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A Study of Clinical Appearances, Histopathological Features, and Demographic Data in Patients with Oral Potentially Malignant Disorders

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Abstract

Background: Oral squamous cell carcinoma is the most common oral cancer. Oral potentially malignant disorders (OPMDs) can be detected before they turn into oral cancer, thus its prevalence and risk factors should be investigated.

Objectives: This research aims to study the prevalence, clinical appearances, histopathological features, and demographic data in patients with OPMDs in Faculty of dentistry, Chiang Mai University during 2017-2020, along with the relationship between dysplasia level and risk factors.

Methods: This was retrospective and analytical study. The following data were collected and analyzed according to patient's diagnosis: demographic data and behaviors, clinical appearances, and histopathological features.

Results: The mean age was 60.6±13.0 years, dominate by female (70.9%). The prevalence for each disease was as follow: leukoplakia (28.6%), erythroplakia (8.2%), lichen planus (39.7%), oral submucous fibrosis (2.2%), actinic cheilitis (3.1%), discoid lupus erythematosus (13.3%), lichenoid reaction (1.8%), and candidal leukoplakia (3.1%). Most disorders are found at buccal mucosa as white plaque or mixed red and white lesion along with burning sensation. In histopathological aspect, mild dysplasia was frequently found in all disorders except lichenoid reaction which no dysplasia was found. Fifty-nine percent of patients with smoking history were found with dysplasia while only 21% of non-smoking patients were found with dysplasia.

Conclusions: OPMDs are frequently found in elderly patients above 6th decade and mostly found in female patient. Lichen planus was the most common found among OPMDs. In this retrospective study the relationship between smoking habit and dysplasia was found. No malignancy transformation was found during the study period.

Keywords: actinic cheilitis, chronic hyperplastic candidiasis, discoid lupus erythematosus, erythroplakia, leukoplakia, lichenoid reaction, lichen planus, oral potentially malignant disorder, oral submucous fibrosis

Introduction

Oral cancer is one of the ten most common cancers found in humans worldwide, and also considered at the top five in Thailand. The most common type is squamous cell carcinoma.⁽¹⁾ Oral potentially malignant disorders (OPMDs) such as leukoplakia, erythroplakia, lichen planus, oral submucous fibrosis, palatal lesions in reverse smokers, actinic cheilitis, discoid lupus erythematosus, hereditary cancer syndromes, lichenoid reaction, and candidal leukoplakia are usually found before cancerous lesions emerge.⁽²⁾ In previous retrospective study reported 7.62% of OPMDs patient diagnosed as epithelial dysplasia had malignant transformation.⁽³⁾ Cancer risk factor such as smoking and alcohol consumption were reported to increase the prevalence of overall OPMDs and heighten the chance of dysplasia found in histopathology for each disease.⁽⁴⁻⁷⁾

Leukoplakia is an oral lesion that appears as a white plaque, which distinguishes it from every other OPMDs as well as non-OPMDs.⁽²⁾ Several risk factors can cause leukoplakia, such as smoking, but it can also occur spontaneously.⁽⁸⁾ Leukoplakia is found in males more than females^(2,9), usually at ages above 40 years, and its likelihood increases with age.^(8,10) The most common site is the buccal mucosa.^(1,11)

Leukoplakia can be clinically categorized into two types. The first is homogeneous leukoplakia, which is homogeneously white; this type is the more common. The second is non-homogeneous leukoplakia, which presents as an uneven mix of red and white.^(11,12) The histology of leukoplakia can be observed as hyperkeratosis, mild dysplasia, moderate dysplasia, through to severe dysplasia and carcinoma *in situ*.⁽⁸⁾ The most common features is hyperkeratosis.⁽¹⁾

Erythroplakia presents as a red lesion that distinguishes it from every other OPMDs and non-OPMDs lesion.^(13,14) It is usually found in patients with histories

of smoking, alcohol consumption, betel nut chewing, or tobacco chewing.⁽¹⁴⁾ It tends to occur in middle-aged to elderly male patients, and the most common sites are the soft palate, the floor of the mouth, and the ventral surface of the tongue.^(13,14)

The clinical features are a red lesion, whose surface can be smooth or rough.⁽¹⁴⁾ More than 50% of histopathological features demonstrate epithelial dysplasia.⁽¹⁵⁾ Of all dysplasia cases, 25% are mild to moderate dysplasia, 47.4% are severe dysplasia, and 27.3% are carcinoma *in situ*.⁽¹⁶⁾

Lichen planus can be a white lesion, or a mixed red and white lesion with patterns such as erythema, atrophy, and erosion together with fine white lines or dots called Wickham's striae. This lesion is commonly found in women aged above 50 years.^(17,18)

The histopathology is unique, featuring band-like lymphocytic infiltration at the connective tissue layer close to the basal lamina. Acanthosis and hyperkeratosis may be found, and liquefactive degeneration of the basal cell layer is common.⁽¹⁸⁾ The most common site for lichen planus is the buccal mucosa.⁽¹⁹⁾

Oral submucous fibrosis is characterized by submucosal fibrosis due to abnormal collagen production, resulting in rigidity and pale coloration or a marble-like lesion of the affected area.⁽²⁰⁾ Patients usually present with trismus, xerostomia, and a burning sensation.⁽²¹⁾ In severe cases, patients might have difficulty speaking, swallowing, and maintaining oral hygiene. This disease is found mostly in females aged 11-60 years, most commonly in the 45-50 age range⁽²²⁾, and its most common site is the buccal mucosa.⁽²³⁾ Oral submucosal fibrosis is strongly related to betel nut chewing.⁽²⁰⁾ The histopathology features atrophic epithelium with fibrosis in the connective tissue from collagen deposition.⁽²⁴⁾

Palatal lesions in reverse smokers, i.e., those who smoke with the lit end in the oral cavity, tend to be found

in particular regions such as India and South America. The clinical appearance can vary as a white lesion, a red lesion, or a mixed white and red lesion on the palate with ulceration.⁽²⁵⁾ Nicotinic stomatitis lesions can also be found, with hyperkeratosis of the palate, and salivary gland inflammation showing as a red dot appearance on the palate.⁽²⁶⁻²⁸⁾

Actinic cheilitis is usually found on the lower lip, resulting from long exposure to sunlight. The clinical presentation is a white lesion on the lip with a dry, rough surface like sandpaper. Patients usually feel tightness in their lips.⁽²⁹⁾

The histopathology could show atrophy or hyperplasia of squamous cells in the epithelium, dysplasia keratinocytes, and drop-shaped rete pegs but with the basement membrane remaining intact.⁽²⁹⁾

Discoid lupus erythematosus is characterized by a round skin rash with defined margins and dilated capillaries at the border.⁽³⁰⁻³²⁾ In the oral cavity, it is usually found as a round, white lesion, featuring an elevated border with white striae.^(32,33) It is commonly found on the labial mucosa, lower lip, and buccal mucosa. Several predisposing factors are reported, such as genetics, smoking, diet, and some drugs.^(30,34)

Common histopathological features are lymphocyte cell infiltration at the surrounding blood vessels, atrophic or hyperplastic epithelium, spongiosis at several layers, and diffuse inflammatory cells at the basement membrane layer and connective tissue.^(30,35)

Hereditary cancer syndromes are a group of genetic disorders with a high risk of developing oral cancer: ataxia telangiectasia, Bloom syndrome, Fanconi anemia, Li-Fraumeni syndrome, and xeroderma pigmentosum.⁽³⁶⁾

Lichenoid reactions can be divided into two subtypes: drug-induced oral lichenoid reactions and lichenoid contact lesions. The clinical appearances of these diseases are similar to lichen planus.⁽³⁷⁾

Several drugs are reported to induce oral lichenoid reactions, such as nonsteroidal anti-inflammatory drugs (NSAIDs) and angiotensin-converting enzyme inhibitors (ACEIs); the latter have the highest chance of inducing lesions.⁽³⁸⁾ Lichenoid contact lesion is commonly found as a white plaque or striae in the oral soft tissue in close contact with dental materials such as amalgam or crown restorations.^(39,40)

The histopathological features are orthokeratinized squamous epithelium with liquefactive degeneration of keratinocytes and lymphocyte infiltration at the submucosa.⁽³⁹⁾

Chronic hyperplastic candidiasis or candidal leukoplakia is a less common lesion caused by *Candida* spp. infection.⁽⁴¹⁾ Common clinical characteristics can be divided into two categories: the first is a white plaque that cannot be wiped off, usually without accompanying symptoms. The second is white nodules or speckles with a burning sensation.⁽⁴²⁾ Several risk factors exist for this lesion, such as smoking, vitamin deficiency, and immunosuppression.⁽⁴³⁾ The disease is more common in males than females, and it is usually found in ages above 50 years.⁽⁴⁴⁾ The most common site is the buccal mucosa.^(42,44)

The histopathological features are epithelial hyperplasia, dysplasia, *Candida* hyphae at superficial areas, and multinucleated white blood cells.⁽⁴⁵⁾ In some cases, *Candida* hyphae will invade the junctional area between the keratin and spinous layers.⁽⁴⁴⁾

The objective of this study was to observe and collect data from a database to identify the demographic data, clinical characteristics, symptoms and histopathological features of each OPMDs. In addition, the relationships between risk factors and dysplasia level were studied.

Methodology

This is retrospective and analytical study of the recorded data from histology and oral examination data archive in Faculty of Dentistry, Chiang Mai University.

Ethical approval

This study was approved prior to the data collection by the Human Experimentation Committee, Faculty of Dentistry, Chiang Mai University, Thailand (NO.16/2020). Patients' identification data were not collected during the retrospective study, hence the informed consent from each patient was not needed.

Sample selection

Inclusion criteria

Patients who arrived at the Oral Diagnosis Clinic, Faculty of Dentistry, Chiang Mai University, from 2017 to 2020, with a clinical and histopathological diagnosis

of an OPMDs: leukoplakia, erythroplakia, lichen planus, oral submucous fibrosis, palatal lesion in a reverse smoker, actinic cheilitis, discoid lupus erythematosus, lichenoid reaction, candidal leukoplakia, or a hereditary cancer syndrome.

Exclusion criteria

- Patient with insufficient data.
- Histopathological reported as inadequate specimens
- Site or location of lesion, Patient symptoms were not reported
- Demographic data were not presented

Data collection method

Patients' data were collected regarding their histopathological diagnoses.

Demographic data and history: age, gender, oral hygiene, drug usage, smoking, alcohol consumption, UV exposure, betel nut chewing, ill-fitting dentures, medication, and medical and dental history.

Clinical characteristics: lesion color, size, border, texture, consistency, site, and symptom.

Histopathological features: histopathological features for each lesion were collected and categorized by the level of dysplasia, carcinoma in situ, hyperkeratosis, liquefactive degeneration, acanthosis, lymphocyte infiltration, fibrosis, collagen degradation, atrophy, and candidal infection.

Statistical analysis

All of the data were analyzed to determine relationships between disease prevalence, clinical and histopathological features, and patient demographic data. Data were analyzed with χ^2 testing and descriptive statistics, using SPSS version 25.0. All biopsy samples were re-analyzed by specialists. The intra-calibration was done by repeating 10 sequence of slides, twice and analyzed with 68.8 percentage of agreement.

Results

We included 561 patients from 2017 to 2020 with OPMDs. The patients were 70.9% females and 29.1% males, with ages ranging from 18 to 87 years and a mean age of 60.6±13.0 years. Some patients had more than one biopsy results, hence the 649 data samples involved (only

samples from same patients with different diagnosis were counted as another samples, if new samples had similar diagnosis as the previous reports, there would be omitted). The prevalence for each OPMDs is shown in Table 1. Lichen planus was the most prevalent, with 39.7% prevalence rate.

In this study, only smoking habit was analysed as it was the only properly recored risk factor in data archive. Dysplasia was found in 20.2% of patients without a smoking history, compared with 58.8% of patients with a smoking history (Table 2). In the non-smoking group, 79.8% of the cases were found as non dysplasia while 16.4% were found as mild dysplasia and 3.8% were found as moderate dysplasia. In the smoking group, 41.2% of the case were found as non dysplasia while 43.8% were found as mild dysplasia, 12.4% were moderate and 2.6% were severe dysplasia (Figure 1) (CI=51.7 ($p>0.001$)). Only eight out of among 10 OPMDs were found during the studied period; palatal lesions in reverse smokers and hereditary cancer syndromes were not found and were excluded from this study. The total sum of clinical appearance and site in some diseases might exceed 100% due to more than one features and sites were reported in some cases. If the clinical characteristics or symptoms were not identified in data record, it would be categorized as "unidentified".

Leukoplakia was more frequently found in females (63.2%) than males (36.8%), with a mean age of 66.0±11.1 years (Table 1). Lesions were mostly found on the buccal mucosa (44.5%), followed by the soft palate (11.6%), gingiva (8.8%), lateral of tongue (7.7%), lower lip(5.5%), alveolar mucosa (5.5%), vestibule (4.4%), ventral of tongue (4.4%), labial mucosa (2.2%), retromolar area (2.2%), dorsal of tongue (1.6%), Floor of mouth (1.1%), corner of mouth (0.5%) (Figure 2). Patient usually have no symptoms (71.2%) or burning sensation (21.1%) and pain (7.7%) (Table 3); 78.5% of lesions were found as a plaque, followed by reticular (7.6%), nodules speckles (7.6%), papular (1.2%) and unidentified (5.1%) (Table 3). Every lesion were found in white color (Table 3). The most common histopathological features were hyperkeratosis (44.8%), followed by Acanthosis (4.9%) and atrophy of epithelial layers(0.5%) were also found to be reported (Figure 3). 43.6% of the cases were found to be mild dysplasia, followed by moderate dysplasia (9.4%), and severe dysplasia (2.2%) (Figure 4). Moreover, 87% of patients with leukoplakia were found to chew betel nuts.

Erythroplakia/Erythroleukoplakia was found in females (56.3%) more than males (43.8%), with the mean age being 66.8 ± 13.2 years (Table 1). The most common site was the gingiva (23.1%), followed by the buccal mucosa (15.4%), hard palate (13.7%), lower lip (8.0%), lateral of tongue (7.8%), soft palate (5.9%), dorsal of tongue (5.9%), ventral of tongue (5.9%), retromolar area (3.9%), vestibule (3.9%), alveolar mucosa (3.8%), upper lip (2.0%), floor of mouth (2.0%), labial mucosa (1.9%) (Figure 2). Patients usually reported a burning sensation (61.6%), no symptom (33.3%) and pain (5.1%) (Table 3). The most frequent clinical characteristic found was a patch or plaque (39.5%), reticular (32.6%), ulcerative (18.6%), nodular (9.3%), and unidentified (2.3%) (Table 3). Lesion came with mixed red and white in color (84.9%) or red color (15.1%) (Table 3). The predominant histopathology was mild dysplasia in (48.6%), followed by moderate dysplasia (14.3%), severe dysplasia (8.6%), non dysplasia (28.5%) (Figure 4). 25.7% was reported with hyperkeratosis and 2.9% was reported with atrophy of epithelial layers (Figure 3).

Lichen planus was found in females (77.5%) more than males (22.5%), with the mean age being 55.2 ± 13.1 years (Table 1). The buccal mucosa was the most common site (70.0%), followed by the vestibular area (8.2%), gingiva (7.8%), lower lip (5.8%), Hard palate (3.1%), retromolar area (2.7%) lateral of tongue (2.7%), dorsal of tongue (2.7%), alveolar mucosa (2.3%), corner of mouth (1.2%), floor of mouth (0.8%) ventral of tongue (0.8%), labial mucosa (0.4%) (Figure 2). A burning sensation was a common symptom (73.9%) followed by no symptom (23.8%), and pain (2.3%) (Table 3). The most frequent clinical characteristic found was reticular (80.5%), then, patch or plaque (12.7%), ulcerative (11.0%), papular (0.8%), nodular or speckle (0.8%), and unidentified (2.5%) (Table 3). The most common color was mixed red and white (63.6%), white color (33.5%), red color (2.9%) (Table 3); Histopathological reported 91.3% of the cases as non dysplasia and 8.7% as mild dysplasia (Figure 4). Additionally 71.1% of the cases was reported as hyperkeratosis followed by acanthosis (15.1%), and atrophy of epithelial layer (7.8%) (Figure 3).

Oral submucous fibrosis was found in females (66.7%) more than males (33.3%), with the mean age being 66.1 ± 14.7 years (Table 1). Every patient had history of betel nut chewing. The most common site was the buccal

mucosa (71.4%), followed by the lower lip (14.4%), corner of mouth (7.1%), and soft palate (7.1%) (Figure 2). Patients usually reported a painful sensation (38.0%), then no symptom (37.0%), and burning sensation (25.0%) (Table 3). Paleness and firm of mucosal tissue at the buccal mucosa (64.3%) and lip (35.7%) was commonly found, along with paleness of the affected area (100%) (Table 3). Moderate dysplasia and non dysplasia were found in histopathological feature equally at 33.3%, Severe dysplasia and mild dysplasia also found equally at 16.7% (Figure 4). Additional histopathological features found were hyperkeratosis (58.3%), acanthosis (50.0%), atrophy of epithelial layer (41.7%) (Figure 3).

Actinic cheilitis was found in females (65.0%) more than males (35.0%), with a mean age of 65.1 ± 10.4 years (Table 1). All of the cases were found on the lower lip (Figure 2). The most common symptom was a burning sensation (72.4%) followed by no symptom (13.8%) and pain (13.8%) (Table 3). Patch lesions were the most common clinical characteristic (60.0%), followed by ulceration (22.2%), reticular (5.6%), and nodular speckle (5.6%) (Table 3). Mix red and white color lesion were the most common (63.2%) followed by white lesion (26.3%), and red lesion (10.5%) (Table 3). Half of the cases were not found to have dysplasia in the histopathology followed by mild dysplasia (30.0%), moderate severe (10.0%), and severe dysplasia (10.0%) (Figure 4). Common histopathological features were hyperkeratosis (65.0%) and atrophy of epithelial layers (35.0%) (Figure 3).

Discoid lupus erythematosus was found in females (74.7%) more than males (25.3%), at a mean age of 57.8 ± 12.8 years (Table 1). The most common site was the buccal mucosa (66.7%) followed by the lower lip (21.0%), gingiva (6.0%), alveolar mucosa (4.8%), soft palate (2.4%), upper lip (1.2%), vestibular area (1.2%), hard palate (1.2%), lateral of tongue (1.2%), dorsal of tongue (1.2%) (Figure 2). Burning sensation is the most common symptom (75.4%) followed by no symptom (14.5%), and pain (10.1%) (Table 3). The lesions were most often reticular features (74.4%), then ulcerative (24.1%), unidentified (9.0%), patch or plaque (6.3%), atrophic (2.5%), papular (2.5%), and nodular or speckle (1.3%) (Table 3). Most common color was mix red and white (76.5%), followed by white color (19.8%), and red color (3.7%) (Table 3). Most of the histopathology was hyperkeratosis (81.2%), with only 9.4% as acanthosis

and 5.9% as atrophy of epithelial layers (Figure 3); only 5.9% showed mild dysplasia while 94.1% did not show any dysplasia (Figure 4).

Lichenoid reactions were mostly found in females (75.0%) than male (25.0%), with a mean age of 58.7±8.8 years (Table 1). Every patient whose diagnosed as lichenoid drug reaction must had clear record of temporal relationship between related medicine or dental restoration and signs and symptoms of the diseases. The most common site was the buccal mucosa (91.7%), and the remaining was at gingiva (8.3%) (Figure 2). The most common symptom was a burning sensation (50.0%) followed by no symptom (33.3%) and pain (16.7%) (Table 3). The most common clinical feature was reticular (45.5%), followed by atrophic area (36.4%), and ulcerative lesion (18.1%) (Table 3). Mixed red and white coloration (58.3%) was mostly found follow by white lesion (33.4%) and red lesion (8.3%) (Table 3). No dysplasia was found in the histopathology (Figure 4); hyperkeratosis was the most commonly found feature (75.0%) with only 8.3% found with acanthosis (Figure 3).

Candidal leukoplakia was found in females (85.0%) more than males (15.0%), with a mean age of 65.2±8.3 years (Table 1). Sixty percent of lesions were found at the buccal mucosa followed by the lateral edge of the tongue (15.8%) with corner of mouth and floor of mouth equal at 5.0% while 14.2% was unidentified (Figure 2). The most common symptoms were a burning sensation (64.3%), no symptom (21.7%) and pain (14.0%) (Table 3). Patches or plaques (35.3%) was most common clinical characteristic found, followed by reticular (23.5%), nodular or speckle (5.9%) and unidentified (35.3%) (Table 3). Mixed red and white was the most common color (47.1%), followed by white lesion (41.0%) and brown lesion (11.9%) (Table 3). Only 2 patients were found to have a related medical condition. One of them had diabetes melitus together with dyslipidemia and the other had HIV infection. The most frequently found histopathological feature was hyperkeratosis (94.7%), followed by acanthosis (52.6%), and atrophy of epithelial layers (5.3%) (Figure 3). Non dysplasia and mild dysplasia was found equally at 47.2%, only 5.6% of the case was found as severe dysplasia (Figure 4).

Table 1: The number and percentage of males and females, age range, mean ages, and prevalence for each OPMDs, 2017-2020.

Lesion	Gender (N/%)		Age (years)			Prevalence (N/%)
	Male	Female	Range	Mean	SD	
Leukoplakia	68/36.8	118/63.2	50-81	66.0	11.1	186/28.6
Erythroplakia/Erythroleukoplakia	23/43.8	30/56.3	43-75	66.8	13.2	53/8.2
Lichen planus	58/22.5	200/77.5	32-70	55.2	13.1	258/39.7
Oral submucous fibrosis	5/33.3	9/66.7	18-87	66.1	14.7	14/2.2
Actinic cheilitis	7/35.0	13/65.0	44-79	65.1	10.4	20/3.1
Discoid lupus erythematosus	22/25.3	64/74.7	38-72	57.8	12.8	86/13.3
Lichenoid reaction	3/25.0	9/75.0	54-68	58.7	8.8	12/1.8
Candidal leukoplakia	3/15.0	17/85.0	46-81	65.2	8.3	20/3.1

Table 2: The percentages of dysplasia in the non-smoking group and smoking group 2017-2020.

	No dysplasia	Dysplasia
Non-smoking	79.8	20.2
Smoking	41.2	58.8

Table 3: The percentage of symptoms, clinical appearances and lesion color for each OPMDs, 2017-2020.

Disease	Symptoms			Clinical appearances								Color				
	Burning sensation	Pain	No symptom	Reticular	Ulcerative	Patch or plaque	Nodular or speckle	Papular	Atrophic	Paleness and firm of mucosal tissue	Unidentified	Red	White	Mix red and white	Brown	Paleness of tissue
Leukoplakia	21.1	7.7	71.2	7.6	-	78.5	7.6	1.2	-	-	5.1	-	100	-	-	-
Erythroplakia/erythroleukoplakia	61.6	5.1	33.3	32.6	18.6	39.5	9.3	-	-	-	2.3	15.1	-	84.9	-	-
Lichen planus	73.9	2.3	23.8	80.5	11.0	12.7	0.8	0.8	-	-	2.5	2.9	33.5	63.6	-	-
Oral submucous fibrosis	25.0	38.0	37.0	-	-	-	-	-	-	100.0	-	-	-	-	-	100.0
Actinic cheilitis	72.4	13.8	13.8	5.6	22.2	60.0	5.6	-	-	-	6.6	10.5	26.3	63.2	-	-
Discoid lupus erythematosus	75.4	10.1	14.5	74.4	24.1	6.3	1.3	2.5	2.5	-	9.0	3.7	19.8	76.5	-	-
Lichenoid reaction	50.0	16.7	33.3	45.5	18.1	-	-	-	36.4	-	-	8.3	33.4	58.3	-	-
Candidal leukoplakia	64.3	14.0	21.7	23.5	-	35.3	5.9	-	-	-	35.3	-	41.0	47.1	11.9	-

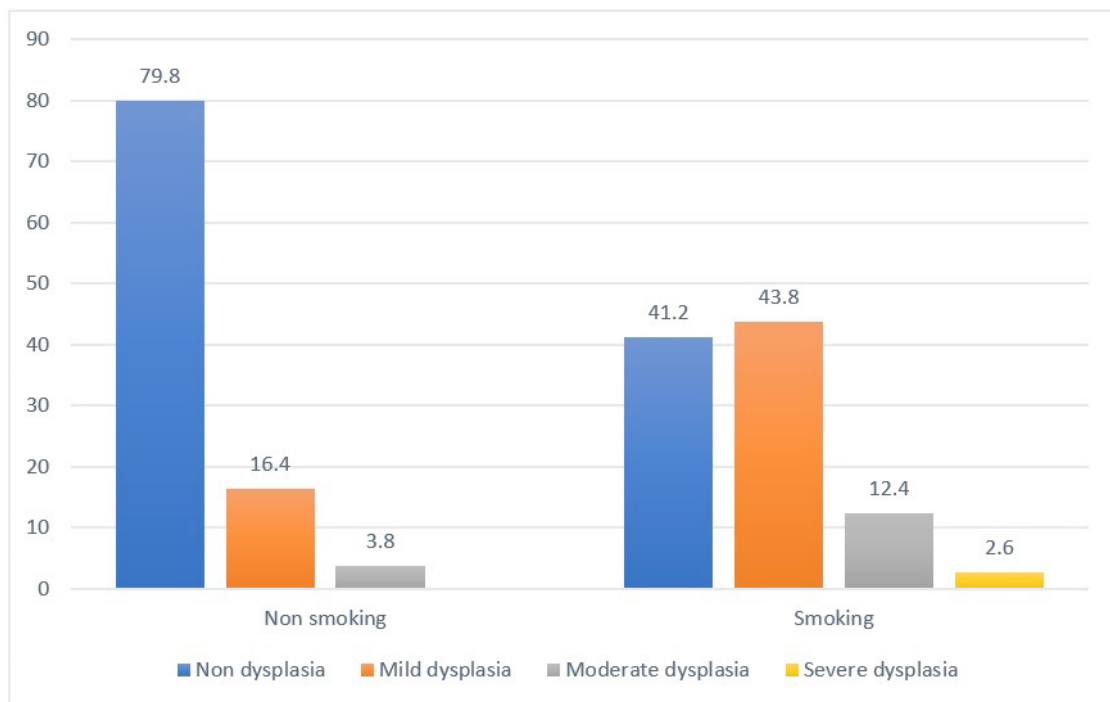


Figure 1: Percentages of patients with OPMDs categorized by smoking and level of dysplasia (CI = 51.7 ($p>0.001$))

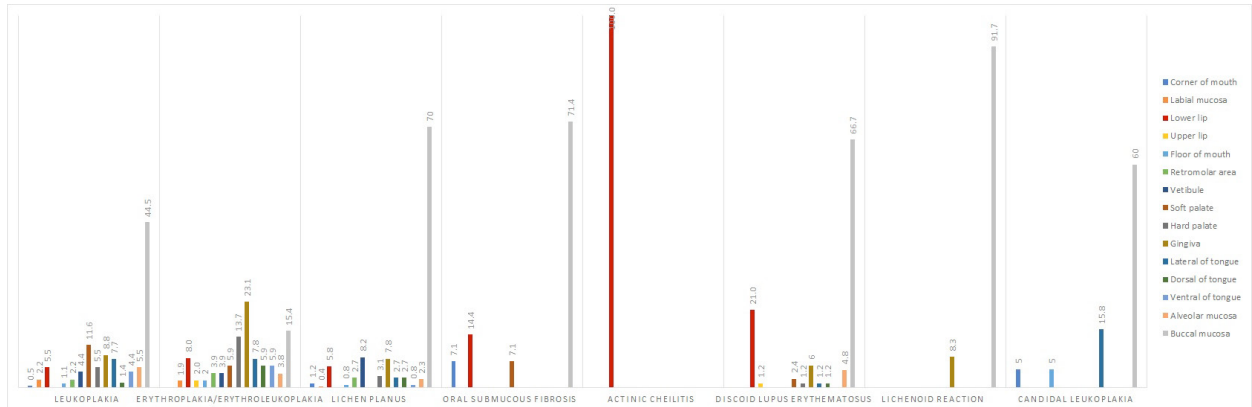


Figure 2: Percentage of lesion's sites categorized by OPMDs

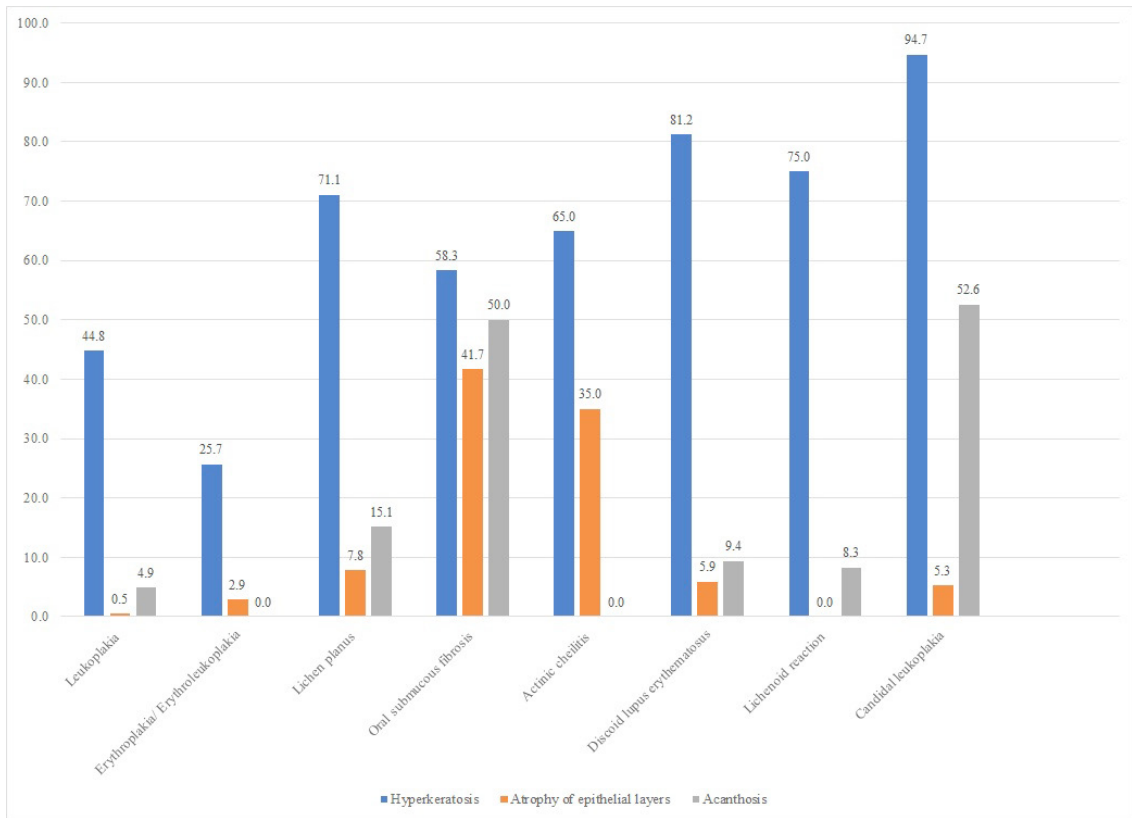


Figure 3: Percentage of common histopathological features categorized by OPMDs

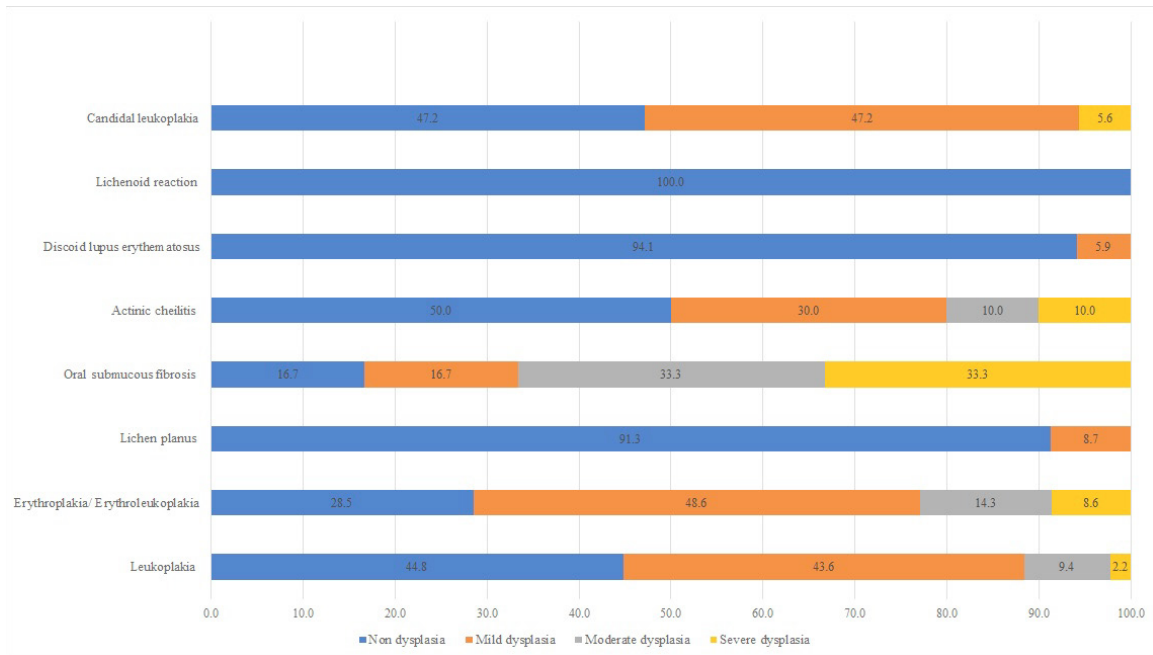


Figure 4: Percentage of dysplasia level found in histopathological result categorized by OPMDs

Discussion

The data were collected from the database of the Faculty of Dentistry, Chiang Mai University. All of the patients diagnosed with OPMDs during 2017-2020 were included, and patients with insufficient data were excluded. In total, 561 cases were included, mainly females (70.9%) and only 29.1% males. Their ages ranged from 18 to 87 years, with a mean age of 60.6 ± 13.0 years which were corresponded to the previous cross-sectional study in Thailand, staging that the most prevalent age was between 6th to 7th decade and predominated by female patients.⁽⁴⁶⁾

Lichen planus had the highest prevalence among all of the patients, which corresponds with literature reviews.^(17,18) Leukoplakia and erythroplakia were found in females more than males, which contradicts other studies.^(2,9) Several factors influenced the study's results, especially the gender representation ratio, since most of the patients included in this study were female. A study from Phudphong in 2020 also indicated that females have more concerns with oral health than males, hence the greater prevalence in female patients.⁽⁴⁷⁾

Similar to previous reports, leukoplakia was found mostly at buccal mucosa with clinical characteristic as white plaque or patch.^(1,11) Hyperkeratosis with non-dysplasia was reported at 44.8% and 43.6% of the cases were report as mild dysplasia which conform with past report.^(1,8) Eighty seven percent of the leukoplakia case was report with betel nut chewing habit, one of the greatest cancer risk factor and could be the cause of higher chance of epithelial dysplasia when compare to other previous studies.^(1,8) Erythroplakia and erythroleukoplakia also show similar tendency as leukoplakia. In this study patient usually came with mixed red and white plaque or reticular which were conformed with other study.⁽¹⁴⁾ However, contradict to the other study, burning sensation or pain at lesion site were found to be the most common symptoms in this study.⁽⁴⁸⁾ Over 70% of erythroplakia cases were found with epithelial dysplasia, significantly higher from another study⁽¹⁵⁾, nevertheless most of dysplasia case were diagnosed as mild dysplasia (48.6% of total case or 68.0% of dysplasia case) with no carcinoma in situ reported, showing better prognosis when compare to other study which reported more higher level of dysplasia case.⁽¹⁶⁾

Recent study has reported that smoking, alcohol consumption, betel nut chewing, and tobacco chewing

correlate with the occurrence of OPMDs; smoking was the most frequently found risk factor.⁽⁸⁾ Some studies also indicated a higher prevalence of oral leukoplakia in smoking patients than in non-smoking patients, including a higher chance of finding dysplasia in smoking patients; this tendency was confirmed in this study.^(9,10)

Lichen planus is the type of auto-immune disease. Lichen planus lesion reported in this study was found predominately at buccal mucosa, mixed red and white with burning sensation were the most common clinical characteristic found which are conformed with previous study.⁽¹⁹⁾ Only 8.7% of lichen planus cases was found with mild dysplasia while the remaining cases were without dysplasia which were within range from previous study.⁽⁴⁹⁾

Oral submucous fibrosis is characterized by epithelial inflammatory reaction with progressive fibrosis of the submucosal tissues result in pale pink and rigidity of affected tissue similar to lesion found in the patient in this study. The disease is closely related with areca or betel nut chewing⁽²⁰⁾, several components such as tanins, arecoline and arecaidine can induce fibroblast stimulation and poliferation. Furthermore, it can inhibit collagenases hence reduce collagen degradation.⁽⁵⁰⁾ Strangely, the common symptoms of oral submucous fibrosis are burning sensation and pain⁽²¹⁾, however around 37.0% of patients do not have any symptom at all. Possibly due to an early detection of the disease before symptom arise.

Actinic cheilitis is the type of OPMDs where epithelial cells or keratinocytes transform due to UV radiation and the most common location is lower lip as it prone to contact with sun light⁽²⁹⁾, which was correspond to the result from this study. Patient with actinic cheilitis has higher chance of having malignant transformation into squamous cell carcinoma (SCC). In addition, the cancer that occur on lower lip have higher chance (11 times) of metastasis when compare to SCC on other skin location.⁽⁵¹⁾ In this study, up to 50% of the cases were diagnosed as dysplasia histopathologically.

Discoid lupus erythematosus is another type of auto-immune disease similar to lichen planus and could be clinically challenged to differentiate between these two disease. Lesion usually came as mixed red and white reticular appearance with burning sensation which are conformed with the result from this study.^(32,33) Discoid lupus erythematosus is a subtype of lupus erythematosus disease and could occur as one of systemic lupus erythe-

matosus manifestation.⁽⁵²⁾ Therefore every patient diagnosed as discoid lupus erythematosus were requested to have their blood test for anti-nuclear antibody screening.⁽⁵²⁾

Lichenoid reactions is also another type of auto-immune disease similar to lichen planus and difficult to distinguish from lichen planus even in histopathology.⁽³⁷⁾ The proper method to identified lichenoid reactions in both subtypes were through history taking especially lesion site and temporal relationship between the lesion occurrence and timing of medication or dental restoration.^(39,40) Similar to lichen planus common clinical appearance show mixed red and white reticular with burning sensation which correspond to this study result.

Candidal leukoplakia is described as white lesion that cannot be wipe off and show histopathological features similar to leukoplakia addition with *Candida* spp. infection detected in histological sample.⁽⁴³⁾ However, there were not possible to define from histological data alone whether *Candida* spp. infection was the cause of disease or patient originally had leukoplakia then infect with *Candida* spp. later on. *Candida* spp. infection is considered to be another cancer risk factor as show in this study; 47.2% of the cases were categorized as mild dysplasia and 5.6% were categorized as sever dysplasia.^(43,45) According to previous reports, candidal leukoplakia might related to some medical conditions such as diabetes mellitus, asthma treated with steroid inhalers, and malabsorption syndrome.⁽⁵³⁾ However, due to lack of proper patient history information, those relationship could not be statistically analyzed.

Conclusion

There were total 649 biopsy samples from 561 patients. Most of the patients were female with overall mean age at 60.3±13.0 years. Almost every disease were found commonly at buccal mucosa, while burning sensation or pain with mixed red and white lesion were common symptoms found. Despite their unique histopathological characteristic, hyperkeratosis was the most common histopathological feature found in every OPMDs. Oral submucous fibrosis had highest dysplasia rate follow by leukoplakia and candidal leukoplakia while there were no epithelial dysplasia reported from patients with lichenoid reaction. Patients with smoking habit had significantly higher level of dysplasia when compared to non smoking group which was confirmed with other previous studies.

Limitations and summary

This was a retrospective study from a database. Some data were missing, such as demographic data and clinical features of lesions. Some diseases were not well-represented, namely erythroplakia, oral submucous fibrosis, angular cheilitis, and lichenoid reactions.

This study suggests that the history-taking and clinical data collection for each patient should be more systematic and detailed to minimize data errors and missing items, which will benefit both patient treatment and future research.

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Conflicts of interest

The authors declare no conflicts of interest.

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