Correlation between clinical and pathologic diagnoses in mucocutaneous biopsies: A 10-year retrospective study, Kerman, Iran

Marzieh Karimi-Afshar DDS, MSc1, Bahareh Ravanbakhsh DDS2, Molook Torabi DDS, MSc3, Ali Taheri DDS, MSc4

Abstract

BACKGROUND AND AIM: Mucosal lesions are in several diseases, such as mucocutaneous disorders. Diagnosis of these lesions is based on background/history, clinical features, and histopathological examination. This study aimed to evaluate the correlation between clinical and pathologic diagnoses in mucocutaneous biopsies during a ten-year period.

METHODS: Based on the existing data, this descriptive, analytical, and retrospective study was carried out on the archives of the pathology departments of School of Dentistry of Kerman University of Medical Sciences and Afzalipour Therapeutic Training Hospital, Kerman, Iran, during March 2008-March 2018. Data were collected using a checklist including the clinical and histopathologic diagnoses of mucosal skin lesions and patients’ demographic characteristics, and were analyzed in SPSS software.

RESULTS: In this study, 650 cases of skin lesions were detected with a conclusive microscopic diagnosis. The lichen planus (LP) with 346 cases (53.23%) and discoid lupus erythematosus (DLE) with 138 cases (23.23%) were the most common lesions, whereas the least cases were related to psoriasis (0.03%). Moreover, buccal mucosa was the most frequent location of lesions, and the prevalence of lesions was significantly higher in female patients, compared to male patients. Furthermore, the most conformity between clinical and histopathologic diagnoses was related to LP. In this regard, the Kappa coefficient as the rate of overall conformity with the histopathologic diagnosis was estimated at 0.542.

CONCLUSION: The conformity between the clinical and the histopathologic diagnoses was within the acceptable range. However, it is recommended that the accurate clinical information of patients be completed to make the correct diagnosis.

KEYWORDS: Mucocutaneous Lesions; Clinical Laboratory Techniques; Oral; Histopathology


found in different patients, including those with mucocutaneous disorders, mucocutaneous lesions are diagnosed based on history, clinical features, and histopathologic findings.1 In this regard, oral lichen planus (OLP), discoid lupus erythematosus (DLE), pemphigus vulgaris (PV), mucous membrane pemphigoid (MMP), and erythema multiforme (EM) are an immune-mediated group of mucocutaneous lesions, clinically observed with the formation of blisters, erosion, or ulcers. In this disease, oral mucosa is often affected, and sometimes, the disease is limited to the mouth.2 Oral manifestations have been reported in more than 90%, 50%-90%, 8%-39%, 20%-60%, 20%, 23%-70%, and 33%-80% of MMP, PV, bullous pemphigoid, OLP, lupus erythematosus, EM,
and lichenoid reactions (LRs), respectively.\textsuperscript{3,4} The prevalence of OLP has been reported as 65.3\%, 62.6\%, and 73.3\% in Isfahan, Mashhad, and Babol Cities, Iran, respectively.\textsuperscript{5-7} The World Health Organization (WHO) describes OLP as a potentially malignant lesion. While the risk of conversion of this lesion into carcinoma is lower, compared to other potentially malignant lesions, patients with this disease should be monitored at short intervals.\textsuperscript{8,9} The most common and severe type of pemphigus is PV initiated with oral lesions and followed by skin lesions.\textsuperscript{10} There is limited epidemiological information of pemphigus. According to reports, the global index of this condition is 0.75-14 cases per 100000 people annually, depending on location. However, it seems that pemphigus is more prevalent in countries lower than the latitude.\textsuperscript{11,12}

The prevalence of pemphigus in Babol and Mashhad has been reported as 14.7\% (in the form of mucocutaneous lesions) and 21.8\% (in the form of skin lesions), respectively.\textsuperscript{6,7} Emerged by the formation of sub-epithelial blisters, MMP is a chronic autoimmune disease that involves the oral mucosa and sometimes the skin.\textsuperscript{13,14} In another study by Sultan et al., the frequency of MMP and PV was reported to be 46\% (n = 26) and 54\% (n = 31), respectively.\textsuperscript{15} EM is a blistering skin lesion, etiopathogenesis of which is unknown. It is an immune-mediated process, even though its cause is not clearly understood.\textsuperscript{4} In a research, oral lesions were reported in 40\% of patients with lupus, and the disease has radial delicate white lines, which is similar to erosive lichen planus (ELP).\textsuperscript{4} Clinical and histopathological diagnoses coincide in 42.9\% of patients with oral lichenoid lesions (OLL) and 52.2\% of patients with OLP.\textsuperscript{16} In a study about clinicopathologic correlation of white non-scrapable oral mucosal surface lesions by Abidullah et al., 78\% of cases correlated with the histopathological diagnosis and 22\% did not correlate.\textsuperscript{17}

Mucocutaneous lesions have various complications and manifestations and their timely diagnosis plays an important role in the decrease of pain and disability and lower drug dose. Given that sometimes, the first signs of disease are found in the mouth, timely identification of lesions by a dentist is crucial. With regard to the lack of similar research on this topic in Kerman, Iran, the present study aimed to evaluate the prevalence of mucocutaneous lesions and their level of clinicopathologic adaptation in the pathology departments of School of Dentistry, Kerman University of Medical Sciences, Kerman, and Afzalipour Teaching Hospital, which is a skin lesion referral center in Kerman.

### Methods
This descriptive, analytical, and retrospective study was performed on records existing in the Department of Maxillofacial Pathology of School of Dentistry, Kerman University of Medical Sciences and the Pathology Department of Afzalipour Hospital during March 2008-March 2018. Clinical diagnoses were established by dermatologists and oral medicine specialist, that for histopathologic evaluation referred to pathology departments of Afzalipour Hospital and Kerman School of Dentistry. In this regard, a trained senior student evaluated the archive of the department and separated all lesions reported in the clinical features of mucocutaneous lesions. The findings extracted were then entered into a checklist, including clinical diagnosis, histopathologic diagnosis, lesions’ location, reference place (hospital or dental school), and demographic characteristics of patients including gender and age. The cases with histopathologic diagnosis written descriptively (even though clinical mucocutaneous lesions do not have a definitive microscopic diagnosis) were re-examined and were excluded from the study in case of lack of definitive histopathologic diagnosis. Data analysis was performed using t-test (to compare the mean age of lesions in men and women), chi-square test (to compare lesions’ frequency in men and women), and Kappa coefficient via SPSS.
software (version 21, IBM Corporation, Armonk, NY, USA). In addition, P-value of 0.05 was considered statistically significant. The project was approved by the Ethics Committee of Kerman University of Medical Sciences with the code of IR.KMU.REC.1396.2293.

### Results

In this research, 638 mucocutaneous lesions with the definitive microscopic diagnosis were observed. Lichen planus (LP) in 346 cases (53.23%) and DLE in 138 cases (21.20%) were the most frequent types observed in the samples. In this regard, the results are shown in figure 1 based on the type of lesion.

![Figure 1. Frequency of lesions based on histopathologic diagnosis](image)

The level of correlation between clinical and histopathologic diagnoses of various lesions is shown in table 1.

### Table 1. Correlation between clinical and histopathologic diagnoses according to type of lesions

<table>
<thead>
<tr>
<th>Lesions</th>
<th>Clinical diagnosis correlation with histopathology</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes [n (%)]</td>
</tr>
<tr>
<td>LP</td>
<td>290 (83.8)</td>
</tr>
<tr>
<td>PV</td>
<td>25 (83.3)</td>
</tr>
<tr>
<td>Benign MMP</td>
<td>4 (50.0)</td>
</tr>
<tr>
<td>Lupus erythematos</td>
<td>100 (67.7)</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>1 (50.0)</td>
</tr>
<tr>
<td>LR</td>
<td>28 (41.2)</td>
</tr>
</tbody>
</table>

LP: Lichen planus; PV: Pemphigus vulgaris; MMP: Mucous membrane pemphigoid; LR: Lichenoid reaction

In this respect, the highest correlation was observed in the diagnosis of LP (83.8%), whereas the lowest correlation was found in LR (41.2%).

In the current study, the mean age of the subjects was 16.06 ± 40.66 years, and lesions were found in 36.9% of male and 63.7% of female patients. Buccal mucosa was the most common place for lesions. The mean and standard deviation (SD) and age range of mucocutaneous lesions are shown in table 2.

As observed, the mean age of patients with benign mucosal pemphigus was higher, compared to other lesions. In addition, the most frequent location for lesions was buccal mucosa, and the most common involved organ in SLE was the kidney. According to the results, there was a significant difference between the frequency of mucocutaneous lesions and gender.

### Table 2. Frequency, age range, mean, and standard deviation (SD) according to type of lesions

<table>
<thead>
<tr>
<th>Lesions</th>
<th>Gender</th>
<th>Age range (year)</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men (%)</td>
<td>Women (%)</td>
<td></td>
</tr>
<tr>
<td>LP</td>
<td>39.3</td>
<td>60.7</td>
<td>6-87</td>
</tr>
<tr>
<td>PV</td>
<td>36.9</td>
<td>62.5</td>
<td>24-66</td>
</tr>
<tr>
<td>Benign mucosal pemphigoid</td>
<td>37.5</td>
<td>62.5</td>
<td>26-78</td>
</tr>
<tr>
<td>EM</td>
<td>25.8</td>
<td>74.2</td>
<td>1-77</td>
</tr>
<tr>
<td>Psoriasis</td>
<td>100</td>
<td>0</td>
<td>16-48</td>
</tr>
<tr>
<td>LR</td>
<td>26.5</td>
<td>73.5</td>
<td>6-81</td>
</tr>
<tr>
<td>DLE</td>
<td>41.3</td>
<td>58.7</td>
<td>14-61</td>
</tr>
<tr>
<td>SLE</td>
<td>13.3</td>
<td>86.7</td>
<td>1-80</td>
</tr>
</tbody>
</table>

LP: Lichen planus; PV: Pemphigus vulgaris; EM: Erythema multiforme; LR: Lichenoid reaction; DLE: Discoid lupus erythematosus; SLE: Systemic lupus erythematosus; SD: Standard deviation
Discussion

In the present study, the most prevalent type of mucocutaneous lesions was LP found in 53.23% of the cases. In a research by do Carmo et al.,\textsuperscript{18} on immune-mediated lesions, 250 of 301 lesion cases were LP, which is consistent with our findings. Our findings are also in line with the results obtained by Shirinbak et al.,\textsuperscript{19} Goncalves et al.,\textsuperscript{20} and Changiz et al.\textsuperscript{6} In the present research, the frequency of LP was higher in female patients, compared to male individuals, which is not in accordance with the results obtained by Rameshkumar et al.\textsuperscript{1} and Munde et al.,\textsuperscript{21} but is consistent with the results obtained by Goncalves et al.\textsuperscript{20} and Changiz et al.\textsuperscript{6} OLP is a mucocutaneous lesion identified with the chronic inflammation process. According to WHO, this disease is a potentially acute lesion, and patients with OLP must be monitored at short intervals, even though there is a lower risk of conversion of the condition into the acute state, compared to other lesions.\textsuperscript{8,9}

In the current research, the mean age of patients with LP was 40.94 years, whereas the mean age of the subjects in the study by Changiz et al.\textsuperscript{6} was 44.85 years, which shows a relative consistence in this regard. In addition, our findings showed that the age range of patients with LP was 6-87 years, which is in congruence with the results obtained by Goncalves et al.\textsuperscript{20} who reported the age range of relevant patients to be 5-88 years. In addition, our findings demonstrated that there was an 83.8% correlation between the clinical and microscopic diagnosis of LP, which is in line with the results obtained by Changiz et al.\textsuperscript{6} In a study by Forouzande et al.,\textsuperscript{22} a good correlation (74.3%) was reported in this respect.\textsuperscript{22} Shirinbak et al. reported the correlation between clinical and histopathologic diagnoses of LP as 42.3%,\textsuperscript{19} which is lower than our findings.

In the current research, the LR involved 11.23% of the mucocutaneous lesions, and the mean age of individuals with LR was 44.01 years. Moreover, 73.5% of the cases with this condition were women. In this context, our findings are in congruence with the results obtained by Changiz et al.,\textsuperscript{6} who reported that 66.7% of the cases were women and the mean age of the patients was 37.13 years. Furthermore, the percentage of clinical and microscopic diagnosis of the LR was 41.2% in the current research. Of 55 lesion cases assessed by Shirinbak et al.,\textsuperscript{19} seven cases were LRs and the correlation percentage of clinical diagnosis was 85.7%, which is higher compared to our findings. This lack of consistency between the results might be related to the similarity of clinical features of LR with LP. Therefore, clinicians should pay more attention to patients’ medical history, drug use, and mucosal contact with restorative materials.

In the present study, PV included 4.61% (30 cases) of the lesions. There were 18 pemphigus cases in the research by Shirinbak et al.,\textsuperscript{19} whereas Changiz et al.\textsuperscript{6} reported 22 cases of PV. In a research by Pires et al.\textsuperscript{10} in Brazil, 12 cases of PV were observed in eight years. On the other hand, Sultan et al.\textsuperscript{15} reported 31 cases of PV, which is in line with our findings. Moreover, Chowdhury et al.\textsuperscript{23} reported 32 cases of PV.

While research methods slightly varied, the prevalence of this disorder seems to be relatively similar in various studies. In the present study, the percentage of referral of patients with pemphigus to the dental school was higher, compared to other studies, which might be due to the fact that the first sign of PV is oral lesions. In addition, pemphigus was more prevalent in female patients of the current research, which is consistent with the results obtained by Changiz et al.\textsuperscript{6} In addition, our findings revealed that the mean age of the patients with pemphigus was 45.07 years, which was similar to the results obtained by Chowdhury et al.\textsuperscript{23} Changiz et al. reported the mean age of the subjects to be 40.55 years.\textsuperscript{6}

In the current research, the conformity of clinical diagnosis with histopathology of pemphigus was estimated at 83.3%, while Changiz et al.\textsuperscript{6} and Forouzande et al.\textsuperscript{22} reported this value at 68.2% and 88.2%,
respectively. On the other hand, Hoseinpour Jajarm and Mohtasham\textsuperscript{24} reported the lowest level of conformity of clinical and histopathologic diagnoses of pemphigus. The high diagnostic concordance regarding pemphigus can be due to the initial oral presentation and classic and apparent clinical specifications of lesions of this disease. Manifestation of the disease includes thin-walled blisters that appear in apparently healthy skin and mucosa, which are rapidly ruptured and spread around and ultimately present in the form of irregular, wide, and diffuse erosions that can be gradually healed. In addition, clinical diagnostic methods (Nikolsky’s sign) and laboratory tests (e.g., immunofluorescence) can help identify pemphigus.\textsuperscript{3,4,25}

In the present research, 21.23\% of the lesions were DLE, all of which were evaluated in a hospital and were more prevalent in women. In this respect, the conformity of clinical and histopathologic diagnoses of the disease was 65.2\%. In the research by Changiz et al.,\textsuperscript{6} only one case of DLE was detected, which was not clinically diagnosed. Our findings revealed that 26.22\% of the cases had lupus lesions, and DLE had the highest prevalence. Moreover, lupus frequency was reported at 33\% by Goncalves et al.\textsuperscript{20} Given the lack of separation of lupus in terms of type, we cannot compare our results with other studies in this regard. In the current research, the rate of lupus was higher in female patients.

In the present study, systemic lupus erythematous (SLE) included 2.3\% of all lesions, and the most involved body organ was the kidney. In addition, this condition was more prevalent in women. In a systematic review, the incidence and prevalence of systemic lupus were reported at 23.2 per 100000 individuals and 24.1 per 100000 people, respectively, in North America.\textsuperscript{26} Similarly, the rate of the disease was higher in women. The results were also indicative of the different prevalence of the disease in various societies. Therefore, more research is required to evaluate genetic and environmental factors in this regard. In the present research, 1.2\% of the lesions were benign mucosal pemphigus, which was more observed in women. The mean age of these patients was 50 years. In this context, our findings are consistent with the results obtained by Changiz et al.,\textsuperscript{6} where 1.3\% of the lesions were benign mucosal pemphigus, which was lower than PV and had a higher prevalence in female patients. Moreover, Sultan et al.\textsuperscript{15} reported that the prevalence of benign mucosal pemphigus was lower, compared to PV. In the current study, the percentage of conformity of clinical and microscopic diagnosis of benign mucosal pemphigus was 50\%. This rate was reported to be 33.3\% in the study by Forouzande et al.,\textsuperscript{22} which was lower than the present research. Furthermore, two cases of psoriasis were observed in the current study, both of them were men and in the hospital. In a research by Babu et al.\textsuperscript{27} in India, 21 cases of 65 patients had psoriasis lesions. According to the results of the present research, the prevalence of mucocutaneous lesions was significantly higher in women, compared to men, which is in congruence with the results obtained by Shirinbak et al.,\textsuperscript{19} Deyhimi and Ferdowsi,\textsuperscript{28} and Changiz et al.\textsuperscript{6}

In the present research, the level of conformity of clinical and histopathologic diagnoses of mucocutaneous lesions was estimated at Kapa coefficient of 0.542, which was higher, compared to the study by Shirinbak et al.\textsuperscript{19} (0.480). Given the fact that the mentioned coefficient was in the range of 0.4-0.6, it seems that the conformity of clinical and histopathologic diagnoses was acceptable. In this regard, the conformity percentage was 62.25\% in the current research. The mentioned variable was estimated at 77.6\%, 88.0\%, and 77.1\% in studies by Ghasemi Moridani et al.,\textsuperscript{29} Changiz et al.,\textsuperscript{6} and Shiva and Sobouti.\textsuperscript{30} This lack of consistency between the results might be related to sample size and lesions assessed in the studies. One of the major drawbacks of
this study was incomplete medical files of patients. The exact location of the biopsy, the patient's age, and clinical signs of the lesion, including the precise form and description of the lesion, the number, duration of the creation, and the accompanying oral and skin lesions can help in the correct diagnosis of the disease and selecting an appropriate treatment for the patient.

Conclusion
According to the results of the present research, LP was the most frequent lesion, and the frequency of mucocutaneous lesions was significantly higher in women. The conformity between the clinical and histopathologic diagnoses was estimated at 0.542, which was within the acceptable range. It is suggested that the medical records of patients be completed to establish an accurate diagnosis.

Conflict of Interest
Authors have no conflict of interest.

Acknowledgments
The authors, hereby, would like to thank the Research Deputy of Kerman University of Medical Sciences for approval and financial support of this project (#9600855).

References