Accuracy of leukoplakia diagnoses: a retrospective study

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The objective of this study was to review the diagnostic accuracy of clinicians identifying leukoplakia and the diagnostic terminology used to indicate leukoplakic lesions at the University of Nebraska Medical Center (UNMC) oral biopsy service. Biopsy archives from the years 1983, 1995, 2005, and 2015 in the UNMC College of Dentistry were reviewed. Cases with a clinical diagnosis of leukoplakia (or white plaque), hyperkeratosis, dysplasia, and/or carcinoma were included in the study. Demographic and clinical information was recorded and descriptive statistics were utilized. Of 6113 cases, 517 lesions (8.46%) from 508 patients met the inclusion criteria. The mean age of the patients was 56.87 years, and the sample included 286 men and 222 women. Of these 517 lesions, 195 (37.72%) were clinically diagnosed as leukoplakia or white plaque. The records revealed that 133 (68.21%) of 195 clinical diagnoses were correct, with lesions histologically exhibiting hyperkeratosis (75 cases), dysplasia (52 cases), or carcinoma (6 cases). The remaining 62 lesions (31.79%) were found to have other histologic diagnoses. Hyperkeratosis made up the largest portion of the correct diagnoses. In general, the ability of clinicians to successfully identify leukoplakia improved over the years (46.15%, 73.68%, 64.29%, and 76.00% in 1983, 1995, 2005, and 2015, respectively). However, clinicians continue to misclassify identifiable pathoses such as lichen planus, lichenoid mucositis, and fibroma as leukoplakia. *Hyperkeratosis* and *dysplasia,* both of which represent histologic diagnoses, appear to be popularly misused clinical terms.

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For decades, clinicians have been classifying white plaques in the oral cavity using the medical term *leukoplakia*, which dates back to the late 1800s and has become widely used in both the medical and dental fields. Are professionals using this term correctly, or has it become an overused diagnosis? According to Regezi et al, "*Leukoplakia* is a descriptive clinical term indicating a white patch or plaque of oral mucosa that cannot be rubbed off and cannot be characterized clinically as any other disease."[1] Thus, by definition, lichen planus, candidiasis, and frictional keratosis should not be identified as leukoplakia. Strictly a clinical term, leukoplakia may vary from benign hyperkeratosis to dysplasia to squamous cell carcinoma when identified microscopically.[1]

This information signifies that not all white plaques should receive the same label. It is a practitioner's duty to gather evidence, including but not limited to clinical presentation, patient demographics, and social history, in order to develop a proper differential diagnosis and associated treatment plan. Relevant social history for the development of white plaques may include smoking, smokeless tobacco use, or parafunctional habits, to name a few.[2]

The present study was conducted to bridge the gap in knowledge in the accuracy of diagnosis of oral leukoplakia and the terms used by dentists to designate leukoplakia. Therefore, this study was designed to review the biopsy archives of the University of Nebraska Medical Center (UNMC) College of Dentistry to determine the clinical diagnostic accuracy of clinicians identifying leukoplakia and evaluate improvement over the last 4 decades, with the hypothesis that there would be a positive trend in the accuracy of leukoplakia as a clinical diagnosis over the years. The secondary objective was to identify the clinical terms used to describe leukoplakia by dentists, serving to highlight the importance of differentiating leukoplakia from other white pathoses.

Methods

This retrospective study included archival material from the UNMC Biopsy Service and was conducted following an expedited UNMC IRB (519-19-EX). Data were gathered from the years 1983, 1995, 2005, and 2015. The inclusion criteria included a clinical diagnosis of leukoplakia (or white plaque), hyperkeratosis, or dysplasia, either alone or in combination. Cases with a diagnosis of carcinoma when used in combination with leukoplakia, hyperkeratosis, or dysplasia were included in the study.

The demographic and clinical information of the cases meeting the inclusion criteria and the histologic diagnoses were recorded in Excel spreadsheets (Microsoft). Descriptive statistics were utilized to analyze the data.

Table 1. Demographics of patients (N = 508) and most common location of lesions included in the study (N = 517).

Year	Women, n	Men, n	Mean age, y	Most common location
1983	22	27	55.19	Buccal mucosa
1995	48	77	55.64	Gingiva
2005	55	73	55.92	Tongue
2015	97	109	58.58	Tongue
Total	222	286	56.87	Tongue

Included cases had a clinical diagnosis of leukoplakia (or white plaque), hyperkeratosis, and/or dysplasia. Cases with a diagnosis of carcinoma were included in the study when the term was used in combination with leukoplakia, hyperkeratosis, or dysplasia.

Table 2. Demographics of patients (n = 192) and most common location of lesions with a clinical diagnosis of leukoplakia (n = 195).

Year	Women, n	Men, n	Mean age, y	Most common location
1983	11	14	56.68	Buccal mucosa
1995	14	24	58.63	Buccal mucosa and tongue
2005	22	34	53.20	Buccal mucosa
2015	32	41	60.37	Tongue
Total	79	113	57.45	Tongue

Results

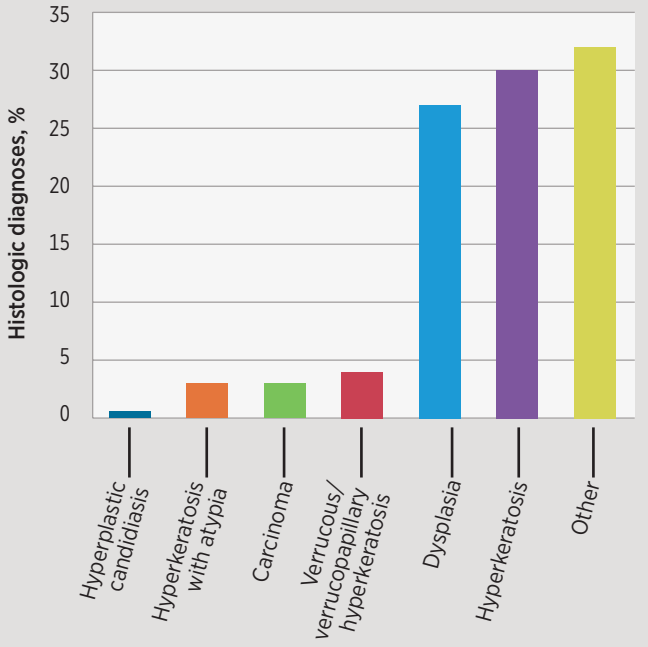
Of the 6113 records within the UNMC biopsy database from the 4 studied years, 517 lesions (8.47%) from a total of 508 patients matched the inclusion criteria. The mean age of the patients was 56.87 years, and the sample included a total of 286 men and 222 women (Table 1). Nine lesions were biopsied from more than 1 location in the patient and were included in the analysis.

The 517 clinical diagnoses included in the study comprised 195 lesions classified as leukoplakia (or white plaque), and 322 lesions classified as hyperkeratosis, dysplasia, or carcinoma. Of the 195 lesions with a clinical diagnosis of leukoplakia (37.72%), 133 (68.21%) were deemed correct, histologically exhibiting hyperkeratosis (75 cases), dysplasia (52 cases), or carcinoma (6 cases). Table 2 shows the demographic information of the patients and the most common location of the lesion for these 195 cases. Hyperkeratosis made up the largest portion of the correct diagnoses, including hyperkeratosis with atypia, hyperplastic candidiasis, and verrucous patterns. Of the 195 lesions clinically identified as leukoplakia, 62 (31.79%) did not match the histologic criteria and were diagnosed as other conditions (Chart 1).

Of the 322 lesions with a clinical diagnosis of hyperkeratosis, dysplasia, or carcinoma, the histologic evaluation confirmed 125 as hyperkeratosis, 83 as dysplasia, and 13 as carcinoma, while 101 (31.37%) were diagnosed as other conditions.

In 1983, incorrect diagnoses of leukoplakia outnumbered correct diagnoses (Chart 2). However, the relative numbers of correct diagnoses increased in 1995, 2005, and 2015.

Chart 1. Histologic diagnoses of lesions with a clinical diagnosis of leukoplakia (n = 195).



Discussion

As previously addressed, *leukoplakia* is a strictly clinical term and is used as a diagnosis of exclusion.[3] Biopsy and histologic examination are the gold standards for diagnosis and treatment of these white plaques. *Hyperkeratosis* and *dysplasia*, histologic diagnostic terms, appear to be misused clinically. These terms were applied in the majority of clinical diagnoses (322 of 517 lesions; 62.28%), despite the fact that these are purely microscopic diagnoses. Lesions such as these require a more appropriate clinical diagnosis, such as leukoplakia or frictional keratosis, which can be achieved through an evaluation of lesion characteristics and patient history.

This study also found that the number of clinical diagnoses of carcinoma and dysplasia increased over the 4 years studied, from just 1 in 1983 to 16 in 1995, 18 in 2005, and 71 in 2015. Of the 322 biopsies submitted with clinical diagnoses of hyperkeratosis, dysplasia, or carcinoma, 125 (38.82%) cases were microscopically diagnosed as hyperkeratosis, while 83 (25.78%) cases showed histologic signs of dysplasia, and 13 (4.04%) cases were diagnosed as squamous cell carcinoma. Earlier studies have found that malignant transformation is present in 5% to 36% of leukoplakic lesions.[4] In the present study, 135 of 517 lesions (26.11%) with a clinical diagnosis of leukoplakia, hyperkeratosis, or dysplasia were histologically dysplastic, while 19 lesions (3.68%) showed squamous cell carcinoma.

Chart 2. Clinical accuracy of clinicians in identifying true leukoplakia in the years studied.

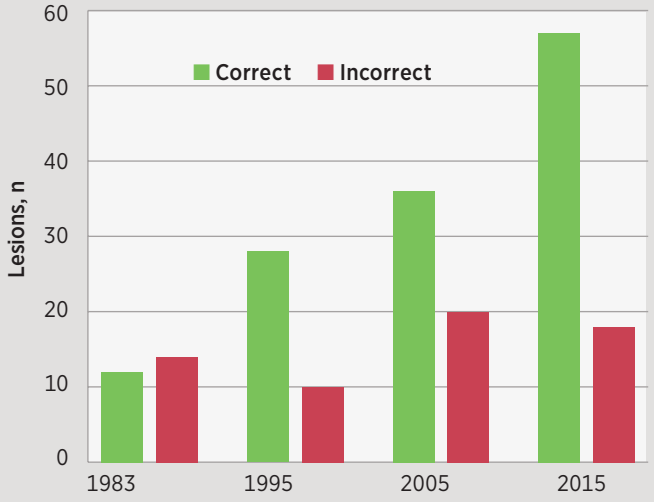
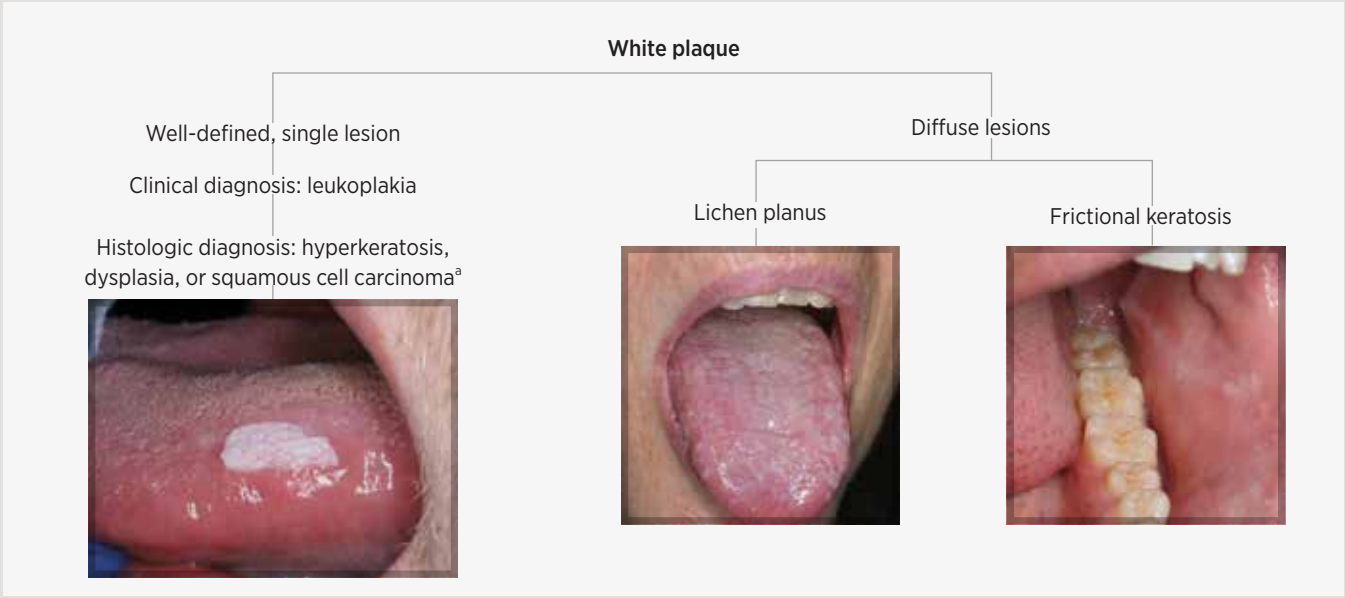


Chart 3. Differential diagnosis of oral white plaques that cannot be rubbed off.



[a]The lesion shown is hyperkeratosis.

In general, clinicians' ability to successfully identify leukoplakia has improved over the years, as 46.15%, 73.68%, 64.29%, and 76.00% of clinical diagnoses were confirmed histologically in 1983, 1995, 2005, and 2015, respectively. This improvement could be due to several factors, including increased focus on oral pathology courses within both undergraduate and graduate level education, increased availability of oral pathology–related continuing education, and a more precise and exclusive definition of leukoplakia. However, clinicians continue to classify identifiable pathoses, such as lichen planus, lichenoid mucositis, and fibroma, as leukoplakia.

Clinicians can better diagnose white plaques based on clinical presentation, patient demographics, social history, location, and demarcation. Lichen planus and frictional keratosis are more diffuse and poorly demarcated. Lichenoid mucositis is often painful, may be erythematous and ulcerated, and may be bilateral instead of unilateral in presentation. Fibromas are well demarcated but typically smooth and nodular in shape. Some fibromas may exhibit keratosis due to friction along the surface but should not be confused with leukoplakia, as fibromas are not premalignant. This distinction is important, particularly prior to establishing treatment plans and alternatives. Chart 3 shows a

flowchart for differential diagnosis of white plaques that cannot be rubbed off.

The mean age of the patients in the present study is consistent with the ages reported in the literature and demonstrates, as is seen in more developed countries such as the United States, that leukoplakia is more common after 40 years of age.[4] Of the total patient pool in the present study, 56.30% were men, which is also in agreement with the literature that localized leukoplakia is more common in men.[5]

The tongue was found to be the most common location of oral leukoplakia, with the buccal mucosa as an alternative location. When leukoplakia is located on the buccal mucosa, lip, or gingiva, other patient-centered conditions should be considered before a definitive clinical diagnosis is established.[6] For some of the cases histologically diagnosed as hyperkeratosis, the provided biopsy information may not have been exacting enough to rule out other diagnoses. For example, if the biopsy specimen was taken from the buccal mucosa but not labeled with the location in relation to the occlusal plane, frictional keratosis cannot be ruled out. If the patient has a habit of placing tobacco in the buccal vestibule, but this identifier is not recognized, tobacco pouch keratosis is still a viable differential diagnosis. Knowledge of the location of the lesion and the social history of the patient will lead to a more definitive diagnosis and more targeted preventive treatment. Distinction of lesions by location is also imperative in terms of potential malignant transformation because a site on the tongue or floor of the mouth is predictive of malignancy.[7]

The wide range of terms currently used to identify white lesions in the mouth can be confusing to both the practitioner and the patient. Establishing a distinct clinical diagnosis is important, particularly for treatment of symptoms, and diagnostic accuracy is highly dependent on the practitioner's capabilities. A clinician who can arrive at an educated, sound diagnosis early can ease the mind of the patient and begin appropriate treatment in a timely manner. Furthermore, a prudent dentist who consistently gathers all available evidence during an examination can better identify suspicious lesions for which immediate histologic evaluation is necessary.

Conclusion

A thorough evaluation and collection of patient information should be conducted in every dental setting before a clinical diagnosis is made. After all of the clinical data are gathered, leukoplakia should be considered as a clinical diagnosis for an idiopathic, unilateral, well-defined white plaque.

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