



A Retrospective Study of Immunological Oral Lesions in Early Adulthood Population in Northeastern Thailand

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Abstract

Immunological disorder-related oral lesions are relatively uncommon in adolescence; however, the condition is chronic and difficult to cure. This retrospective study aimed to examine the distribution of oral lesions related to immunological disorders in Northeastern Thai Oral Pathology Databases. The data were retrieved from the Oral Pathology Databases of the Faculty of Dentistry, Khon Kaen University, during 2000-2019. A total of 1,858 lesions with histopathology data derived from patients aged between 16-35 years were analyzed. Among these, 56 lesions (3%) were diagnosed as related to allergic/immunological disorders, with no preference on sex ratio ($p=0.36$). The prevalence of immunological oral lesions was increased with age ($p<0.001$). However, oral lichen planus (62.5%), pemphigus vulgaris (14.3%), and benign mucous membrane pemphigoid (BMMP) (5.3%) that are commonly reported in the middle-aged patients were found in the samples aged 20 years and under. The most common site was buccal mucosa (66.7%), followed by gingiva (20.6%). Findings from this study have provided a glimpse into the prevalence and distribution of immunological oral lesions in the early adulthood population from one of the largest databases in Thailand. The information indicated that oral health screening for early adulthood should include a thorough examination of the soft tissue. It is very important that these lesions should be early diagnosed and treated appropriately to minimize the risk of turning into malignancy, leading to a better prognosis and improved quality of life for the patient.

Keywords: Allergic/immunological disorder, Early adulthood, Oral and maxillofacial lesions

1. Introduction

Common oral diseases refer to dental caries, periodontal diseases, and oral cancers. Although dental caries could affect individuals across the life course with different patterns, the incidence of periodontal diseases and oral lesions appears to be increased with age. Epidemiologic studies within the population at different life stages could give a better understanding of the trajectory and transition of oral lesions. Based on the recent Thailand National Oral Health Survey reported in 2017 (Bureau of Dental Health, 2017), an oral lesion screening was included in the survey only for the adult population. Among 4,683 of the 35-44-year-old subjects examined, only 5 cases were reported with soft tissue lesions: red, white, mixing red-white, ulceration or nodule/mass, one on each category. This finding appeared to be underestimated compared with the reports in other countries, which showed the range between 15.7%-17.1% in the US (Weir, Davenport & Skinner, 1987) and 8.3% in Malaysia (Zain et al., 1997). Whereas the information is abundant for the geriatric population, less is known about the prevalence of oral maxillofacial lesions in early adulthood in Thailand.

Immunological abnormalities, including allergic disorders, may be apparent as mucosal lesions in the oral cavity, which, in some cases, is the most obvious sign or the first site detected (Harman et al., 2017; Leuci et al., 2019). The occurrence of oral immunological lesions has been reported more frequently in the middle-aged population but can also be observed in the younger or older age groups. Due to the nature of diseases that are chronic and unlikely to be treated, some of them, such as resistant oral lichenoid mucositis, have been considered as oral precancerous lesions (Messadi, 2013). Although the lesion may retain in a precancerous stage for decades, a fraction of them could potentially transform into malignancy later in the



patient's life. Early detection with close monitoring as well as increased awareness in high-risk patients should be emphasized.

In Thailand, epidemiologic studies of oral and maxillofacial pathology are still limited, and most of the studies are only available for either pediatric (Dhanuthai, Banrai & Limpanaputtajak, 2007; Laphanasupkul et al., 2015) or geriatric populations (Intercountry Center for Oral Health, 2020). Faculty of Dentistry, Khon Kaen University, is known to be one of few centers providing histopathology services in Northeastern Thailand. The archive of over 20 years could provide an additional resource for the retrospective study. Thus, this preliminary study focused on investigating the prevalence of oral maxillofacial lesions related to allergic/immunological disorders in the Northeastern Thai early adults and assessing the demographic distribution of histopathological diagnosis regarding different age ranges and genders.

2. Objectives

To investigate the distribution of histopathologically diagnosed oral lesions related to oral immunological lesions in Northeastern early adults recorded in KKU Oral Pathological Database.

3. Materials and Methods

This retrospective study analyzed the data available from Oral Pathology Databases of the Faculty of Dentistry, Khon Kaen University, over a period of 20 years, from 2000 to 2019. The study was approved by the Center for Ethics in Human Research, Khon Kaen University (Approval No. HE642025). Required data were retrieved from the KKU Oral Pathology database and transformed into an electronic spreadsheet using Microsoft Excel. Most of the histopathological diagnoses were interpreted from the hematoxylin and eosin (H&E) staining specimens. Approximately 20% of the samples with an initial diagnosis of pemphigus vulgaris and pemphigoid will be confirmed using direct immunofluorescence (DIF). The studied samples were histopathological data from individuals aged between 16 and 35 years old. The samples diagnosed as "normal tissue" or those with missing information (e.g., age and gender, no clinical impression, or no histological diagnosis) were excluded from further analysis. The histopathology diagnoses were categorized into either lesions related to allergic/immunological disorders or others. Data analysis performed using SPSS 26.0 (Armonk, N.Y., USA). A Chi-square test was carried out to analyze the relationship between types of histopathology diagnosis on different age groups and genders. The statistical significance level was set at 5%.

4. Results and Discussion

4.1 Results

A total of 9,026 specimens were archived from 2000 to 2019 in the Oral and Maxillofacial Pathology Database. There were only 1,858 samples (approximately 20%) that met the inclusion criteria with the age range between 16 to 35 years old. The mean age of the studied samples was 24.35 (SD=5.789 years), of which 706 samples (37%) were derived from males and 1,152 samples (63%) were derived from females.

Of the 56 samples with histopathology diagnosis related to allergic/immunological disorders, 49 samples observed in this study included benign mucous membrane pemphigoid (BMMP), lichen planus, lichenoid mucositis, lupus erythematosus, pemphigus vulgaris. Seven samples were categorized as "unspecified" because the interpretation was suggestive for allergic or immunologic-related pathological characteristics; however, more clinical information or additional tests were required before a definite diagnosis could be made. Table 1 shows the distribution of histology diagnosis according to histological types and age groups. When grouping the samples according to the age range of 5 years, the numbers of cases with disorders appeared to be increasing with age. Approximal one-third of the cases were aged between 31-35 years old. However, 9 cases, aged 20 years or under, were also diagnosed with lichen planus, pemphigus vulgaris, and BMMP, whose onsets were not commonly found at this early age.

The predominant pathohistological diagnoses in this group were lichen planus (62.5%), followed by pemphigus vulgaris (14.3%).

**Table 1** Distribution of allergy/immunological disorder with respect to the age groups

Age-groups (years)	Histological type (%)						Total (%)
	Lichen planus (%)	Pemphigus vulgaris (%)	Unspecified (%)	BMMP (%)	Lichenoid mucositis (%)	Lupus erythematosus (%)	
16-20	4 (44.5)	2 (22.2)	1 (11.1)	1 (11.1)	1 (11.1)	0 (0.0)	9 (16.0)
21-25	3 (50.0)	2 (33.3)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	6 (10.7)
26-30	6 (60.0)	1 (10.0)	2 (20.0)	0 (0.0)	0 (0.0)	1 (10.0)	10 (18.0)
31-35	22 (71.0)	3 (9.6)	4 (13.0)	1 (3.2)	1 (3.2)	0 (0.0)	31 (55.3)
Total	35 (62.5)	8 (14.3)	7 (12.5)	3 (5.3)	2 (3.6)	1 (1.8)	56 (100.0)

Table 2 shows the distribution of immunological lesions according to the site of specimens. Regarding the anatomical location, most of the lesions (66.7%) occurred at buccal mucosa, followed by the gingiva (20.6%), tongue (7.9%), labial mucosa (3.2%), and palate (1.6%).

Table 2 Distribution of allergy/immunological lesions with respect to anatomical locations

Location's site	Total	%
Buccal mucosa	42	66.6
Gingiva	13	20.6
Tongue	5	8.0
Labial mucosa	2	3.2
Palate	1	1.6
Total	63*	100.0

(*) some cases had more than one site of lesion

Statistical analysis was to test whether the immunological lesions might be associated with the sex and age of the studied population. Table 3 shows the distribution of immunological and other lesions according to sexes. Chi-square test demonstrated that there was no statistical significance ($p=0.36$) in the association between the type of lesions and sex (Chi-square = 0.84, $df = 1$, $p = 0.36$).

Table 3 Distribution of oral and maxillofacial histopathology with respect to sex

Sex	Diagnostic categories		Total (%)
	Immunological related (%)	Others (%)	
Male	18 (2.5)	688 (97.5)	706 (100.0)
Female	38 (3.3)	1,114 (96.7)	1,152 (100.0)
Total	56 (3.0)	1,802 (97.0)	1,858 (100.0)

Chi-square test at $p>0.05$

When divided the cases according to the age groups into youth (16-25 years old) and early adulthood (26-35 years old), the analysis indicated that the immunological lesions were significantly associated with the older group (Chi-square = 26.65, $df = 1$, $p<0.001$). Table 4 shows the distribution of immunological and other lesions according to the age groups.

Table 4 Distribution of oral and maxillofacial histopathology with respect to the age groups

Age groups (years)	Diagnostic categories		Total (%)
	Immunological related (%)	Others (%)	
Youth (16-25)	15 (1.3)	1,101 (98.7)	1,116 (100.0)
Early adulthood (26-35)	41 (5.5)	701 (94.5)	742 (100.0)
Total	56 (3.0)	1,802 (97.0)	1,858 (100.0)

Chi-square test at $p<0.05$

4.2 Discussion

The purpose of the present study was to provide preliminary data on the prevalence of immunologically related cases among all oral lesions existing in the KKU Oral Pathology Database, the



largest archive available for Northeastern Thailand. This study was focusing on the early adulthood population. The distribution of the patients' age, sex, and locations were shown according to the histopathology diagnosis.

The KKU Oral Pathology Database was established as an electronic archive in 1992. There were 3-5 oral and maxillofacial pathologists interpreting these submitted specimens. Sample providers included general dentists and various specialists from KKU Dental Hospital, community hospitals, advanced hospitals, and private clinics. These oral care services were mainly from 3 Health Districts covering 15 provinces, in the northeast region of Thailand. The number of cases requiring pathological diagnosis by KKU pathologists had escalated after 2000 when the number of trained dental specialists has increased in Thailand. In the present study, cases from 2000-2009 were triple in a decade later, during 2010-2019. The database served as a valuable resource for a retrospective study when a clinical study involving such a large population could not be easily conducted during the time of the pandemic.

Oral mucosal diseases are not only correlating with inherent factors, mainly genetics, and the immune system. Extrinsic factors such as trauma, medication usage, and oral hygiene also play an essential role in developing the diseases (Jainkittivong, Aneksuk & Langlais, 2002). Besides, several risk factors, such as local infection diseases, i.e., virus or bacteria, metabolic disorders (Villanueva-Vilchis et al., 2016), drug reaction and lifestyle, i.e., consumption of tobacco or betel quid (Arya et al., 2017), may also affect the oral cavity as oral mucosal diseases (Harris et al., 2004). In this study, most biopsy specimens received were in the "other" group in which diagnostic categories varied from inflammatory, cysts, benign tumors, malignant, salivary gland pathology, and developmental pathology. The range of diagnoses within-group "other" appeared to be similar to those reported in other retrospective studies using the database (Dhanuthai et al., 2016a); Dhanuthai et al., 2016b). The age range of the cases in this present study was from 16 to 35 years old, considering to be youth and early adulthood. Whereas the reactive or inflammatory lesions and cysts has a high prevalence in the first and second decades of life, the peak distribution of immunological lesions was known to be during the fourth and fifth decades (Dovigi et al., 2016; Intercountry Center for Oral Health, 2020; Joseph et al., 2019). These findings are consistent with our data that only three percent of the studied samples featured as an immunologically related lesion. The National report in 2016 by the Department of Health, Thailand Ministry of Health, also categorized the potentially malignant disorders (PMD), which included lichen planus, lichenoid mucositis, leukoplakia, and erythroplakia, as one of the oral lesions in the examination (Intercountry Center for Oral Health, 2020). Based on the dental treatment records. The report summarized that the PMD was accounted for only 0.42% (426 cases) of all lesions recorded (99,312 cases) in the patients aged 15-34. The prevalence increased to be 1.37% (2,414 PMD:175,665 lesions) in the 35-59 years old age group and 2.4% (3,677 PMD:152,808 lesions) in the 60 years old onward group.

The oral lesions related to allergic and immune disorders are considerably uncommon in the youth and early adulthood population. Most allergic or irritated lesions could be recovered when the sources were removed. For most of the autoimmune lesions, mechanisms underlying the disease remain unclear and controversial, although more associated factors have been identified up to date. Cellular and/or humoral immune responses play a central role (do Carmo et al., 2014), while the other studies showed that smoking was associated with having oral potentially malignant disorder (Villa & Gohel, 2014). Treatment outcomes for these chronic diseases may not be favorable as the "cured" stage. They have been considered premalignancy due to their high potent in becoming oral cancer over some time (Jaafari-Ashkavandi et al., 2011). Having physically and mentally suffered from such chronic lesions could also compromise the quality of life of these patients. In this study, the prevalence of immunologic lesions is significantly higher in the early adulthood cases when compared with that of the youth. However, a few youth patients in their teen-year received a histopathological diagnosis of oral lichen planus and benign mucous membrane pemphigoid. The diagnosis confirmation would hopefully be a warrant for these patients to be placed into a close surveillance program after the appropriate treatment depending on the clinical stage (Eisen et al., 2005; Leuci et al., 2019).

Our analysis further showed that the prevalence of immunological lesions among the oral lesions in females was not significantly different from that of the male patients. This trend was consistent with the national report (Intercountry Center for Oral Health, 2020) but controversial to those reported in other



populations, which stated that females appeared to have more prevalence of immunological disorder (Scully, 2012; Villa & Gohel, 2014). In this present study, the immunological disorder seems to increase with age among the early adulthood (5.5%) more than youth (1.3%), especially during the third decade of life. These results were similar to other studies in that these lesions also occurred in the middle-aged adults with a mean age of 31.93 ± 10.37 (third decade of life), and the peak occurrence of this lesion was in the sixth decade of life. So, the increasing age was found to be a risk factor for the immunological disorder diagnostic category (Almoznino et al., 2015; Villa & Gohel, 2014). The predominant lesion found in this study was oral lichen planus, which is also commonly found in other studies (Arisawa et al., 2008; do Carmo et al., 2014). The higher sample numbers of lichen planus might be due to their distinct clinical features that were well recognized by most clinicians. The common anatomical sites that the lesions were biopsied appeared to be buccal mucosa and gingiva in this study, which was agreeable to other studies in which buccal mucosa was the highest incidence of lichen planus (Thongprasom et al., 2010; Arisawa et al., 2008). Recently, an increased incidence of oral lichen planus in the young was emphasized among dermatologists and oral medicine specialists (Eisen et al., 2005). This finding should also be made aware among the dentists who provide care for children and adolescences.

Histopathology of oral lesions is always crucial to confirm the clinical diagnoses that are differentiated by the clinician, which would lead to an appropriate treatment protocol. For some autoimmune lesions, such as mucous membrane pemphigoid, the immunology test is also critical to ascertain the clinical features and histopathology. Pathologists would suggest further immunofluorescence tests for most vesiculobullous lesions prior to making the definite diagnosis. However, in our database, about one-fifth of such samples had proceeded for DIF at the private laboratory. The decision for further investigation depends on the patient's consent and the clinician's suggestion. Seven samples in this data set were labeled as "unspecified." More clinical information had been acquired along the diagnosis process. The clinicians should be reminded that clinical features such as whether there were multiple lesions or were bilateral, the site of other lesions, systemic involvement, and medical history should be given in detail when submitted the specimens for pathological investigation.

Over the past decades, the incidence of premalignant lesions and oral cancer has been increasingly detected in the middle-aged and elderly population in Thailand. Early detection of high-risk conditions has been one of the effective procedures to prevent mortality and significantly improve the prognosis. The allergic/immunological disorders manifested as oral lesions are not uncommon. More studies and cases had been reported to affect the younger age group. The data available in the KKU Oral Pathology Database could be underestimated prevalence in the population. Systematic screening and recording of the oral lesions ought to be performed as part of the national oral health survey and extended to cover the younger age group.

5. Conclusion

This study reported the prevalence of oral lesions associated with allergic/immunological disorders and the demographic data in the early adulthood samples. Higher cases were observed in early adulthood than in the youth group. Findings from this study support the importance of including oral soft tissue screening as part of routine check-up for the adolescence.

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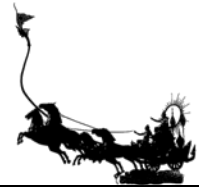
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