Available online at **www.ijmrhs.com**

ISSN No: 2319-5886

International Journal of Medical Research & Health Sciences, 2018, 7(10): 109-120

Oral and Genital Lichen Planus in a Cohort of Iraqi Females

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ABSTRACT

Lichen planus is a chronic, inflammatory, mucocutaneous autoimmune disease that affects various surfaces such as the mucous membrane of the oral cavity, genitalia, skin, nail scalp esophagus, and eye. The lesion may affect many sites and at the same time, it may affect inter and extra orally. The lesion appears as a sequence of different types of lesion mostly intra orally and extra orally. The lesion may be associated with symptoms of pain and burning or with candida growth. ***Objective:*** *To evaluate a correlation between oral LP with age, GLP changes among Iraqi females patients, to isolate and identify Candida species from the mucous membrane of LP patients and to find its role to aggravate these symptoms and its effects on the clinical investigation in that individual who had been used carrageenan for treatment burning sensation.* ***Material and methods****: The study was performed at the college of dentistry, University of Baghdad. The sample consisted of 15 LP patients. Candida species were isolated from the oral cavity of patients (affected and unaffected sites).* ***Results****: The most frequent affecting age was 45-54 and the buccal mucosa was the most commonly affected site. The lesion was the Bilateral, symmetrical and reticular type of lesion appeared in 73.3% cases. Burning sensation at the buccal mucosa was the most prevalent complain of about 86.6 patients while 2/3rdof the sample had genital symptoms. The vulval lesion was present in about 60 of genital lesions. High significant correlation was found between the genital lesion and the site of OLP lesion at buccal mucosa and gingiva. Carrageenan showed strategies to treat OLP symptoms. Candida growth was more at the affected site of OLP lesion than the normal site of the same patient. This may give an indication about its role in incidence and aggravation of lesion.* ***Conclusion:*** *The diagnosis and management of LP lesion can be challenging for oral medicine and gynecologist specialist because of the lack of familiarity between these two branches and patient embarrassment in history recording. Therefore, genital LP should be considered among individuals with oral LP lesions.*

Keywords: Oral lichen planus, Genital lichen planus, Oral symptoms, Candida species, Carrageenan gel

INTRODUCTION

The term lichen planus (LP) is derived from the Greek word lichen meaning tree moss and the Latin planus meaning flat. Erasmus Wilson first described the condition LP in 1869 [1]. Lichen planus is chronic, inflammatory, a mucocutaneous autoimmune disease that affects various surfaces. OLP Patients may have the disease in one or more extraoral sites [2], vulvar and vaginal involvement, cutaneous lesions scalp, nails, esophagus, and eyes (rarely occur). Andreasen classified oral lichen planus into six clinical forms [3], including reticular the most common type with a feature of white lines (Wickham's striae), plaque-like, papular, atrophic, erosive, and bullous [4,5]. The mouth lesions may occur in the absence of skin lesions and usually appear in multiple and symmetrical distributions [6]. In 1978, the World Health Organization has defined OLP clinically. Lichen planus was discovered in both the oral and genital mucosa in a relatively high percentage of patients [7]. Vulvar LP (VLP) may often be associated with desquamative inflammatory vaginitis (DIV), which is secondary to erosive or blistering epithelial disease that occurs in the vagina [8].

Genital lichen planus appears in a different morphology. A female patient has an erosive form by scarring, pain, and discomfort [9,10]. The patients present with desquamated peeled eroded gingivitis complained of pain, burning and involved buccal, labial mucosa. While reticular lesions of GLP are relatively asymptomatic, unlike erosive GLP Scarring was not seen [9]. Oral lesions preceded the development of genital lesions. Prognosis of genital symptoms for spontaneous remission is poor. Most patients continue to suffer from the disease for years [11].

Candida species had been associated with different oral lesions with various percentage especially OLP [12,13] identified by culture methods. Candida overgrowth or infection may exacerbate OLP signs and symptoms, while using antifungal treatment for erosive lesions with Candida may change it to reticular form as shown in many studies [5,14].

Carrageenan was used as a thickening agent back in the 1400's in Europe [15]. In a dental aspect, carrageenan was used as a toothpaste and impression material [16,17].

Carrageenan is extracted from red seaweed [18]. It is a polysaccharide extracted with hot water or alkali and it consists of potassium, sodium, calcium, magnesium, and ammonium sulfate esters of galactose and 3,6-anhydrogalactose copolymers [16].

Extensive studies have demonstrated the treatment effect of carrageenan on oral lesion may allow the use of K-carrageenan as a base or primary compound in dental practice besides the other compounds like chlorhexidine [19]. It showed that after application of carrageenan, it was found that there was taste alteration, burning mouth syndrome, dry mouth. The biological activity of Carrageenans was shown a bacteriostatic agent [20]. It was also capable of inhibiting virus replication so it is used in the delivery of antiviral drugs [21]. It also acts as an antitumor agent and antimalarial [22,23]. Carrageenan is used as an antacid and to cure peptic and duodenal ulcer. Several studies were conducted all over the words regarding OLP. Up to our knowledge, few of these studies were emphasized on the genital aspect of LP especially in Iraq. Therefore this study intensively showed the relevance of genital changes in female patients with OLP disease.

The aim of the study:

1. To evaluate the genital involvement associated with oral changes among Iraqi females with lichen planus
2. To isolate and identify the Candida species in patients complaining from lichen planus and correlate the above mention results with burning mouth sensation, types of lichen planus, and systemic disease
3. The effect of carrageenan on burning mouth sensation in patients with lichen planus

PATIENTS AND METHODS

Patients and Methods

The study group consisted of 15 females with clinical evidence and who were histologically diagnosed with OLP. They attended the Oral Diagnosis Department of Dentistry College of Baghdad University from March 2017 to April 2018. All patients were examined in gynecologist's clinic at the same period study group. Each patient gave her informed consent to the study and to the use of personal data.

Clinical and Histopathological Examination

Information related to age at presentation, duration of the OLP lesion and associated symptoms like pain and burning sensation, other skin lesions, the presence of any systemic diseases, commonly affected site of oral mucous and types of lesion were collected from each patient. Oral examination was done by a specialist of oral medicine (College of Dentistry University of Baghdad). The Diagnosis was based on clinical and histopathological findings [24] according to the modified World Health Organization 2003 [25].

All patients referred to the gynecologist private clinic for examination. The genital examination was based on the American criteria 2014. Vulva was examined by inspecting the color of skin and surface, poison, symmetry if there is any ulceration, rushes, and warts present. Histopathological diagnosis of OLP was confirmed by an oral pathologist (College of Dentistry University of Baghdad). Histopathological criteria proposed by Van der Meji and Van der Waal [25] for the diagnosis of OLP. Only patients with sufficient features were considered to be diagnostic. The features include hyperorthokeratosis and parakeratosis, degenerative changes of basal cells, and a band like subepithelial infiltration of lymphocytes.

Microbial Study

Two separated swabs were rubbed and rotated vigorously to collect the deepest-seated micro-organism. It was then inoculated into transported media (Nutrient Broth) for candida species taken from the affected site mucous of OLP lesions and normal site mucosa in the same patient. The swab was then transferred to Sabourad's Dextrose Agar (SDA) media at room temperature (20°C) For 48 hours.

The diagnosis of Candida colony was based on the morphology, colors, odor done by microbiologist specialist.

The carrageenan gel was prepared according to Appendix 2. The carrageenan gel was applied to the patients with burning sensation two times daily for 10 days. The patients were treated with carrageenan without any combination of other medication like topical or systemic corticosteroid which when taken twice daily after meal allows long standing on the affected sites without interference by drinking or eating. The patients were then asked to follow up and were asked about improvement or not of pain. Burning sensation examination of the lesion intra-orally was also done.

RESULTS

Distribution of the Sample According to Age Group

The study sample consisted of 15 females who were diagnosed clinically and histopathological having OLP and GLP. The age range 26-69 years were divided into five groups of 10 years interval. The age group (55-64) years was the highly affected age group (40%) while (45-54) was the lowest percentage (6.66%) as described in Table 1. Mean age of the study group was 49.9 and SD=14.17.

Table 1 Age groups with percentages and their sites of involvement

Age group	No. of patient	Percentage %	Bilateral Sites	Unilateral Site	CHI square	P-Value
25-34	4	26.66	3	1	5.002	0.025*
35-44	1	6.66	1	0	0.313	0.576
45-54	2	13.33	2	0	0.323	0.577
55-64	6	40	3	3	9	0.003**
65 and above	2	13.33	1	1	5.003	0.025*
Total	15	100	10	5	7.87	0.049*
			66.70%	33.30%		
*significant p<0.05, **highly significant, non-significant p>0.05.						

Site of Involvement

The oral lesion appeared as bilateral most commonly among our sample 10 of 15 (66.7%) while the unilateral appeared in only 5 of 15 (33.3%). A significant correlation (P value=0.049) between the bilateral distribution of OLP and age was present. It was highly significant (p=0.003) with age group (55-64) as shown in Table 1.

Buccal mucosa was the most commonly affected site (100%) the gingiva (46.66%), the tuberosity and retro molar area (33.33%), the tongue (40%), and floor of mouth (6.66%), lip and hard palate (13.33%), It was found that each Ten of 15 females have more than one affected site as describe in Table 2.

Table 2 Distribution of the sample according to the site of involvement

Site	One site affected	Two sites	Three sites	More >3 sites	Percentage %
Buccal mucosa	5	3	3	4	100%
Gingiva and gum		2	1	4	46.66%
Tongue			3	3	40%
Floor of mouth				1	6.66%
Lip				2	13.33%
Palate				2	13.33%
Retro molar and tuberosity		1	1	3	33.33%

Distribution of the Sample According to the Types of the Lichen Planus

The lesions were simply classified as a white Reticular lesion which was the predominant type of OLP. It appeared as a white area, smooth patches with or without striae (Wickham striae) and pigmented white-gray lesion. Pure reticular lesion (26.66%) while the mixed (red and white) lesion appeared in (73.3%) of the sample.

The erosive type was (53.33%) of patients, erythematous (20%), atrophic type (13.33%).

Table 3 Distribution of sample according to types of lesion

Type of Lesions	No. of patients	Percentage	Age group(55-64)
Reticular	15	100%	6
erythematous	3	20%	0
Erosive	8	53.33%	5
Atrophic and vesical	2	13.33%	1

Chi square=8.260; p value=0.041.

There was a significant relation between age group (55-64) and types of the lesion (P-value 0.041) was shown in Table 3.

Distribution of the Sample According to the Associated Symptoms with Different Location Involvement

Burning sensation was the main complaint of the OLP patients in different sites. It was in buccal mucosa in 12of 15 (86.66%) of affected sites, gingiva (53.33%), at tongue (40%), lip and palate (6.66%), for each pain associated with burning (20%) as shown in Table 4A.

Table 4A Distribution of sample according to the site of burning sensation

Sites of burning	Number of patients	Percentage %
Buccal mucosa (BM)	13	86.66%
Tongue	6	40%
Gingiva	8	53.33%
Lip	1	6.66%
Palate	1	6.66%
Burning associated with pain	3	20%

Regarding the Symptoms Associated with Genital Lesions

Ten of the fifteen complain of both genital and oral symptoms (66.7%), the rest (33.3%) have a genital lesion with free of symptoms. Genital symptoms can be classified as itching, burning and or dyspareunia as in Table 4B.

Table 4B Symptomatic GLP with OLP symptoms

Symptomatic GLP	Symptomatic OLP (Yes)	Percentage %
Yes	10	66.7%
No	5	33.3%
Total	15	100%

Distribution of Lesions According to Genital Involvement

Gynecologist clinical examination showed vulval lesions in 9 of 15 (60%) vaginal localization (VVGS) in 3 of 15 (20%). In the further three of 15 (20%) no cervical lesion was found as shown in Figure 1.

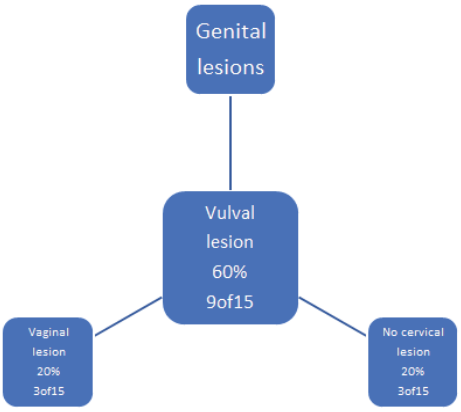

Figure 1 Distribution of genital lesion

Genital LP lesion was correlated with sites of OLP lesion. This relation varies from highly significant (p<0.001) at commonly affected sites like buccal mucosa, gingiva to significant (p<0.043). The less common sites lip, palate, floor of the mouth are shown in Table 5.

Table 5 Correlation between GLP and site of OLP

Site of olp lesion	Genital lp patients	Correlation p-value
Buccal mucosa	15	P<0.001**
Gingiva	7	
Tuberosity and retro molar	5	
Tongue	6	P<0.043*
Floor of mouth	1	
Lip	2	P<0.047*
Palate	2	
*significant p value; **highly significant p-value		

OLP and GLP duration: The duration of OLP vary in our study group from 2 months to 9 years. In most of the cases, GLP was discovered after OLP only in a single case where GLP preceded OLP by 2years.

Distribution of Sample According to Medical History and as Associated with the Genital Ulcer

The diabetes mellitus was found in 3 of 15; hypertension in 3 of 15. 2 of 15 had both DM and HT while 7 of 15 were systemic disease free. All patients had a genital lesion. 6 of them had skin lesion. High significant relation (p=0.01) was found between the medical history of those patients and genital lesion. Also, significant relation (p=0.048) with skin lesion appeared in Table 6A.

Table 6A The relation between medical history and both genital and skin lesions

Systemic diseases	Genital lesions	Skin Lesions
Diabetes mallets	3	
Hypertension	3	2
Both DM &HT	2	1
Non	7	3
P-value	0.01*	0.048*
*significant relation p<0.05		

The highly significant correlation was found between the skin and genital lesion (p=0.001) as shown in Table 6B.

Table 6B The relation between skin lesion and a genital lesion in the sample

Skin lesion	Genital lesion (Yes)	Percentage of patients
Number of patients	Number of patients	
Yes	6	40%**
No	9	60%
Total number	15	100%
**Highly significant (p=0.001)		

Distribution of Sample According to Candida Growth

Two candida swabs were taken for the same patient intraorally one from the affected mucosa and the second from normal look like mucosa as shown in Table 7.

Table 7 Difference of candida growth on both affected and normal site of the oral mucosa

Candida Growth affected site	Growth	Scanty growth	No growth	Scanty growth	Heavy growth	Heavy growth	Heavy growth	Scanty growth	Scanty growth	growth	Heavy growth	Scanty growth	Heavy growth	Scanty growth	Scanty growth
Candida Growth Normal site	No growth	No growth	No growth	Scanty growth	Scanty growth	No growth	growth	growth	No growth	No growth	Scanty growth	No growth	growth	No growth	No growth
No growth=no; Growth=yes; Scanty growth=yes+; Heavy growth=yes++															

A significant correlation was found between duration of OLP and candida growth at both affected and normal sites (p=0.028), (p=0.001) respectively as shown in Table 8.

TABLE 8 The relation between candida growth at (affected and normal) sites with systemic disease; duration of OLP; burning sites of lesions

	Affected Site Candida				Normal Site Candida		
Systemic Disease	**No growth**	**Growth**	**Scanty growth**	**Heavy growth**	**No growth**	**Growth**	**Scanty growth**
Diabetes mellitus (DM)			2	1		1	
Hypertension (HT)		1	2				1
Both (DM) and (HT)				2			2
P-VALUE	0.039*				0.037*		
Duration of OLP							
2mon.-1year	1	2	2	5	6	2	2
>1year			5		3	1	1
P-value	0.028*				0.001**		
Site of burning							
Buccal Mucosa		2	3	3	6	3	
Tongue		1	1	1	3		1
Gingiva			3	2	2	2	1
Lip	1				1		
Pain With Burning	1		1	1	1		2
P-value	0.021*				0.035*		

*significant p-value; **Highly significant p-value.

No difference in correlation was found between medical history of sample group and candida growth at both normal or affected sites, but the slight difference was found between sites of burning sensation and pain of OLP and candida growth at affected site and normal sites.

DISCUSSION

Oral lichen planus is a chronic inflammatory autoimmune disease [26,27]. It is seen worldwide affecting nearly 1–2% of the population twice in women than in men, most often in perimenopausal women [28]. Lichen planus can appear at any age, but most cases occur between 30 and 60 years of age [27].

It was more prevalent in 4th and 5th decade of life [29]. In this study, (mean age was 49.9 years) which is lower than the mean age reported in Central China (50.4 years), UK (52.0 years), Spain (56.4 years), and Italy (56.7 years) [2,29,30-33]. In spite of that our age group (55-64) was more compatible with previous authors since it is the highly affected group about 40% of all age group.

While it was higher than another study that was shown by Munde et al [34], it was more prevalent in the 3rd decade of life (mean age 36.9 years). This was probably due to the ethnic population, geographic difference and smaller samples compared to previous reports.

Regarding the site of involvement, OLP was recognized as bilateral. It appeared symmetrical in 66.7% of the sample which coincides with most of the previous study that shows predominantly bilateral and symmetrical distribution of OLP [30,31,34-36], whereas unilateral appeared in 33.3% [37]. Andreasen in 1968 reported that unilateral lichen planus was detected in 6 of 115 patients about 1.8% of all patients [3].

The buccal mucosa was the most common site of involvement followed by the gingiva and the tongue [2,30,31,35,36,38,]. This is similar to the findings of this study. Clinically the most common location was the buccal mucosa with the prevalence of 100% which coincide and slightly higher than other studies prevalence (80%-95%) [2,8,32,39], while gingiva was secondly involved in this study (46.66%) and the result was the same [8,30,40,41]. Other study showed gingival involvement in about 10% of OLP patients [42] followed by the tongue (40%), while other studies showed that tongue appeared secondly affected after buccal mucosa (30%-50%) [2,30,32].

The interesting point is that 66.7% of patients had multiple affected sites with OLP. Buccal mucosa concomitant gingiva and tongue were the most common multiple oral sites. On the other hand, isolated lesions were located on the palate, lip, retro molar area, tuberosity and mouth floor.

The type of lesion in those multiple sites was predominantly mixed lesion [43] (white and red) about (73.3%) while one site lesion mostly were white reticular area or patches with striae or white-grey pigment. During the rational investigation of the location of LP (26.66%) of our sample exhibited one site of location in reticular form This finding unlike previous study [2,44,45] that shown a single location, erythematous-erosive lesions were more common to find (44.4%), including desquamative gingivitis [42,45]. In patients with multiple affected locations of 2-4 sites, the reticular-papular was the most frequent lesion [2,29,44,45]. According to the fact that a characteristic reticular form is associated with erythematous areas and vice versa [29,43], this was compatible with our finding that the white reticular form is associated with red form in about 66.66% of the sample group.

A significant correlation was found between age and both type and site of lesion in this study, while such a relation was found between the clinical type and extension of the lesion in other studies [2,29,44,45]. Reticular type of OLP was the most common form and was present in all patients and was manifested as bilateral, asymptomatic Wickham striae on the oral mucosa. The reticular form with striae was found in 2 of 15 of this sample. Pigmentation was a prominent feature in reticular form and was diffuse or in patches, ranged from brown to black in color and seen especially on the buccal mucosa [34]. In this study, only one patient had a grey-white pigmentation associated with the erosive and reticular form. However, this could be explained by the facts related to racial factors, skin type and habit [34]. The erosive form was observed in 53.33% of the sample. This form leads to ulcerated, painful, erythematous areas that superimposed by secondary infection, such as Candidiasis [27]. The erythematous form was found in 20% and atrophic form in 13.33%. This result agreed with other study done by Anita d. Munde et al [34,36,46].

An overall vision of the attitude toward the location of the OLP showed that the majority of the patients (86.66%) from this study complained of burning sensation, pain or soreness at the buccal mucosa. The second affected site was gingiva followed by the tongue. Less common sites were lip and palate as reported in other studies [6,11,46,47]. In the previous studies, it was observed that 20%-34% of all patients with OLP develop lesions on the skin [38,39,41,46,47].

Skin lesions are present frequently as pruritic flat-topped violaceous papules and plaques, predominantly on the flexor aspects of the wrists or ankles, extensor aspects of the lower legs, the skin of the lower central back and the natal cleft [48].

In this sample, 40% of the patients presented lesions on the skin. The prevalence of skin lesion was higher in this study than others like Ingafou et al [30] and Jin Lin et al [32] that reported a prevalence of 13%, 11.5% respectively.

Patients report genital involvement with features similar to skin lesions. This study supports a reasonable fact that skin involvement was highly significantly correlated with genital lesion (p=0,001). Regarding the genital lesion, a high percentage of genital lesions in this study was recorded as compared to other studies [11,49-51].

The hair-bearing genitalia and proximal thighs are not the common places for lichen planus. On modified mucous membranes or on true mucous membranes, lichen planus lesions were white or erosive rather than red and popular [9].

Genital involvement was estimated in all of the sample patients. Linear, white striae appear on the vulva and vagina. Reticular papules or severe erosions may appear on the vulva. Anyhow further complications were associated like urethral stenosis, dyspareunia, pruritus, deep erythema. Resorption of the vulvar contours is common with vulvar and vaginal lesions [49,52] that extend to involve the labia mineral. However, the investigation of the genital complication was beyond the aim of this study and need further study to be clarified.

Erosive lichen planus is the common morphology on the moist skin of the vulva and within the vagina. Erosions are frequently accompanied by white lesions [9]. However, this could be explained by the fact that most of these studies were based on the information available on the patient's own report and not on a consistent examination of the genital mucosa [51].

There are many researches that gave along speech about the evidence on the symptoms associated with OLP. About 66.66% of the study group had genital symptoms compared with 100% with oral symptoms. This result was similar to another study which showed 60% of the study group had genital symptoms to 95% oral symptoms [11,49]. Most genital symptoms emerged after oral symptoms in only one case in our sample in which the genital symptoms appeared 2 years before oral symptoms. Our result was higher than another study that showed 33.6% symptoms [2].

The complementary articles regarding the LP and the systemic disease showed a minor or non-significant association between OLP, and hypertension and Diabetes. Grinspan was the first to describe the triad that can be seen clinically

and is called Grinspan‘s syndrome. Although it may simply represent an OLR medication used to treat hypertension and diabetes rather than a true syndrome [1,53]. In this study, sample showed a significant relation between systemic disease and both genital and skin lesions (p=0.01) and (p= 0.048) respectively.

The value for treatment of OLP symptoms by using carrageenan gel twice daily in reducing the symptoms without affecting on severity and extent of oral PL lesions was investigated in this study. This is could be explained by the fact that carrageenan had a biological activity which decreases the over growth of micro-organism at the site of the oral lesion. These micro-organisms may aggravate the condition of any oral lesion and make it symptomatic.

Reports showed *Candida albicans* is present in about 37% of oral LP lesions [13]. *C. albicans* is most frequently been identified by culture methods [12,54]. Prevalence of Candida infection is more in OLP patients and more in erosive type [14,54,55]. This is supporting an association between Candida species and OLP [12,54]. During the study of the general fundamental effect of the candida, this study’s result agreed with previous studies that showed predominant candida growth at affected site by approximately one or more time if compared to the normal mucosal site of the same patient if we take each patient separately.

Symptoms of oral LP may be exacerbated by candida overgrowth or infection. This could explain the result about the relation between burning sensation at the site of OLP lesion and candida growth [5]. This study shows slightly high significant p-value at the affected site if compared to normal. This could be explained by the fact that Yeast possesses phospholipase activity which is capable of promoting the destruction of cellular membranes [56,57]. These observations support the possibility that this yeast is pathogenic in OLP [14].

Open field to the antifungal treatment of erosive lesions with Candida can change the lesions to the reticular form [5]. Also, systemic immunosuppressive therapy is predisposed to candidiasis if used to treat OLP [14]. The hypoglycemic and antihypertensive agent reduce salivary flow in general [58], these medications are associated with a high frequency of isolation of Candida species from subjects with OLP [12]. These previous studies support that the subjects with OLP are more likely to be orally colonized with Candida than subjects with healthy oral mucosa [59-61]. This result disagrees with the finding of this study which showed no difference in the relation between the medical history or systemic disease and candida growth at both sites. However the difference between this type of study and other is not surprising to take into consideration due to lack of the objective criteria demographic, ethnic and epidemiological factors.

SUGGESTIONS

Further studies are needed in Iraq for the prevalence of genital LP in patients with oral LP with a larger sample to clarify which sex is more affected with this type of disease.

Regarding the carrageenan treatment, further studies in Iraq is required to show the effect of carrageenan on oral lesions.

DECLARATIONS

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

APPENDIX 1

Modified WHO diagnostic criteria of OLP and OLL (2003).

Clinical Criteria

Presence of bilateral, more or less symmetrical lesions. Presence of a lacelike network of slightly raised gray-white lines (reticular pattern) Erosive, atrophic, bullous, and plaque-type lesions are only accepted as a subtype in the presence of reticular lesions elsewhere in the oral mucosa. In all other lesions that resemble OLP but do not complete the aforementioned criteria, the term clinically compatible with should be used.

Histopathologic Criteria

Presence of a well-defined, band-like zone of cellular infiltration that is confined to the superficial part of the connective tissue, consisting mainly of lymphocytes Signs of liquefaction degeneration in the basal cell layer Absence of epithelial dysplasia. When the histopathological features are less obvious, the term histopathologically compatible with should be used.

Final Diagnosis of OLP or OLL

To achieve a final diagnosis, clinical as well as histopathological criteria should be included. OLP A diagnosis of OLP requires fulfillment of clinical and histopathologic criteria.

OLL: The term OLL will be used in the following conditions:

1. Clinically typical of OLP but histopathologically only compatible with OLP
2. Histopathologically typical of OLP but clinically only compatible with OLP
3. Clinically compatible with OLP and histopathologically compatible with OLP

APPENDIX 2

The carrageenan preparation methods and chemical ingredients [62]

Ingredients	Percentage
Carrageenan(semi-refined)	0.9 gm
Sugar(sucrose)	20 gm
Citric acid (2-hydroxypropane-1,2,3-tricarboxylic acid)	0.45gm
Potassium citrate (tripotassium citrate)	0.35gm
Deionized distilled water	100 ml
Benzoate of soda (sodium benzoate)	0.5 gm

Methods of Preparation

1. The carrageenan gel (0.9 g) was dissolved in 30 ml distilled water (D.W.) in a water bath at 80°c for about 20 minutes with continuous stirring until fully dissolved
2. Sugar solution was prepared by dissolving 20 gm of it in 30 ml of D.W
3. A citric acid solution prepared by dissolving 0.45gm of it in 10 ml of D.W
4. Then a solution of potassium citrate was prepared by dissolving Sodium benzoate solution prepared (as a preservative) by dissolving 0.5 gm in 15 ml of D.W
5. The sugar solution, carrageenan solution, citric acid solution, potassium citrate, and sodium benzoate were mixed together and completed to 100ml with continuous stirring. Then the mixture was cooled at 8°C to evolve gelation 0.35 gm of it in 15 ml of D.W

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