All case files of patients with diseases of the oral mucosa consulted in the Department of Periodontology and Oral Mucosa Diseases, Faculty of Dental Medicine, Medical University of Plovdiv for a period of 5 years
- The pathohistological file cards of all biopsied patients at the Department of Periodontology and Oral Mucosa Diseases, Faculty of Dental Medicine, Medical University of Plovdiv for the same period

Study Design

This was a retrospective study in which data were extracted and analyzed from the archives of the Department of Periodontology and Oral Mucosa Diseases, Faculty of Dental Medicine, Medical University - Plovdiv, in order to achieve the set goals. The observation period was between 2012-2016. According to the records, all biopsies have been taken at the Department of Periodontology and Oral Mucosa Diseases, and the histological examination of all biopsied patients has been performed at the Department of General and Clinical Pathology, Faculty of Medicine, Medical University of Plovdiv. The study was conducted in accordance with the Declaration of Helsinki. The research protocol was approved by the Ethics Committee of Medical University Plovdiv (R3716/07.10.2014).

Frequency distribution of the diseases of the oral mucosa

The journal books of the patients with mucosal diseases consulted in the Department of Periodontology and Oral Mucosa Diseases for the period 2012-2016 were retrospectively reviewed. The diagnoses filled in there were made by an oral pathology specialist from the department based on clinical data (medical history and clinical findings) and do not reflect the results of additional paraclinical examinations.

Gender and age distribution of the patients with OLP

To determine the distribution of patients with OLP by gender and age, only those with a histologically confirmed clinical diagnosis were included in the statistical analysis after checking the results from the pathohistological file cards

Clinico-pathological correlation in the diagnosis of OLP

A retrospective analysis of the pathohistological file cards of all biopsied patients in the Department of Periodontology and Oral Mucosa Diseases between 2012-2016 was conducted. The clinical diagnoses of the cases were categorized as either: 1- oral lichen planus or 2-other definable lesions and were retrieved from the dentist report that refers the biopsy. The histological diagnoses extracted from the pathohistological file cards were divided into three categories: the first one included 'evident oral lichen planus,' the second category was 'compatible' with oral lichen planus, and the third was another definable lesion.

Statistical analysis

SPSS 13 software was used for data analysis. A chi-square test was performed to determine the statistically significant difference between the presence of OLP lesions in different age groups and sexes. P values less than 0.05 were considered statistically significant.

RESULTS

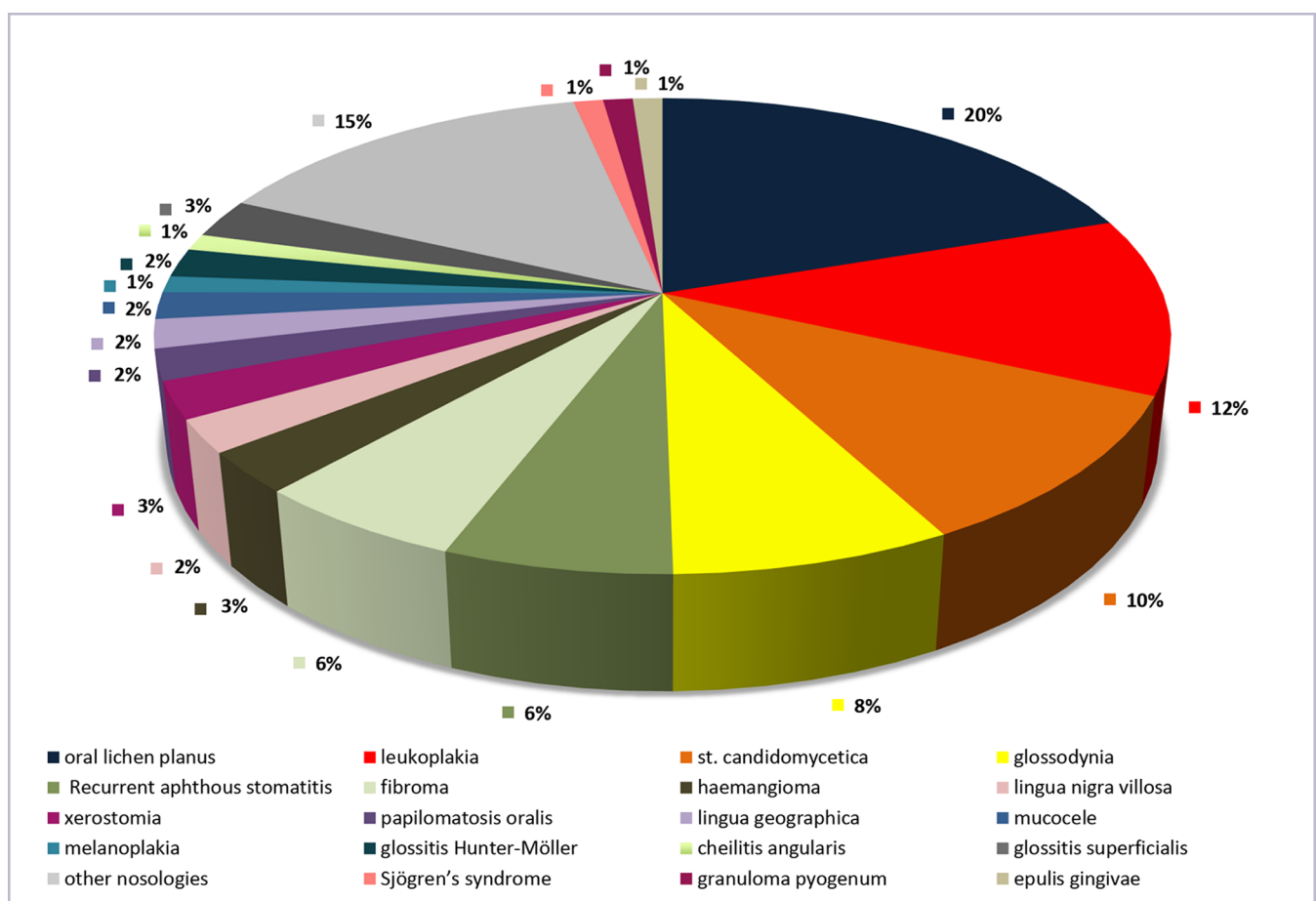
Frequency distribution of the diseases of the oral mucosa

A total of 714 patients have been diagnosed with a disease of the oral mucosa for the period 01.01.2012-31.12.2016. The distribution of clinical diagnoses made is

shown in Figure 1. The prevalence of OLP is relatively high (average of 28 patients per year, 141 patients in total), with the disease accounting for the largest proportion (20%) among the analyzed cohort, exceeding that of leukoplakia (12%) and oral candidiasis (10%). The number of patients with other nosologies was significantly lower, including: pemphigoid (n=7; 0.98%); herpes labialis (n=7; 0.98%); ulcus decubitalis (n=7; 0.98%); morsicatio buccarum (n=7; 0.98%); verruca vulgaris (n=6; 0.84%); epulis fissuratum (n=6; 0.84%); allergic stomatitis (n=6; 0.84%); desquamative gingivitis (n=5; 0.70%); fibroepithelial polypus (n=5; 0.70%); carcinoma spinocellulare (n=4; 0.56%); bisphosphonate osteonecrosis (n=4; 0.56%); burning mouth syndrome (n=3; 0.42%); naevus pigmentosus (n=3; 0.42%); pemphigus vulgaris (n=2; 0.28%); herpangina (n=2;

0.28%); leucoedema (n=2; 0.28%); cheilitis exfoliativa (n=2; 0.28%); an amalgam tattoo (n=2; 0.28%); cheilitis granulomatosa (n=2; 0.28%); epidermolysis bullosa hereditaria (n=2; 0.28%); phlebectasia lingue (n=2; 0.28%); melanosis oris (n=2; 0.28%); cheilitis glandularis (n=1; 0.14%); cheilitis actinica (n=1; 0.14%); herpes zoster (n=1; 0.14%); condyloma acuminatum (n=1; 0.14%); stomatitis ulceronecroticans (n=1; 0.14%); lipoma (n=1; 0.14%); electrogalvanic stomatitis (n=1; 0.14%); sialadenitis gl. minors (n=1; 0.14%); stomatitis nicotinic (n=1; 0.14%); erythema multiforme (n=1; 0.14%); cornu cutaneum (n=1; 0.14%); ranula (n=1; 0.14%); ulcus traumaticum (n=1; 0.14%); lichenoid reactions (n=1; 0.14%); friction hyperkeratosis (n=1; 0.14%); Stevens-Johnson syndrome (n=1; 0.14%); Blue rubber bleb nevus syndrome (n=1; 0.14%).

Fig. 1. Frequency distribution of diseases of the oral mucosa based on clinical diagnosis.



Sex and age distribution of the patients with OLP

Of 141 patients clinically diagnosed with oral lichen planus, 88 had a biopsy performed, and 74 had the diagnosis confirmed. Of them, 61 (82%) were women and 13 (18%) were men. OLP patients were in the age range from 21 to 86 years (mean age 54.6 years), with a peak age between 51-60 (n=25; 33.78%) and over 61 years (n=23; 31.08%). Women were most commonly affected over the age of 51 years - 36.07% (51-60 years) and 36.07% (>61

years), while for men, the highest incidence of OLP was between 41-50 years (46.15%). The percentage of male patients with OLP under 30 years of age was 15.38% versus 4.92% of female patients in the same age group. There was a notable difference in the presence of OLP lesions in the different age groups according to gender, although it was not statistically significant (p=0.06). The epidemiological characteristics of OLP are presented in Table 1.

Table 1. Distribution of patients with OLP by sex and age

Age of Patients	Male		Female		Total	
	n	%	n	%	n	%
<30	2	15.38	3	4.92	5	6.76
31-40	1	7.69	3	4.92	4	5.41
41-50	6	46.15	11	18.03	17	22.97
51-60	3	23.08	22	36.07	25	33.78
>61	1	7.69	22	36.07	23	31,08
Total	13	17.57	61	82.43	74	100

Clinico-pathological correlation in the diagnosis of OLP

For the period 2012-2016, a total of 304 patients have been biopsied in the Department of Periodontology and Oral Mucosa Diseases. 88 biopsies have been referred to the Department of General and Clinical Pathology for histological examination with a clinical diagnosis OLP (Observatio: Oral lichen planus). Histological confirmation of this diagnosis has been obtained in 74 (84.1%) of them (Table 2). Of the remaining 14 cases, 7 have been

histologically diagnosed as 'compatible' with oral lichen planus, 3 - as leukoplakia, 2 - as pemphigoid, 1 - as pemphigus and another 1 - as plasma cell granuloma. On the other hand, another 9 cases (10,84%) histologically diagnosed as OLP have been misdiagnosed clinically as leukoplakia (n=8) or papillomatosis (n=1) (Table 2). The total number of patients with a clinical diagnosis of OLP was 88 (28.95%) versus 83 (27.30%) with a histological diagnosis of OLP. Consensus between clinicians and pathologists was present in 84.1% of cases.

Table 2. Comparison of clinical and histopathological assessment results of OLP

Histological diagnosis \ Clinical diagnosis	Evident OLP		'Compatible' with OLP		Other definable lesions		Total	
	n	%	n	%	n	%	n	%
OLP	74	89.16%	7	100%	7	3.27%	88	28.95%
Other definable lesions	9	10.84%	0	0%	207	96.73%	216	71.05%
Total	83	27.30%	7	2.30%	214	70.39%	304	100%

DISCUSSION

Oral lichen planus is a relatively common mucosal disease of the middle-aged, with female predominance [3, 4, 6]. The demographic characteristics of the disease have been well-described in the literature. However, ethnic and geographic differences have been demonstrated by some authors [5]. For example, in a cohort of 128 OLP patients in the rural population of India, Munde et al. observed lower mean age (36.9 years) of the patients and male predominance [5]. In this regard, the epidemiological characteristics of OLP among the Bulgarian population are poorly studied.

The present retrospective study shows the 5-years incidence rate of OLP among patients with oral mucosa diseases in the region of Plovdiv, Bulgaria. In addition, the distribution of the disease by age and gender is given. Retrospective studies have many limitations; however, they are useful in evaluating patient populations. We

found oral lichen planus to be the most common mucosal disease among the cohort we analyzed. OLP cases outnumbered those of leukoplakia and oral candidiasis. The incidence of oral leukoplakia has been shown to be greater than that of oral lichen planus, with a total estimated global prevalence of 3.41% [13] versus 1.01% for OLP [3]. In our study, patients with OLP (n=141) were almost twice as many as those with leukoplakia (n=85). Based on these results, we may speculate that OLP is of great clinical importance in our country.

For the presented OLP cohort, the male to female ratio was 1:4. Additionally, OLP was shown to be most prevalent in the 5th decade of life (51-60 years). The mean age of 54.6 years for our sample coincides with the mean ages reported in central China (50.4 years), the United Kingdom (52.0 years), Spain (56.4 years) and Italy (56.7 years) [5]. These results are consistent with data from most OLP studies [3, 7] and demonstrate that the distribution

of OLP patients by gender and age in Bulgaria does not differ from that of OLP patients in different parts of the world. We found no statistically significant difference ($p=0.06$) between the presence of OLP lesions in different age groups and sexes. However, it is noteworthy that the onset of the disease in men is at an earlier age. The percentage of male patients with OLP under 30 years of age was 15.38% versus 4.92% of female patients in the same age group. In addition, almost half of the men with OLP were in the age range between 41 and 50 years, while 72.14% of women were over 51 years of age. Other authors have also reported similar results [4, 5]. No childhood cases were observed in our study.

Diagnosing OLP is often a difficult task. The first clinical and histopathologic definitions of OLP were formulated by the WHO in 1978 [11]. Application of these criteria as a diagnostic tool led to inter- and intra-observer variability in the clinical [14] and histological [15] assessment of oral lichen planus, as shown in the studies of van der Meij et al. That means that we cannot rely on a clinical or histopathologic diagnosis alone. Therefore, confirmation of the clinical diagnosis by histopathological examination is necessary. Moreover, OLP is included in the group of premalignant oral lesions. The present study showed that of a total of 141 patients clinically diagnosed with oral lichen planus, only 88 have been biopsied. This paper aims to encourage Bulgarian clinicians to perform histological examination whenever patients from this contingent give consent.

Given that OLP is considered to be a clinic-pathological diagnosis, we decided to assess the degree of agreement between clinicians and pathologists in obtaining it. A lack of clinico-pathological correlation in the diagnosis of oral lichen planus has been previously reported by some authors [4, 10]. A comparison of the results of clinical and histopathologic assessment of OLP in the present analysis showed consensus in 84.1% of cases. 15.9 % (14 out of 88) of the cases for which the clinicians have considered that the clinical picture is diagnostic of OLP have not completed the histopathological criteria. Conversely, 10,84% (9 out of 83) of the cases histologically diagnosed as OLP have been misdiagnosed clinically. The observed clinico-pathological discrepancy can be explained by the following: First, OLP can be present in six different clinical forms. This diversity of clinical findings makes it easy to misdiagnose OLP as another mucosal disease. Secondly, histologically, OLP demonstrates typical but not pathognomonic features. Many of the typical microscopic features of OLP, such as Civatte

bodies and so-called interface mucositis (dense band-like inflammatory infiltrate consisting mainly of lymphocytes and confined to the superficial lamina propria), can also be seen in other diseases [12, 16]. Third, choosing the most appropriate area for biopsy may play a role. Areas of ulceration should be avoided, as the latter often lack an epithelial compartment. Since most of the typical features of OLP, such as Civatte bodies and keratinocyte liquefaction degeneration, are found in the basal epithelial cell layer, the latter must be present to ensure a histological diagnosis. Finally, the difficulty in differentiating oral lichenoid drug/contact reactions from “idiopathic” OLP might be partially responsible for the lack of clinico-pathologic correlation [10]. In this regard, out of a total of 714 patients consulted in the department, only one has been diagnosed with oral lichenoid reactions. The latter, on the other hand, mimic the histological findings of OLP but may also present some differences, such as polymorphic inflammatory infiltrate containing eosinophils, plasma cells, and neutrophils; inflammatory infiltrate in deeper areas; focal perivascular infiltrate [12], and therefore can be defined histologically as “compatible” with oral lichen planus. 7 of 14 cases with a clinico-pathological discrepancy in our study have been histologically diagnosed as ‘compatible’ with oral lichen planus, meaning they may have been oral lichenoid reactions instead of OLP. In 2003, van der Meij et al. proposed a set of modified WHO diagnostic criteria (including clinical as well as histopathological criteria) aimed at easier differentiation between OLP and oral lichenoid lesion (OLL), including OLR [10].

The results of the study support the opinion that for the correct diagnosis of OLP, it is necessary to conduct both a clinical and a pathomorphological examination.

CONCLUSION

Based on the findings of the present study, we can conclude that oral lichen planus is of great clinical importance in our country, as it was the most common mucosal disease among the analyzed cohort. The demographic characteristics of OLP in the Bulgarian population are consistent with those reported from different parts of the world, being a middle-aged disease with a female predominance. Additionally, we demonstrated that there is a lack of clinico-pathological correlation in the diagnostic evaluation of OLP in a relatively high percentage of cases. There is an urge to introduce and follow stricter diagnostic criteria in order to obtain a more reproducible diagnosis of OLP.

REFERENCES:

1. El-Howati A, Thornhill MH, Colley HE, Murdoch C. Immune mechanisms in oral lichen planus. *Oral Dis.* 2023 May;29(4):1400-1415. [PubMed]
2. Warnakulasuriya S, Kujan O, Aguirre-Urizar JM, Bagan JV, Gonzalez-Moles MA, Kerr AR, et al. Oral potentially malignant disorders: A consensus report from an international seminar on nomenclature and classification, convened by the WHO Collaborating Centre for Oral Cancer. *Oral Dis.* 2021;27:1862-1880. [PubMed]
3. Manchanda Y, Rathi SK, Joshi A, Das S. Oral Lichen Planus: An Updated Review of Etiopathogenesis, Clinical Presentation, and Management. *Indian Dermatol Online J.* 2023 Dec;15(1):8-23. [PubMed]
4. Layla SY, Al-ani BDS. Oral lichen planus clinical study with the clinicopathological correlation in the diagnosis of O.L.P. *J Coll Dent.* 2005;17(1):57-60.
5. Munde AD, Karle RR, Wankhede PK, Shaikh SS, Kulkurni M. Demographic and clinical profile of oral lichen planus: A retrospective study. *Contemp Clin Dent.* 2013 Apr;4(2):181-185. [PubMed]
6. Mutafchieva MZ, Draganova-Filipova MN, Zagorchev PI, Tomov GT. Oral Lichen Planus - Known and Unknown: a Review. *Folia Med (Plovdiv).* 2018 Dec 1;60(4):528-535. [PubMed]
7. Aghahosseini F, Arbabi-Kalati F, Fashtami LA, Fateh M, Djavid GE. Treatment of oral lichen planus with photodynamic therapy mediated methylene blue: a case report. *Med Oral Patol Oral Cir Bucal.* 2006;11:126-129. [PubMed]
8. Andreasen JO. Oral lichen planus. A clinical evaluation of 115 cases. *Oral Surg Oral Med Oral Pathol.* 1968 Jan;25(1):31-42. [PubMed]
9. Silverman S Jr, Gorsky M, Lozada-Nur F. A prospective follow-up study of 570 patients with oral lichen planus: Persistence, remission, and malignant association. *Oral Surg Oral Med Oral Pathol.* 1985 Jul;60(1):30-34. [PubMed]
10. van der Meij EH, van der Waal I. Lack of clinicopathologic correlation in the diagnosis of oral lichen planus based on the presently available diagnostic criteria and suggestions for modifications. *J. Oral Pathol. Med.* 2003;32: 507-512. [PubMed]
11. Kramer IR, Lucas RB, Pindborg JJ, Sobin LH. Definition of leukoplakia and related lesions: An aid to studies on oral precancer. *Oral Surg. Oral Med. Oral Pathol.* 1978;46:518-539 [PubMed]
12. Cheng YS, Gould A, Kurago Z, Fantasia J, Muller S. Diagnosis of oral lichen planus: A position paper of the American Academy of Oral and Maxillofacial Pathology. *Oral Surg. Oral Med. Oral Pathol. Oral Radiol.* 2016;122:332-354. [PubMed]
13. Zhang C, Li B, Zeng X, Hu X, Hua H. The global prevalence of oral leukoplakia: a systematic review and meta-analysis from 1996 to 2022. *BMC Oral Health.* 2023 Sep;23(1):645. [PubMed]
14. van der Meij EH, Schepman KP, Plonait DR, AxeAll T, van der Waal I. Interobserver and intraobserver variability in the clinical assessment of oral lichen planus. *J Oral Pathol Med.* 2002 Feb;31(2):95-98. [PubMed]
15. van der Meij EH, Reibel J, Slootweg PJ, van der Wal JE, Jong de WFB, van der Waal I. Interobserver and intraobserver variability in the histologic assessment of oral lichen planus. *J Oral Pathol Med.* 1999 Jul;28(6):274-277. [PubMed]
16. Reddy R, Fitzpatrick SG, Bhattacharyya I, Cohen DM, Islam MN. Seventeen New Cases of Chronic Ulcerative Stomatitis with Literature Review. *Head Neck Pathol.* 2019 Sep;13(3):386-396. [PubMed]

Please cite this article as: Mutafchieva M. Demographic profile of oral lichen planus patients in the Bulgarian population. Clinicopathological correlation in the diagnosis of the disease. *J of IMAB.* 2024 Oct-Dec;30(4):5895-5900. [Crossref - <https://doi.org/10.5272/jimab.2024304.5895>]

Received: 07/08/2024; Published online: 06/12/2024



Address for correspondence:

d-r Maria Mutafchieva, PhD
Department of Periodontology and Oral Mucosa Diseases, Faculty of Dental Medicine, Medical University of Plovdiv;
3, Hristo Botev Str., 4000 Plovdiv, Bulgaria.
E-mail: mariya.mutafchieva@mu-plovdiv.bg