

Correlation between WHO and Modified WHO Classification Systems in the Histopathologic Diagnosis of Oral Lichen Planus Using Intraobserver and Interobserver Variability

Abstract

Background: Oral lichen planus (OLP) is a relatively common chronic autoimmune disease. In the present study, we tried to correlate the histopathological criteria of WHO and modified WHO (mod.WHO) classification systems using two methods, namely, intraobserver and interobserver observations in these samples. **Methods:** This cross-sectional study was performed on 64 microscopic slides with the diagnosis of the OLP lesions, based on both clinical and histopathological features. At first, each pathologist individually (as intraobserver) examined microscopic slides based on both histopathologic diagnostic criteria. Later, three pathologists in a group (as interobserver) reevaluated microscopic slides 2 months later in the second phase of the study, based on both systems. Eventually, the findings were statistically analyzed with Cohen's kappa coefficient (κ) and reported. **Results:** According to the results, the lichen planus was detected in 8 cases using the WHO method, and in 41 cases using the Mod.WHO method. Intrarater Kappa coefficients were $\kappa = 0.114$, $P = 0.299$; $\kappa = 0.181$, $P = 0.012$; and $\kappa = 0.062$, $P = 0.424$ for three pathologists, respectively. The findings showed no reproducibility ($\kappa = 0.148$, $P = 0.024$) and there was no correlation between the two systems. Statistical analysis revealed that the histopathological criteria of the WHO classification for detecting the lichen planus microscopy were more sensitive but the Mod.WHO classification criteria were more specific for detecting the lichen planus. **Conclusions:** Due to the higher specificity of the histopathological criteria of Mod.WHO classification rather than WHO classification, it seems that Mod.WHO classification has more important and useful criteria for histopathological diagnosis. Finally, we can conclude that the use histopathologic criteria of the Mod.WHO classification is more useful in the diagnosis of lichen planus, although it should be in combination with clinical information.

Keywords: Modified WHO classification system, oral lichen planus, WHO classification system

Introduction

The oral lichen planus (OLP) is a chronic autoimmune disease that accounts for 0.5%–2.6% of the population and develops a variety of manifestations of skin, hair, nails, and mucous membranes.^[1,2] In 1869, Dr. Wilson, for the first time described the OLP clinically as an epithelial disease with unknown etiology. Its name is derived from the Greek word “lichen” meaning tree moss and Latin word “planus” meaning flat.^[3] Some studies have suggested that the OLP may have malignant potential, hence the early diagnosis and follow-up of the lesions are important to prevent and/or at least reduce possible problems in people's lives.^[4,5] It affects the quality of life of the patients due to complications such as pain, discomfort, stress, restlessness, and

depression when compared with the healthy population. Contrary to the cutaneous lichen planus, which is reported in most patients with good treatment response, the OLP has resistance to treatment.^[6]

It is difficult to diagnose this condition often due to manifestation of various clinical subtypes, including reticular, atrophic, papular, erosive, and bullous and erythematous.^[7] The most commonly involved sites are buccal mucosa, gingiva, dorsal surface of the tongue, and vermilion border.^[7] In addition to the mouth, the OLP can also affect various areas including esophageal mucus and genital area.^[8]

Given the importance and effectiveness of this disease in the individual life, it seems very necessary to develop appropriate diagnostic criteria. The clinical and histopathological

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diagnosis of this lesion was established on the basis of the WHO system in 1978 however, this classification system was relatively subjective and had insufficient reproducibility and validity.^[9] The absence of correlation between the clinical and histopathological diagnostic criteria of this classification system, in the sense that each of these criteria alone is unable to determine the definitive OLP, led to clinical and histopathological reconsideration in the WHO classification system and consequently the development of the Mod.WHO classification system by Van der Meij *et al.* in 2003.^[10] Although the other modification and classification have already been introduced,^[11,12] the results of some studies found higher clinicohistopathological correlation and more objectivity in the new classification system compared to the WHO classification system. This means that the Mod.WHO classification system will be able to better assess the disease and achieve a more definitive outcome than the WHO classification system.^[13] However, other research^[14] in 2014 showed a relatively weak correlation for clinicohistopathological diagnostic criteria based on the Mod.WHO system.

The WHO classification is as follows:

Clinical diagnostic criteria

1. White papule, reticular, plaque-type lesions, gray-white lines radiating from the papules
2. Presence of a reticular pattern
3. Appearance of atrophic lesions with or without erosion and bullae.

Histopathological diagnostic criteria

1. Thickened ortho- or para-keratinized layer in normally keratinized sites, and thin keratinized layer in nonkeratinized site [Figure 1]
2. Presence of Civatte body in the basal layer, epithelium, and superficial part of the connective tissue [Figure 2]
3. Presence of a band-like area of lymphocyte infiltration in the superficial part of the connective tissue
4. Signs of liquefaction degeneration in the basal cell layer.^[15]

The Modified WHO classification is as follows:

Clinical diagnostic criteria

1. Bilateral and symmetrical lesions
2. Manifestations of reticular, erosive, atrophic, bullous, and plaque-type lesions.

Histopathological diagnostic criteria

1. Presence of a band-like area of lymphocyte infiltration in the superficial part of the connective tissue
2. Signs of liquefaction degeneration in the basal cell layer [Figure 3].
3. Absence of epithelial dysplasia.^[10]

Therefore, due to the presence of these contradictions and the importance of diagnosing this disease, the current study

was conducted to investigate the histopathology of OLP samples in the archives (2006–2017) of the Department of Oral and Maxillofacial Pathology, Faculty of Dentistry, the Islamic Azad University of Tehran based on WHO and Mod.WHO using two methods of intraobserver and interobserver observations to verify the diagnostic accuracy of the criteria and the correlation between the two classification systems. Although clinical features can really help us for diagnosis of lichen planus but the correlation between the histopathological criteria, of these two classification systems, is further useful for diagnosis and differentiating lichen planus from diseases such as lichenoid drug reaction, contact lichenoid hypersensitivity reaction “lupus erythematosus”, “chronic ulcerative stomatitis with a similar clinical picture”.^[16]

Methods

Study design and sample

This was a cross-sectional study which was conducted on samples that were collected before, and they had a confirmed diagnosis of OLP. The diagnoses were made and confirmed based on both clinical and histopathological features. Other similar lesions were ruled out by same features. All samples were entered in the study anonymously from the archives of the Department of Oral and Maxillofacial Pathology, Faculty of Dentistry, Islamic Azad University of Tehran ($n = 64$). The study protocol was approved by research council of Islamic Azad University of Tehran (Code: 25612). We just used old archived paraffin blocks without any clinical information about the patient. And on the first day of acceptance of the samples, patients' consent to use blocks prepared in research articles was obtained. Consequently, consent has not been used again in this article.

Procedures

Intraobserver variability: Three pathologists examined all slides independently. They first evaluated all slides with histopathologic diagnostic criteria of the WHO system and recorded their diagnosis based on slide numbers, which was made by the first author in a form. Slide number sequence was changed later by the principal investigator. Pathologists examined the slides again using the mod. WHO system. The detected positive and negative cases by each pathologist were recorded separately.

Interobserver variability: Two months after the first examination as a washout period, in the second phase of the study, three pathologists as a group (as interobserver) reevaluated microscopic slides, based on both WHO and Mod.WHO classification systems.^[13-14,17] They first evaluated all slides by WHO classification system. Then, after a change in the sequence of slides by the principal researcher, they evaluated them by Mod.WHO classification systems again. Slides which were diagnosed as positive or negative by all three pathologists also were recorded.

Statistical analysis

Statistical analysis was conducted using SPSS 16. Cohen’s Kappa coefficient was used to measure the agreement between two classification methods. Firstly, Cohen’s Kappa coefficient was calculated for each pathologist separately (intraobserver variability). Later, it was calculated for cumulative diagnosis as interobserver variability. The Kappa coefficients were interpreted as follows: values ≤ 0 as indicating no agreement and 0.01–0.20 as none to slight, 0.21–0.40 as fair, 0.41–0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1.00 as almost perfect agreement.^[17]

Results

The results indicated: As outlined in Table 1, out of 64 samples, the lichen planus was detected in 8 cases using the WHO method, and in 41 cases using the Mod.WHO method. The findings showed no reproducibility between WHO and Mod.WHO ($\kappa = 0.148$) and no correlation between the two systems. On the other hand, according to Table 1 displaying the cumulative Kappa coefficient values for different observers, it was determined that none of these two classification systems had expertise dependence design.

A statistical analysis revealed that 100% of cases diagnosed with OLP, according to the WHO classification system, was confirmed also by the Mod.WHO classification system. However, 33 (58.9%) out of the 56 samples undiagnosed with OLP by the WHO system was detected with OLP using Mod.WHO system. On the other hand, only 8 (19.5%) out of 41 samples diagnosed with OLP by the Mod.WHO system was detected with OLP using the WHO method. However, 100% of cases undiagnosed with OLP by the Mod.WHO method was also undiagnosed by the WHO system. Thus, it can be highlighted that the histopathologic criteria of the WHO classification are more sensitive to the microscopic diagnosis of the Lichen planus however, the Mod.WHO classification criteria are more specific for diagnosis of the Lichen planus.

Discussion

Attained results showed the absence of correlation between the two, WHO and Mod.WHO classification systems. Considering the poor Kappa coefficient obtained in these

two systems, it can be concluded that the histopathological criteria of these two classification systems are subjective and the use of these criteria alone is not effective for the diagnosis of lichen planus.

Despite the fact that the subject matter of the research has special diagnostic importance, no extensive studies have been carried out in this context and limited studies have been conducted to examine the clinical and histopathological criteria of the diagnostic systems used in the diagnosis of lichen planus. On the other hand, our research is the first study to compare both classification systems in the diagnosis of lichen planus.

Van der Meij *et al.* in 1999,^[18] examined the interobserver and intraobserver variability in the histologic assessment of OLP based on the WHO classification system. They found that interobserver agreement varied from poor-to-moderate, consistent with our findings. However, they used only the diagnostic criteria of the WHO classification system and no comparison was made between WHO and Mod.WHO classification systems.

Van der Meij *et al.* in 2002,^[8] examined inter-observer and intra-observer observations in the clinical diagnosis of OLP based on the WHO classification system. After observing the clinical images of the lesions from 60 patients according to the criteria in the system, the interobserver opinion (0.62–0.92) was acceptable to good. Comparing the results with the previous study of these researchers showed that although the clinical criteria of the WHO method for the diagnosis of OLP are more reproducible than histopathological criteria, there is still a significant degree of subjectivity in the use of this definition.

Rad *et al.* in 2009,^[13] examined the correlation between clinical and histopathological criteria for the Mod.WHO classification system in comparison with the WHO classification system and concluded that there is a higher clinicohistopathological correlation in the Mod.WHO system compared to the WHO system, inconsistent with our study so that we saw the absence of correlation between the two systems.

It should be noted that we did not use the clinical criteria in the diagnosis of lichen planus and employed only

Table 1: Frequency distribution of data obtained from observers based on classification systems

Observers	Lesion detection (Code 1: Presence of Lichen Planus, Code 2: Absence of Lichen Plan)	WHO system Frequency (%)	Mod.WHO system Frequency (%)	Total (%)	Cohen’s kappa coefficient (κ)
Observer 1	1	42 (65.6%)	26 (40.6%)	64 (100%)	$\kappa = 0.114, P=0.299$
	2	22 (34.4%)	38 (59.4%)		
Observer 2	1	13 (20.31%)	46 (71.9%)	64 (100%)	$\kappa = 0.181, P=0.012$
	2	51 (79.7%)	18 (28.1%)		
Observer 3	1	18 (28.1%)	49 (76.6%)	64 (100%)	$\kappa = 0.062, P=0.424$
	2	46 (71.9%)	15 (23.4%)		
Cumulative	1	8 (12.5%)	41 (64.06%)	64 (100%)	$\kappa = 0.148, P=0.024$
	2	56 (87.5%)	23 (35.9%)		

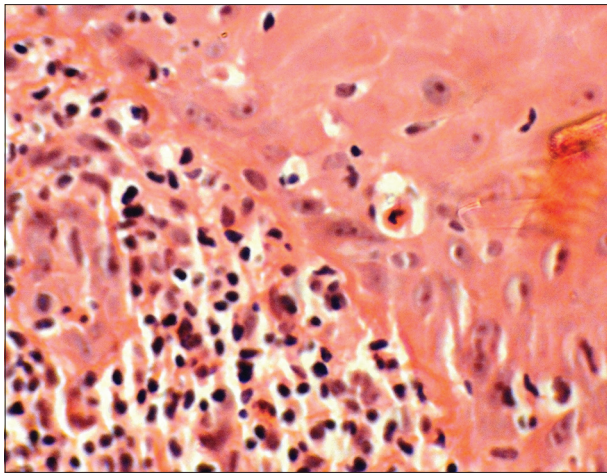


Figure 1: Civatte body formation in OLP under ×400 magnification

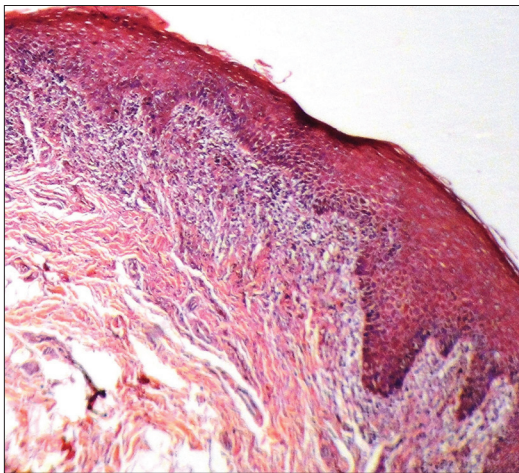


Figure 2: Band like infiltration of chronic inflammatory cells under ×200 magnification

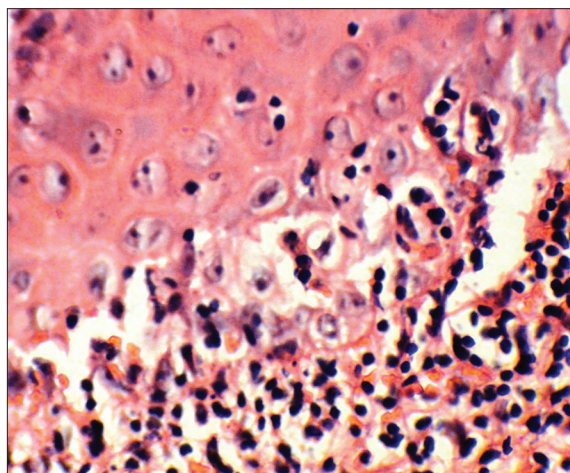


Figure 3: Basal cell degeneration

histopathological criteria to examine the correlation and the reproducibility of the criteria; this could be a reason for the inconsistency of the results of these two studies. It can also be assumed that the clinical criteria for the

diagnosis of this lesion are more objective and have higher reproducibility in the diagnosis of lichen planus. In line with our study, van der Waal *et al.* in 2009,^[19] investigated oral lichen planus and oral lichenoid lesions and reported that there are several oral lesions that are clinically and histopathologically indistinguishable from OLP but have a certain etiology, and sometimes it is difficult to distinguish them from each other but not impossible. Given that the histopathological diagnostic criteria of the existing lichen planus have no true reproducibility; it is impossible to detect the lichen planus only by this method.

One of the limitations of our study is that there were not negative cases to differentiate between the two classifications. All blocks used were Lichen planus selected by a third person. And the fellow pathologists in the project were unaware of this and thought it was white lesions in general.

Conclusions

This study demonstrated that not only was there a lack of correlation between the two histopathological criteria, but also none of them allowed for definitive diagnosis. Therefore, the clinical presentation is paramount and the histologic evaluation, although not definitively diagnostic, presents supportive diagnostic data. However, it should be noted that this diagnostic support will be more accurate using the histopathologic criteria of the Mod.WHO. In addition, it was determined that none of these two classification systems had expertise dependence design, so for precise diagnosis of lichen planus, would be better integrating the opinions of specialists and holding calibration workshops to harmonize their views and to specify criteria with greater certainty and reproducibility.

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Conflicts of interest

There are no conflicts of interest.

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