ASSOCIATION BETWEEN CLINICAL SIGNS AND QUALITY OF LIFE IN THAI PATIENTS WITH ORAL LICHEN PLANUS

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A Thesis Submitted in Partial Fulfillment of the Requirements

for the Degree of Master of Science in Oral Medicine

Department of Oral Medicine

FACULTY OF DENTISTRY

Chulalongkorn University

Academic Year 2019

ความสัมพันธ์ระหว่างอาการแสดงทางคลินิกและคุณภาพชีวิต ในผู้ป่วยไทยโรคไลเคนแพลนัสช่องปาก

พ.ท.หญิงศศิรินทร์ เยี่ยมสถาน

วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
สาขาวิชาเวชศาสตร์ช่องปาก ภาควิชาเวชศาสตร์ช่องปาก
คณะทันตแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
ปีการศึกษา 2562

Thesis Title	ASSOCIATION BETWEEN CLINICAL SIGNS AND QUALITY OF LIFE IN THAI PATIENTS WITH ORAL LICHEN PLANUS
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ศศิรินทร์ เยี่ยมสถาน : ความสัมพันธ์ระหว่างอาการแสดงทางคลินิกและคุณภาพชีวิตในผู้ป่วยไทยโรคไลเคนแพลนัสช่องปาก. (ASSOCIATION BETWEEN CLINICAL SIGNS AND QUALITY OF LIFE IN THAI PATIENTS WITH ORAL LICHEN PLANUS) อ.ที่ปรึกษาหลัก : รศ.ทญ. ดร.พรพรรณ พิบูลย์รัตนกิจ, อ.ที่ปรึกษาร่วม : ศ.ทญ. ดร.สุดาดวง กฤษฎาพงษ์

อาการของผู้ป่วยแต่ละบุคคลและคุณภาพชีวิตในมิติสุขภาพช่องปากได้ถูกแนะนำให้รวมเข้าในการศึกษาโรคไลเคนแพลนัสช่องปาก วัตถุประสงค์เพื่อประเมิน 1) ความสัมพันธ์ระหว่างอาการแสดงทางคลินิกโรคไลเคนแพลนัสช่องปากกับคุณภาพชีวิตในมิติสุขภาพช่องปากและความสัมพันธ์กับความเจ็บปวด 2) ความสัมพันธ์ระหว่างความเจ็บปวดกับคุณภาพชีวิตในมิติสุขภาพช่องปาก วิธีการ ผู้ป่วยไทยที่ได้รับการวินิจฉัยเป็นโรคไลเคนแพลนัสช่องปาก หรือโรคไลเคนอยด์สาเหตุจากยาจำนวน 69 คน เก็บข้อมูลการสัมภาษณ์ด้วยสเกลวัดความปวดแบบตัวเลขและดัชนีโอไอดีพี ตรวจอาการแสดงทางคลินิกโรคไลเคนแพลนัสช่องปากถึงตำแหน่ง ชนิดรอยโรค และความรุนแรงของรอยโรคประเมินด้วยระบบคะแนน Thongprasom ผลการศึกษาพบว่า 1) มีความสัมพันธ์อย่างมีนัยสำคัญทางสถิติระหว่างความรุนแรงของรอยโรคไลเคนแพลนัสช่องปากกับระดับความเข้มข้นของผลกระทบคุณภาพชีวิต ค่าสัมประสิทธิ์สหสัมพันธ์สเปียร์แมน (r_s) เท่ากับ 0.490 ($p < 0.001$) และมีความสัมพันธ์กับความเจ็บปวดอย่างมีนัยสำคัญทางสถิติ ค่า r_s เท่ากับ 0.298 ($p = 0.013$) ระดับความเข้มข้นของผลกระทบคุณภาพชีวิตและความเจ็บปวดเพิ่มขึ้นตามความรุนแรงของรอยโรคทางคลินิก รอยโรคไลเคนแพลนัสชนิดแผลถลอกมีอาการเจ็บปวดมากที่สุดและมีผลกระทบอย่างมากต่อคุณภาพชีวิต รอยโรคไลเคนแพลนัสที่เพดานอ่อนมีผลกระทบต่อคุณภาพชีวิตอย่างมาก 2) มีความสัมพันธ์อย่างมีนัยสำคัญทางสถิติระหว่างความเจ็บปวดกับระดับความเข้มข้นของผลกระทบคุณภาพชีวิต ค่า r_s เท่ากับ 0.400 ($p = 0.001$) สรุป ผลการศึกษานี้แสดงถึงความใช้ได้ของดัชนีโอไอดีพี ในการประเมินคุณภาพชีวิตเมื่อเทียบกับระบบคะแนน Thongprasom ที่ใช้ประเมินความรุนแรงทางคลินิกของโรคไลเคนแพลนัสช่องปาก การใช้ตัวชี้วัดทางคลินิกอย่างเดียวไม่เพียงพอ การประเมินคุณภาพชีวิตในมิติสุขภาพช่องปากจะช่วยเติมเต็มให้กับการประเมินด้วยตัวชี้วัดทางคลินิก

สาขาวิชา เวชศาสตร์ช่องปาก ลายมือชื่อนิสิต .....

ปีการศึกษา 2562 ลายมือชื่อ อ.ที่ปรึกษาหลัก .....

ลายมือชื่อ อ.ที่ปรึกษาร่วม .....

6175843932 : MAJOR ORAL MEDICINE

KEYWORD: Oral lichen planus, Quality of life, Oral impact on daily performance, OIDP, Oral health related quality of life, Pain

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Subjective patient's symptoms and oral health-related quality of life (OHRQoL) were recommended to be involved in oral lichen planus (OLP) studies. Objectives: to evaluate 1) the association between OLP clinical signs and OHRQoL as well as pain perception. 2) the association between OLP pain and OHRQoL. Methods: Sixty-nine OLP or oral lichenoid drug reaction (OLDR) Thai patients were recruited. Data were collected through personal interview with the Numeric Rating Scale (NRS) and Thai version of Oral Impacts on Daily Performance (OIDP) index. OLP signs were examined in aspects of localization, type and clinical severity according to the Thongprasom sign scoring system. Results: 1) there was statistically significant association between OLP clinical severity and the intensity of oral impacts (Spearman's correlation (r_s) = 0.490, $p < 0.001$) and with OLP pain (r_s = 0.298, p = 0.013). The intensity of OLP impacts and pain intensities were increased along with OLP clinical severity, except for the clinical score 1. The ulcerative OLP lesions equivalent to clinical score 4 and 5 were the most painful symptom and had substantial impacts on OHRQoL. Presence of OLP at soft palate had considerable worsened OHRQoL. 2) there was statistically significant association between OLP pain and the intensity of oral impacts (r_s= 0.400, p = 0.001). Conclusion: The results showed the OHRQoL measure would valid against OLP clinical measure. As the discrepancy based on its measurement, using merely OLP clinical indicators were insufficient. OHRQoL measures could complement OLP clinical measures.

Field of Study:	Oral Medicine	Student's Signature .....
Academic Year:	2019	Advisor's Signature .....
		Co-advisor's Signature .....

ACKNOWLEDGEMENTS

This thesis would not have been accomplished without the contribution from these people. Firstly, I own my deepest gratitude to my supervisors, Associate Professor Dr. Pornpan Piboonratanakit and Professor Dr. Sudaduang Krisdapong for their patience, motivation and immense knowledge. Without their persistent help, this thesis would not have been possible. Secondly, I wish to show my gratitude to all of faculty staff for helping me in the clinic. Lastly, I would like to thank my family for kept me going on and supporting me spiritually throughout my life. I would also like to make a special reference to Support Services Department, Royal Thai Armed Forces Headquarters for sabbatical leave approval.

Sasirin Yiemstan

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ABBREVIATIONS

HRQoL	Health-Related Quality of Life
OHRQoL	Oral Health-Related Quality of Life
QoL	quality of life
OLP	oral lichen planus
PROM	Patient-Report- Outcome Measurement
COMDQ	Chronic Oral Mucosal Disease Quality of Life Index
CSS	Change in symptom scale
NRS	Numerical Rating Scale
SD	standard deviation
OIDP	Oral Impact on Daily Performances Index
OLL	oral lichenoid lesion
cm	centimeter
cm^2	square centimeter
CS	Condition-specific
WHO	World Health Organization
OHIP	Oral Health Impact Profile
OLDR	Oral lichenoid drug reaction

CHAPTER 1

BACKGROUND AND RATIONALE

*O*ral lichen planus (OLP) is one of the common chronic inflammatory diseases with manifestations in the oral mucosa, affecting of daily life activity of patients. It has been increasing concern within oral health problems because this disease can lead to open sore in the mouth. OLP can be found in many clinical forms (1, 2). Most clinical forms are white lesion, red lesion and mixed lesion representing as clinical manifestations such as reticular, papular, plaque-like, atrophic and ulcerative type (2). Many studies demonstrated that the majority of patients were female and the lesion onset occurred during the middle age (3). Regarding the sites of the lesion, buccal mucosa is one of the most affected sites, followed by tongue and gingiva (4).

The main symptom in OLP varied from burning sensation to severe painful chronic pain (5). The issue of oral pain and discomfort has received considerable critical attention. Several attempts have been made to relieve symptomatic pain. A considerable amount of literature has been published on various empirical treatments. Most studies focused on pharmacological modalities such as corticosteroids, retinoid, cyclosporin, immunosuppressive agents and also herbal drugs (3, 6). Despite its long clinical success, medication has a number of side effects such as increasing of oral candidiasis for using topical corticosteroid and increasing risk for other systemic conditions for systemic corticosteroid such as hypertension, diabetes mellitus, gastric ulceration, bone mineral density loss, and cataract formation if it is used for long term (7). Therefore, approaches based on non-pharmacological treatment modalities are examined with fewer side effects such as photodynamic therapy, laser therapy and periodontal surgery (8, 9).

In order to categorize the clinical OLP conditions, many clinical indices which based on OLP clinical characters such as size, color and site-based lesion distribution have been developed; however, no existing scales have been accepted worldwide (10). In addition to the nature clinical course of OLP that varies between remission and exacerbation, it could be found that there are differences in distribution patterns and clinical types, making a reproducible measurement impossible (11, 12). For these reasons, using merely clinical scoring scale is not suitable for clinical setting or clinical trial. Therefore, there is also suggestion of including a subjective patient's symptom and Oral-Health-Related Quality of Life (OHRQoL) in the research studies (10, 13).

Since the concept of health now extends beyond the clinical interpretation. Nowadays patient-based outcome measures have been established to amount the concerns of impaired oral health from the patient's perception, frequently mentioned as OHRQoL (14, 15). There are five aspects of patient-report-outcome measurement (PROM) including pain, psychological status, emotional status, social impacts and quality of life (QoL) (16). These reflect that it is essential for clinicians to understand disease from the patient's perspective (13, 17). OLP is a chronic condition for which cure is not possible (11). There are periods of remission and exacerbation (18). Patients suffer from pain or discomfort (19). As pain is one aspect of PROM, several attempts have been made to assess pain perceptions; these pain measurement tools include Numerical Rating Scale (NRS), McGill pain questionnaire, Visual Analogue Scale (VAS), and Change in symptom scale (CSS) with patient's verbal description of their oral condition (16, 20). Besides, the literature available tools used to evaluate pain are unidimensional scales which measure only intensity not the multidimensional evaluation of the

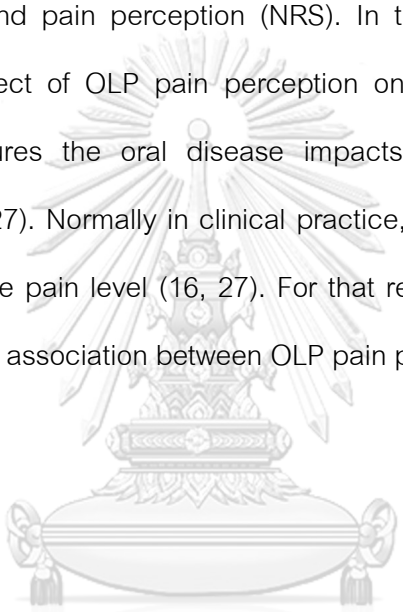
pain perception (21). Therefore, leaning on pain scale data alone is not ample (22). There is a need of research in this area to know the existence of pain perception of each patient in relation to QoL.

QoL can be noted as an index. The use of QoL measures in OLP studies is mostly conduct with three techniques that are population-based studies, questionnaire-based studies and treatment-based studies (14). A variety of QoL measurement tools, both General-Health and Oral-Health related QoL Index, had been involved (6, 13). Moreover, Ni Riordain et al. in 2011 developed a QoL questionnaire for a chronic oral mucosal disease which refers to a specific to Chronic Oral Mucosal Disease Quality of Life Index (COMDQ) (23). Although a specific instrument allows for better measurement of QoL than generic questionnaires (24). There is a need of cross cultural adaption and validation methodology for using these instruments (25).

Oral Health Impacts Profile (OHIP), generic OHRQoL instrument, is widely used in OLP studies (16). This index is designed to assess the oral impact in several dimensions from functional limitation, physical pain, and psychological discomfort to handicap (26). Nevertheless, OHIP index is not a measurement of impacts within behaviors. Therefore, Oral Impact on Daily Performances Index (OIDP) is a measurement instrument developed to evaluate only the ultimate oral disease impacts which beyond the intermediate impacts of pain, discomfort, functional limitation and appearance dissatisfaction. The OIDP ultimate oral impact, including 3 aspects of physical difficulty, psychological difficulty and social difficulty, are impacts on 8 daily life performances. The impacts on daily life performances include eating, speaking, cleaning the mouth, relaxing including sleeping, maintaining general emotional state without being irritable, smiling,

laughing and showing teeth without embarrassment, carrying out major work or social role and contact with people (27). It had been undergone testing to evaluate their measurement properties with reliability, validity and precision (28).

To date, no studies have considered the impact of OLP clinical signs on specific OHRQoL within normal daily activities. Therefore, our main purpose of this study was to find the association between OLP clinical signs, OHRQoL by using OIDP inventory and pain perception (NRS). In the meantime, no studies have evaluated the effect of OLP pain perception on OHRQoL. Even though OIDP instrument measures the oral disease impacts which past the intermediate impacts of pain (27). Normally in clinical practice, the clinicians usually count on patients' subjective pain level (16, 27). For that reasons, another purpose of this study is to find the association between OLP pain perception and OHRQoL.



CHAPTER 2
REVIEW OF LITERATURE

2.1 Oral lichen planus

Oral lichen planus (OLP) is a chronic inflammatory mucocutaneous disease affecting oral mucosa and may accompany by skin lesions. Although the primary etiology is still unknown, current etiopathogenesis of OLP is associated with dysregulated T-cell-mediated disorder, triggering apoptosis of basal keratinocytes. The evidence shows that cytotoxic T cells (CTL or $CD8^+$ T cells) bind to keratinocytes and cause apoptosis of basal cell layer. Keratinocytolysis occur in accordance with the helper T cells (Th cells or $CD4^+$ T cells) and other cells such as myeloid dendritic cells, mast cells and NK cells. The basal cell layer is toxified with the secretion of various cytokines, chemokines and intercellular adhesion molecules (2, 29).

Even if, the causative factors of OLP remain unknown. There are many associated factors seen in OLP, including stress/anxiety, trauma, drugs, chemicals, viral infections, genetic influences (1, 29, 30). The estimated prevalence of OLP is between 0.5% and 2.2% of the general population with variations between different countries (31). In Chiangmai, Thailand, the prevalence of OLP is approximately 3.8% (4, 32).

2.1.1 Clinical features

In general, most patients with OLP are middle-aged adults between 30 and 60 years of age with a female predominance. The buccal mucosa is the most common location affected by OLP; however, OLP may occur at any oral mucosal sites such as lateral and dorsal tongue, gingiva, palate, floor of the mouth and lower lip (33).

Clinically, OLP can be classified as reticular, atrophic, erosive / ulcerative, papular, plaque-like and bullous types. There is also frequently overlap between types, with a blend of reticular, erosive/ ulcerative, and atrophic lesions (2, 19). Reticular OLP is the most common form, usually asymptomatic and involves the posterior buccal mucosa bilaterally. Interlacing white lines, also referred to as Wickham striae, are its characteristic pattern. Atrophic OLP appears as inflamed areas of the oral mucosa, covered by thinned erythematous epithelium. This lesion probably progresses to erosive form when the thin epithelium is abraded or ulcerated (33). Although not as common as the reticular form, erosive or ulcerative forms of OLP is more significant for the patients because the lesions are usually symptomatic, range from a mild burning sensation to severe pain (34). Clinically, this form demonstrates atrophic, erythematous areas with central ulceration of varying degrees and peripheral keratotic white striae. In some cases, atrophic and erosive/ ulcerative forms LP are limited to the gingival mucosa, creating bright red patches and ulcers that involve the full width of the attached gingiva. This reaction pattern is termed desquamative gingivitis (35-37). Bullous form is relatively rare presentation resulting from epithelial separation from the underlying connective tissue. The bulla eventually rupture, leaving erosive areas on the mucosa (38). Plaque-like OLP presents as isolated white patch that similar to leukoplakia. This form is usually located on the tongue (38).

2.1.2 Diagnosis

Although history and clinical appearance can usually be used to make a diagnosis, lesional biopsy is often indicated to differentiate from other conditions for confirmation of the definitive diagnosis and also to exclude malignancy (39).

According to modified World Health Organization (WHO) diagnostic criteria (2003), a diagnosis of OLP requires fulfillment of both clinical and histopathologic criteria (40). The interlacing white striae appearing bilaterally on the posterior buccal mucosa are virtually pathognomonic. Therefore, the diagnosis of reticular OLP can often be made based on the clinical findings alone (41). Conversely, diagnosis of erosive/ ulcerative OLP is sometimes more challenge. Biopsy, often with direct immunofluorescence studies, is usually performed to rule out other ulcerative or erosive diseases (42). Furthermore, patients with solitary erosive lesions, as well as papular and plaque-like OLP, particularly those of the soft palate, the lateral and ventral tongue, or the floor of the mouth, should be obtained for biopsy to rule out dysplastic changes and leukoplakia (41).

Histopathologic features of OLP are characterized by varying degrees of hyperkeratosis of the surface epithelium, degeneration of the basal epithelial layer, and a band-like subepithelial infiltrate of lymphocytes. However, these features are not specific, because other conditions may also demonstrate similar microscopic findings, such as oral lichenoid lesions (OLL): oral lichenoid drug reaction (OLDR), lichenoid contact lesion (OLCL), oral graft-versus-host disease (GVHD), lupus erythematosus (LE), chronic ulcerative stomatitis, and oral mucosal cinnamon reaction (43).

Direct immunofluorescence studies of OLP show deposition of shaggy fibrinogen at the basement membrane zone in most cases. Deposition of clusters of IgM-staining cytoid bodies in the peribasalar area is highly suggestive of lichen planus (44, 45). Serum immunoglobulins G and complement (C3) are also observed (46).

2.1.3 Treatment modalities

There are various treatment modalities for OLP. But there is still no intervention which can completely cure OLP because of its remission nature. The treatment goal is for reduction of symptoms and lesional inflammation. Controlling good oral hygiene should be advised in order to improve healing. As well as concerning the irritation from calculus, sharp teeth or dental restorations and poorly fitting denture should be removed to avoid exacerbation of the lesions. Moreover, amalgam restoration and medication taking should be considered to be caused of oral lichenoid reaction (3).

Pharmacological treatment

The most commonly used medication in OLP is corticosteroid. Topical and systemic corticosteroids are widely used for reducing inflammation (47). Topical coricosteroids, for instance triamcinolone acetonide, fluocinolone acetonide, fluocinonide, betamethasone valerate, clobetasol propionate and hydrocortisone, have been used effectively in several preparation; orabase, lozenge, spray, mouthwash, ointment, and oral suspension (3). Systemic corticosteroid should be only used when lesions do not response to topical corticosteroids or in patients with diffuse, multiple or mucocutaneous lesions (33). The usage of antifungal drugs together with corticosteroids has been reported to improve symptoms of OLP since Candida infection may exacerbate symptomatic

OLP (47). Furthermore, other several medications were used for treat OLP including cyclosporin, retinoids, tacrolimus, aloe vera gel, curcuminoids, tumor necrosis factor-α (TNF-α), antimalarials, azathioprine, dapsone and interferon (48).

Non-pharmacological treatment

Isolated and non-healing erosive lesions were recommended to do surgical excision. Likewise, cryosurgery, CO_2 laser and photochemotherapy have been used to treat severe OLP and resistance to other treatment (49, 50). Due to oncogenicity, photochemotherapy with psoralen ultraviolet A (PUVA) should be concerned (43). Other alternative treatment is free gingival graft surgery which can completely remove localized erosive lesions but it may also develop lichenoid reaction from mechanical trauma (3).

2.2 Oral lichenoid lesions (OLL)

There is also the lichen planus- like lesion caused by a known trigger such as a variety of drugs and restoration. In addition, there is also OLL in patients with acute or chronic graft-versus-host disease (GVHD) (43). OLL present in several clinical characters:

Oral lichenoid contact lesions (OLCL) are localized to the mucosa in close contact with the restoration. They are a result from allergic contact stomatitis with delayed type immune mediated hypersensitivity (51). These lesions are seen in direct topographic relationship to dental restorative materials, most commonly in corroded amalgam (52). Likewise, they can be frequently found in other contacted agents including cinnamon which are widely used in chewing gum, toothpaste and confectionary (43).

Oral lichenoid drug reactions (OLDR) are triggered by a very wide range of drugs. The more common causes are oral hypoglycemic drugs, beta-blockers, captopril, angiotensin-converting enzyme inhibitors, nonsteroidal anti-inflammatory drugs (NSAIDs), gold salts and penicillamine (53). The cause of drug reactions is still unrevealed. It is quite difficult to find the causative drug since the reaction may persist months or years after administration. Proof of causation requires withdrawal and re-challenge after healing (54).

Oral lichenoid lesions of graft-versus-host disease (OLL-GVHD) are occurred in bone marrow transplant patient which transplanted lymphocyte attacks the recipient's tissue. The diagnosis is made primarily with history and effects in other organs (55).

Features suggesting a lichenoid lesion are onset occurrence closely associated with the potential cause, unilateral or unusual distribution, localized lesion in contact with potential cause. Since they share similar clinic-pathologic pictures, the role of biopsy is used to exclude other conditions, rather than distinguish lichen planus form a lichenoid reaction (56).

2.3 OLP pain measurement

Pain is defined as unpleasant sensory and emotion experience associated with tissue damage (57). The nature of pain is subjective and there are no obvious objective measures (58). To quantify their pain, clinicians must rely on patient to provide key information of type, localization and pain intensity (59). In addition, current evidence provides a general recommendation that pain is needed to be treated. Therefore, clinicians should assess as well as record their patient's pain

levels and pain estimation in routine practice and in clinical settings (60). For these purposes, several pain intensity scales had been developed and validated (21).

Pain or burning sensation is one of the most common chief complaints reported by OLP patients (61). The most common pain rating scale used in OLP studies are Visual Analog Scale (VAS), Numeric Rating Scale (NRS) and Verbal Rating/ Descriptor Scale (VRS/ VDS) (16). All three tools were found to be valid and reliable in both clinical practice and research (20).

The VAS scale, comprise of 100 mm line, is the most common used in OLP studies. This scale can be used by asking patients to indicate which point along the line that represents their pain. Since the VAS scale has ratio properties, the normal distribution data is allowed for parametric analysis (62). Although the VAS scale had advantages, a number of studies found difficulties in practical use particularly in the elderly and impaired cognitive level population (63).

The NRS scale is secondly used tool. This consists of 11-point scale where the end points are “no pain” and “extremely pain as bad as it could be”. This scale can be delivered or presented written or verbally. The patients are requested to state the number representing their level of pain intensity (64). The NRS scale, an easy-to-use instrument, is extremely simple to administer and score. The tool can be used from ages of children older than 8 years of age who are able to

understand numbers and also adults (62). For statistical point of view, the NRS scale is interval scale which allows processing data for parametric analysis, which is more powerful than non-parametric testing (62).

Moreover, Change in Symptom Scale (CSS) is also used. The CSS consists of a numeric list of adjectives which describe change in symptom. The scale comprises of a numeric list of adjectives which describe change of pain. Patients are told to choose the word which represents their pain level (64). The older adults and children find it easier to use (21). In contrast to VAS and NRS, this scale provides data in a categorical scale thus limiting the precision (62).

All 3 pain rating scales are widely accepted. Nevertheless, these provide data only pain intensity levels which is not comprehensive approach. The evidences suggest of understanding in more complex multidimensional pain perception (21). Further studies have advocated for development or improvement of special pain scale on QoL for specific patients (21).

2.3.1 Oral health-related quality of life (OHRQoL) and OLP pain

Existence of discomfort or pain is one of 4 topics in OHRQoL research field (65). Furthermore, evaluation of the pain of OLP is important for monitoring disease progression and treatment responses (66). Therefore, there is a need for instruments to measure the signs and symptoms of OLP that are easy to use and

sensitive enough to monitor changes in signs and symptoms and in response to treatment.

The study of Chainani-Wu et al. in 2008 had validated the VAS, NRS and CSS in measuring symptoms of OLP. The result indicated that the 3 scales showed good correlation with each other. The NRS had stronger correlation with OLP clinical signs that may reveal the better accuracy of this scale (20).

Hee-Kyung Park et al. in 2012 conducted the study of the correlation of OLP semiquantitative scoring system, the reticulation/keratosis, erythema and ulceration (REU) system, with pain. They showed that this scoring system correlated with the NRS pain scale for pain (66).

2.4 OHRQoL assessment

The disease affects not only a body but also mind. So, it has become a necessity to determine the feelings and perceptions of patients (67). QoL is gaining importance in public health research and also clinical practice (67, 68).

OHRQoL is assessed by the patient's judgment in four groups of factors that affect their well-being. These comprise of how their mouth functioning, pain/discomfort, psychologic aspects and social aspects (16, 67). Essential aspects of assessment cover both qualitative and quantitative measurement methods. In general, these broadly defined concepts and domains focus on opportunity, health perceptions, social, psychologic and physical functional status (69). Quantitative assessment methods of OHRQoL consist of many indices. For this purpose, a large number of standardized questionnaires had been developed. Those undergone testing for reliability, validity and precision. In order to adequately reflect the impact of oral conditions on an individual's personal and

social well-being, both generic and disease-specific instruments exist for that purpose (28, 69).

There are various approaches to the assessment of OHRQoL. Provided with three categories of OHRQoL measures, assessment of the societal impact to oral conditions, global self-ratings and multiple-item questionnaires are commonly used (69). There are differences in focus, length and format of questionnaires. Some limited to a few dimensions while others capture more dimensions ranging from chewing to social relations. General health and general oral health instrument had been used in studies of populations or groups of patients (70, 71). Mostly OLP studies administered QoL instrument, namely the Oral Health Impact Profile (OHIP), Oral Health-Related Quality of Life-UK (OHRQoL-UK) and Chronic Oral Mucosal Disease Quality of Life Index (COMDQ). These instruments are generic to a range of chronic oral mucosal diseases (16, 72).

Different QoL instruments have their advantages and disadvantages. There is significant heterogeneity in the focus, length and the format of the response. As indicated, these questionnaires focus on content area limited to an inquiry about the frequency, the severity and the importance of a specific problem (28, 69). The potential of these disorders is significantly affected on oral function, orofacial appearance and social interaction. Thus, OHRQoL measures, including objective and subjective assessment, are useful for evaluating efforts to prevent disabling chronic diseases and assessing their effectiveness.

2.5 Oral Impact on Daily Performances index (OIDP)

OIDP is a model for measuring oral health. The patients answer an interview questionnaire evaluating the impact of the disease on the QoL. OIDP had

been introduced by Adulyanon et al. in 1997. This index evaluates OHRQoL with impacts on daily life performances in 3 dimensions measured including physical difficulty, psychological difficulty and social difficulty (27). The theoretical framework was modified from Locker's framework in 1988 (73) and International Classification of Impairment, Disability and Handicap (ICIDH) from the World Health Organization (WHO) in 1980.

The OIDP instrument is a multiple-item index, composed of 8 questions which measure of performances focusing on function, pain and discomfort, self-image and social interaction. This concept is known as the following three levels (69).

Level 1: Oral impairments

Level 2: Intermediate impacts: Pain discomfort, functional limitation, appearance dissatisfaction.

Level 3: Ultimate impacts: Impacts on daily life performances in physical difficulty, psychological difficulty and social difficulty.

Oral impacts to daily performances in each dimension are (69)

- **Physical difficulty**: Eating, speaking and cleaning the mouth.
- **Psychological difficulty**: Relaxing including sleeping, maintaining general emotional state without being irritable and smiling, laughing and showing teeth without embarrassment.
- **Social difficulty**: Carrying out major work or social role and contact with people.

All questionnaires are limited to the negative impacts of oral diseases. The index assesses oral impacts during the past six months with the performance of 8 daily activities.

Example of questions includes 4 parts of questions. These questions will be asked both frequency and duration period which the impact affected them in 8 activities such as (69)

A: In the past six months, do you have dental problems caused one difficulty in eating and enjoying food? If any oral impact is detected on a patient, the frequency and the severity of their effect on daily life may be asked.

B: Have you had this difficulty on a regular periodic basis or for a period?

C: During the last six months how often have you had this difficulty?

D: Using a scale 0 to 5, which number reflects what impact the difficulty in eating and enjoying food had on your daily life?

Frequency scores range from 0 to 5. The OIDP questions had following response format. “Every or nearly every day” = 5, “three to four times a week” = 4, “Once or twice a week” = 3, “Once or twice a month” = 2, “Less than once a month” = 1, “Never affected” = 0.

The patient are asked to rate the severity of impacts on daily performances resulted from each activity problems on a 6-point Likert scale “Very severe” = 5, “Severe” = 4, “Moderate” = 3, “Little” = 2, “Very little” = 1, “Never affected”= 0.

OIDP scores are calculated by multiplying the frequency score by the severity score which is a performance score (ranging from 0-25). Then, the sum of

eight activity scores results in the total impact score. The total score of the questionnaire ranges from 0 – 200. The score is then divided by the maximum possible score which is 200. Then, the score is multiplied by 100 to get a percentage score. Finally, the overall score ranges from 0 to 100 (74). The higher scores indicate poorer OHRQoL.

Moreover, OIDP outcomes can be expressed in different ways. Oral impacts will be demonstrated in scope with extent and intensity of impacts. The extent score is the number of performances with impacts (PWI). That demonstrates how broad the effect of the mouth on QoL (ranges 0-8) (74).

In addition, the concept of the intensity of oral impacts was presented. The intensity of oral impact was classified according to the highest performance score among the eight performances. Table 1 demonstrated the distribution of the performance scores calculated by multiplying the frequency score by the severity score and were graded into 5 groups: very little (1-2), little (3-5), moderate (6-12), severe (15-16) and very severe (20-25). The intensity of impacts reflected how severe of the impact on QoL (74, 75).

Condition-specific (CS) impacts are impacts caused by specific oral conditions, recognized as the oral conditions perceived to be the main causes of impacts. CS impacts include caries, periodontal diseases, edentulism, oral lesions, discolorations, malocclusion, traumatic dental injuries and natural processes (76). The importance of CS impact is analyzed as responses in numerical scores.

Table 1 Classification of oral impact intensity

Index	Frequency/severity score		Frequency/severity score	Performance score (Frequency score x Severity score)	Intensity level*
OIDP	1 2	x	1 1	1 2	Very little
	3 4 2 5	x	1 1 2 1	3 4 4 5	Little
	3 4 3 5 4	x	2 2 3 2 3	6 8 9 10 12	Moderate
	5 4	x	3 4	15 16	Severe
	5 5	x	4 5	20 25	Very severe

* The intensity of oral impact was classified according to the highest performance score on any activity among the eight performances

There are considerable numbers of OHRQoL studies in Thailand. Among these OIDP measure is widely used. The OIDP index had been validated and tested reliability in all-aged group of Thai people both in Thai children, adolescents and older Thai individuals (74, 77, 78).

In a study of Srisilapanan et al. in 2003, the cross-sectional study conducted in 707 older individuals, 60-74 years in metropolitan area of Chiang Mai. They selected the OIDP to evaluate the oral impact on daily performance in older people. With obtained data, the author formulated the model of impact-related treatment needs to assess the partial denture treatment need estimation.

They concluded that there was large difference of estimated prosthetic treatment need. In addition, they also reported the prevalence of oral related impacts on the QoL in older Thais (78).

Since the concept of OHRQoL measures for children should be different from those for adults or elderly. Gheranpong et al. in 2004 had modified the OIDP index and evaluated its psychometric properties in 513 children, aged 11-12 years, in Suphan-buri province (79). They concluded that CHILD-OIDP index consisted of validity, reliability and practical measurement of OHRQoL in 12-year-old Thai children (74). Moreover, the CHILD-OIDP index had been used in nationally representative of the children aged 12 and 15-year-old in the sixth Thailand National Oral Health Survey (80). Thai national survey was conducted in 2007 for assessment of the prevalence and characteristics of oral impacts on daily life. The result showed that impacts were mostly on eating performance which toothache and oral ulcers were the two significant perceived causes. Later then in 2012, Krisdapong et al. explored the association between OIDP scores and other indicators. They had formulated proposal for oral health goal in 12-year-old children (76). As above mentioned, these confirmed that OIDP instruments have been previously validated in all Thai populations. Moreover, OIDP measures were also used in the seventh and eighth Thailand National Oral Health Survey (81).

Additionally, the OIDP index had been validated in university clinical settings in various fields such as surgery and prosthetic patients (82, 83).

The mode of administration of OIDP consists of both interview and self-administration (84). The advantage of interview is detailed information such as attitudes, feeling and opinion that can be evaluated in depth analysis. The interview can help to get the sufficient information as needed because the relation between the interviewer and the interviewee can be developed. Likewise, the conversations have ability to find out the actual reasons behind the problem. Finally, one of the major advantages of interview is feasible that depends on the situation it can be framed differently (28).

On the other hand, the main disadvantages of interviews are time consuming. The process includes preparation for the interview, taking interview and interpretation of the response which required much time (28). In addition, the success of an interview depends on the efficiency of the interviewer which requires the trained interviewer (69).

2.6 The rationales for selecting OIDP index

The rationales for selecting OIDP index used in a research question because it is a valid and reliable measure for use in clinical trials or in population studies (35). In addition, there is evidence of reliability, feasibility and acceptability of OIDP measure. The index was set up and also validated in an adult Thai

population by Adulyanon et al. in 1997 and later in the study of assessing prosthodontic dental treatment needs in older adults in Thailand by Srisilapanan et al. in 2003 (27, 78). It can also be comprehensible for every age group (74). It had been translated into languages other than English including Portuguese (85), Malagasy (86), Persian (87), Swedish (88), Malay (89), Kiswahili (90), Arabic (91), Nepali (92), Spanish (93), Korean (94), Norwegian (95), Croatian (96), French (97), Bosnian (98) and Albanian (99).

2.7 Findings from cross-sectional population studies of OLP impact in normal daily activities

Although OLP is generally not life-threatening; the consequence of OLP can impact on many aspects of QoL (12). The evidence shows that it has a negative influence on daily activities (24). There are the direct and indirect impacts of OLP on the well-being of those affected in these following activities

2.7.1 Eating

Eating has been reported in association with several medical conditions and significantly affects QoL (100). OLP patients always complain of mouth sensitivity from usually tolerated spices, acidic liquid or spicy flavours (101). The temperature of food is also related to the discomfort. Owing to their sensitive oral mucosa, patients usually complain of painful gums and discomfort when eating with some particular foods. They found difficulties with some types, texture and temperature of food (12, 102). Spicy or acidic food seems to be the most dietary problem (100). Besides, the rough and crusty food has been also reported to be the problem (100). Therefore, the goal of treatment will be providing erosive lesions to heal and reduce pain and difficulty in eating and drinking (102).

Due to mouth pain and mouth sensitivity, OLP patients frequently avoid exacerbating symptoms or chronic soreness by altering some diet and limiting the types of food and drink. These include foods of a softer, more liquid consistency and the avoidance of highly seasoned, spiced, or acidic food. In severe cases, avoiding eating or drinking may lead to weight loss or malnutrition (100). Patients reported a different degree of bother from ulceration and avoidance of food. Because eating and drinking are essential sources of pleasure. Food satisfaction may be compromised thus affecting joy, social ability and QoL (100).

2.7.2 Speaking

Pain or discomfort when speaking is a symptom with an ulcerative form of OLP. The study of Larsen et al. in 2017 found that patients with OLP, lichenoid lesions and generalized stomatitis reported more prevalent xerostomia symptom than the healthy patients. A questionnaire regarding xerostomia was used and then gave the scoring of the severity of xerostomia. They found that 12.2% of the patients reported they experienced an annoying feeling of dry mouth thus making speech difficult (103). Also, Baker et al. in 2006 studied the xerostomia patients with the psychometric properties by using both of short forms of OHIP and OIDP. Although they indicated that OHIP accomplished better than did OIDP in xerostomia populations, both measures appeared beneficial measures of OHRQoL in xerostomia (104). Chronic xerostomia remains a significant burden for many individuals, particularly affecting speech (105).

2.7.3 Cleaning abilities

Atrophic or erosive OLP lesion is commonly present on the buccal mucosa, tongue and gingiva. The involvement of gingival OLP leads to the worse

of the periodontal status as compared with the healthy persons (106, 107). The affected gingival epithelium is very fragile and easily detached in response to any minor trauma. The symptom presents with gingival pain and bleeding. Patients always complain of having discomfort or pain when carrying out daily oral hygiene practices. Therefore, careful attention should be paid to oral hygiene measures. In addition, the study of Larsen et al. in 2017 indicated that OLP patients had discomfort with particular dentifrice. The study reported that there might be an allergic reaction in oral hygiene products which their suggestion of mild dentifrice is strongly indicated in OLP patients (108).

Limited daily oral hygiene routine causes plaque accumulations thus adversely affects patient's gingival lesions and periodontal status (107, 109). Many studies provide evidence that effective plaque control with rigorous oral hygiene is a fundamental prerequisite for the treatment of any oral mucosal diseases (110, 111). Painful gingival lesions of OLP can be improved by effective plaque control and periodontal treatment (111-113). Therefore, efficient gentle oral hygiene practices with appropriate method minimizing injury to the gingival tissue should be considered. The motivation of behavioral skill protocol should be introduced to encourage patients having adequate self-performed plaque control (114). Efficient cleaning ability of home oral hygiene may contribute to the improvement of OLP lesion and periodontal status which favoring the QoL (110, 113).

2.7.4 Relaxing and sleeping

Sleep disorders are common problems that lead to neuropsychology deterioration. The study of Adamo et al. in 2014 showed that OLP patients had higher sleep disturbances when compared with healthy persons

(115). Many studies showed that poor sleep quality could lead to chronic fatigue, depression, hypertension, loss of concentration, anxiety, irritability, reduced activity, loss of alertness during the day. Lack of sleep also affects the pain threshold prone to increased sensitivity to pain (116). There may be from amplifying pain signals, being paid greater attention and more focusing on the related negative emotion (117). Lastly, an impact to habitual sleep efficiency may contribute to using of sleeping medication (115).

2.7.5 Demonstrating in emotional stability

Psychological alteration is associated with poor oral health (118). It is also associated with some oral pathology such as burning mouth syndrome, recurrent aphthous stomatitis and OLP (119-121). Although the existence of psychological changes may not be a direct etiologic factor for oral diseases, it should be remembering that stressors may play a key role in occurring of these diseases. Any causal association between psychological disorders and OLP are also vague (122). It is not clear whether the latter precedes the former or vice versa. Moreover, stress and the absence of psychological well-being worsen their symptoms (122, 123). Various OLP studies reported the correlation of the presence of stressful life events with the time of onset/exacerbation of OLP (124).

OLP has interesting been linked to psychological and mental health issues. Some observational studies reported that greater stress and anxiety and higher levels of depression scores in OLP patients compared with healthy patients (125, 126). Patients with multiple erosive lichen planus had more sign of depression than patients with unilocal erosions (125). Patients were stressed when their oral symptoms were severely preventing themselves from social contact such as eating and drinking with others (127).

2.7.6 Smiling without feeling embarrassment

A beautiful smile is placed on healthy dental anomalies and soft tissue. This smiling composed of harmony between the teeth, gingiva and lips. Preferences of color and texture account for facial attractiveness. Lips are highly visible, thus, changes in lip color and texture might affect self-perceived satisfaction with smiling (128). Women patients may have difficulty in the application of make-up (129). The patients may have dissatisfaction with appearance or eventually affect the QoL, related to aesthetic deterioration.

Patients with lichen planus at lips quite complains of eroded or dry, cracked lip and possibly painful. The patients reported symptoms including pain, burning, bleeding and crusting. Clinically, lip color of OLP lesion shows erythema and keratosis with exfoliation of the vermillion border (129). The lip clinical characters show various forms including keratotic plaque, white striae, erythematous atrophic area and ulceration (129). Moreover, the resolution of OLP is often accompanied by post-inflammatory hyperpigmentation which shows in brown or black color (130). Lip texture presents with rough area and ulceration (129).

2.7.7 Carrying out major work or social role (For the elderly, this item is changed to carry out light physical activities)

Many chronic conditions can compromise the QoL and create limitations and disability. WHO inspires the economic consequences of chronic diseases involving the estimation of the economic burden (131). From an economic perspective, the OLP disease might affect the financial cost. In 2016 Ni Riordain et al. reported the economic burden of OLP in a UK population. OLP

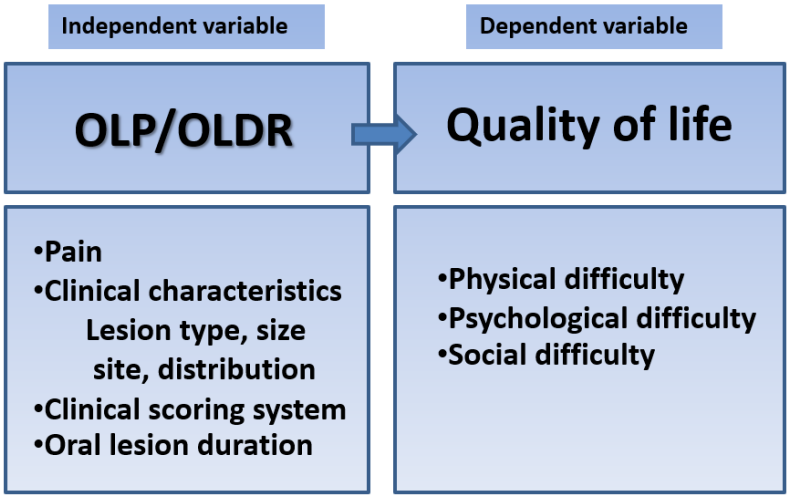
patients had their dental visits in the oral medicine unit and also involved with their general medical practitioners as well as their general dental practitioner more frequently (132). Furthermore, social cost and work loss or school absence might be also affected. The annual leave used for dental visits might equate to decreased productivity and can have a major effect on the population's burden of illness in a given year. Lastly, socio-economic disparities in disability days are meaningful to the economy (133).

2.7.8 Socialisation

The social impact of OLP would cause the disruption of social activities or avoidance of social interaction consisting of the difficulty of social gathering or eating out parties (11).

From the study of Ni Riordain et al. in 2011, there are other issues affecting on the patients' quality of life including treatment limitations and side effects, unpredictable flare-up with OLP and the delay issue of diagnosing condition (12).

2.8 CONCEPTUAL FRAMEWORK



KEYWORDS

Oral lichen planus, Quality of life, Oral impact on daily performance, OIDP index, Oral health related quality of life, Pain

RESEARCH OBJECTIVES

1. To associate OLP clinical sign with OHRQoL and pain perception.
2. To associate pain in OLP with OHRQoL.

RESEARCH QUESTIONS

1. Is there an association between OLP clinical sign and OHRQoL as well as pain perception in Thai OLP patients?
2. Is there an association between pain and OHRQoL in Thai OLP patients?

RESEARCH HYPOTHESES

1. More severe OLP clinical signs associates with poorer OHRQoL and more pain.
2. More pain in OLP associates with poorer OHRQoL.

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CHAPTER 3
RESEARCH METHODOLOGY

A cross-sectional study was carried out to collect data of sociodemographic, oral chief complaint, patient's pain intensities, OLP clinical characteristics and OHRQoL. This chapter explains all research methodological procedures including sampling design, data collection, study implementation and data analysis.

3.1 Sample

3.1.1 Study area

A cross-sectional study was conducted in dental setting at the Oral Medicine Clinic, Faculty of Dentistry, Chulalongkorn University.

3.1.2 Study participants

New or follow-up OLP patients who already had a previously definitive diagnosis of OLP at the Oral Medicine Clinic, Faculty of Dentistry, Chulalongkorn University were included in the study.

Inclusion criteria

1. Patients with clinically and histopathologicaly diagnosed as OLP or compatible with OLP (40).
2. OLDR patients with history of taking medications at least 1 type that was associated with this reaction.
3. Patients with Thongprasom sign score from 1 to 5
4. Patients aged 18 years and above.
5. Patients can communicate.
6. Patients can provide consent.

Exclusion criteria

1. OLP patients have no oral lesion (complete remission)
2. Patients have pregnant.
3. Current smokers or ex-smokers with evidence of smoking within the past 6 months.
4. Patients with current active infection or acute illness of any kind.
5. Patients with presence of any other oral mucosal lesions.
6. Patients are unable to communicate.

3.1.3 Sampling design and sample size calculation

The sample size was calculated for estimation the difference between two proportions. The sample size per group was given as shown in equation.

$$\text{Sample size } n = \left[\frac{Z\,\alpha/2\sqrt{2P(1-P)}+Z\beta\sqrt{p_1(1-p_1)+p_2(1-p_2)}}{(p_1-p_2)^2}\right]^2$$

When p_1 was proportion of outcome in the first group

p_2 was proportion of outcome in the second group

P = (p1+ p2)/2

$Z\,\alpha_{/2}$ = Standard normal variate (at 5% type I error ($P < 0.05$) it is 1.96

$Z\beta$ = Standard normal variate (at the power of 80%) it is 0.84

In terms of sample size calculation, estimated proportions of OLP patients was used to calculate sample size in this study. Sample sizes related in the literature for similar studies were taken into consideration. From the previous study of Taboli et al. in 2009, the QoL in patients with oral mucosal disease in dermatological practice had been studied. Proportion of OLP patients with painful

aching effecting QoL as 35.40% while proportion of patients with painful recurrent apthous stomatitis effecting QoL as 60.9% (71). The sample size was calculated by using 80% power and 95% confidence interval level. The estimated sample size was 57. Ten percent oversampling was 63. To allow for the total number, the estimated total sample size of 70 patients was sufficient to obtain relevant results from a statistical point of view.

3.2 Data collection

Parameters including five parts were sociodemographic data, patient's self-symptoms perception, pain intensities, impact on OHRQoL and the characteristics of OLP. Data were collected through personal interview and oral examination.

3.2.1 Sociodemographic data

The data including age, sex, patient type and OLP duration since first diagnosis were collected from dental chart review.

3.2.2 Patient's self-symptoms perception

Reported oral symptoms were assessed by the question "Have you experience the presence of "burning sensation", "roughness", "abrasion or ulceration" or "blisters". Each symptom was assessed as presence or absence. The others except above mentioned were defined "others".

3.2.3 Pain intensities

Participants were asked about their current pain intensities using NRS scale. It consists of 0 to 10, in which "0" signified no pain at all and "10" presented the worst imaginable pain. Patients were asked to rate the number that

best represented their pain intensities. Later, the NRS scale was categorized as mild pain (0-3), moderate pain (4-7) and severe pain (8-10) (21).

3.2.4 OHRQoL

For OHRQoL measure, participants were interviewed by one well-trained and calibrated interviewer using the Thai version of Oral Impacts on Daily Performance (OIDP) index (27). Subjects were asked about whether their OLP lesions restricted their ability in any of the 8 performances during the recall memory period of past 6 months. The difficulties on 8 daily activities include: a) eating: b) speaking and pronouncing clearly: c) cleaning the mouth: d) relaxing including sleeping: e) maintaining general emotional state without being irritable: f) smiling without embarrassment: g) carrying out major work or social role: and h) contact with people were assessed. The questions involved if the OLP lesions caused any difficulties within 8 daily activities as above mentioned. If no impact was experienced, then a zero score was assigned.

If a respondent experienced an oral impact for each of the aforementioned performances, the frequency of oral impacts on a performance were asked. The patients were asked about how often OLP have caused any difficulties during the past 6 months. For chronic pattern of the impact, the frequency of the effect was scored using 6-point scale, in which “0” signified never affected, “1” presented less than once a month, “2” presented once or twice a month, “3” presented once or twice a week, “4” presented three to four times a week and “5” presented every or nearly every day. In case of the oral impacts which occurred in periodical pattern, the frequency of the effect was scored in the total day of the oral impact in which “1” presented 1-5 days, “2” presented 6-15

days, “3” presented 16-30 days, “4” presented 1-3 months and “5” presented more than 3 months.

Lastly, severity of the performance impacts had on daily life were assessed. The questionnaire items provided information about the severity of burdens that participants had experienced. Participants were asked to rate the severity of impact using 6-point Likert scale in which “0” indicated never affected, “1” indicated very little, “2” indicated little, “3” indicated moderate, “4” indicated severe and “5” indicated very severe.

3.2.5 Clinical characteristics

The data about clinical characteristics of OLP or OLDR were recorded. Participants were examined for OLP clinical signs by one trained and calibrated dentist.

The lesion types including clinically morphologic findings presenting as white reticular type (R), atrophic type (A), erosive/ulcerative type (U), bullous type (B), pigmented type (P) and plaque type (Pa) were recorded (2). The OLP lesion sites were examined including the buccal mucosa, tongue, lip, gingiva, palate, floor of the mouth and soft palate.

The OLP lesion distribution in the buccal mucosa was recorded each of the right side and the left side. The tongue was examined in dorsal and ventral side. The lip was examined in upper and lower lip. The gingiva was recorded as upper arch and lower arch. The palate, floor of the mouth and soft palate were examined.

The Thongprasom sign scoring criteria was used in which was categorized into a 5-rank scale as demonstrated (61).

score 5: white striae with erosive area ≥ 1 cm^2

score 4: white striae with erosive area <1 cm^2

score 3: white striae with atrophic area ≥ 1cm^2

score 2: white striae with atrophic area <1 cm^2

score 1: mild white striae only

score 0 indicate no lesions or normal mucosa.

3.3 Study implementation

3.3.1 Preparation of documents

The standard forms and criteria used for clinical oral examinations and personal interview were used in the study (Appendix A, B, C).

3.3.2 Training and calibration exercises

a) Training

One interviewer was trained and calibrated before collecting data against the gold standard. Extensive training and the calibration procedure were carried out at the Oral medicine dental setting, Faculty of Dentistry, Chulalongkorn University. Ten participants were collected for calibration against gold standard. The inter-rater reliability of study measurement was estimated against the gold standard with intraclass correlation coefficient (ICC). Reliability tests was done through the evaluation of correlation among items according to the criteria for each condition. The analyses on inter-examiner reliability showed high inter-examiner reliability (ICC = 0.910, $p < 0.001$).

b) Intra-examiner reliability

Ten percent of participants were re-examined and re-interviewing for testing intra-examiner reliability. The analyses on intra-examiner reliability exhibited very good agreements (ICC = 0.911, $p < 0.001$).

3.4 Data analysis

All statistical analyses were performed by IBM SPSS statistics for Windows, version 22.0. The continuous variables including the OIDP percentage score and the NRS score were checked for normal data distribution with the Kolomogonov Smirnov normality test. Data were not normally distributed ($p < 0.001$). Therefore, nonparametric tests including the Kruskal-Wallis test and the Mann-Whitney U test were used for comparison test across groups. The level of significance was set at $p < 0.05$. Statistical analyses included the followings:

3.4.1 Descriptive statistics

Descriptive data was presented as frequencies, percentage, mean ± standard deviation (SD), median and range which were:

a) Sociodemographic characters: gender was assessed as female and male. Age was presented in continuous data and dichotomized into two groups of younger (18-32 years) and older (33-85 years) (134).

b) Pain perception intensity: the NRS score was described in terms of continuous data (0-10) and was categorized in to 3 levels of mild pain (0-3), moderate pain (4-7) and severe pain (8-10) (21).

c) Patient's self-symptom perception: the presence of burning sensation, roughness, abrasion or ulceration and blisters of the surface of the oral mucosa were reported.

d) OLP clinical variables: the diagnosis of OLP and OLDR, patients type including new patient, recall patient with strictly medication adherence and recall patient with infrequent medication adherence were assessed. Oral lesion duration was reported with mean and sub grouped into 3

groups: under 1 year, between 1-5 years and more than 5 years (135). The distributions of OLP lesion type including reticular, atrophic, erosive or ulcerative, bulbous and plaque type were included. The involved lesion sites at the buccal mucosa, tongue, lips, gingiva, palate, floor of the mouth and soft palate were presented. In addition, number of OLP affected sides and of OLP clinical severity according the Thongprasom sign scoring system were also displayed.

e) OHRQoL data: The prevalence of experiencing impaired QoL for at least one aspects and each of 8 daily performances were reported. The OIDP score calculation in this study presented with the percentage score (0-100) and the intensity level (0-5). To obtain the overall OIDP score, the performance score (0-25) for each activity was calculated by multiplying the frequency score (0-5) by the severity score (0-5). Then, the sum of eight activity scores resulted in the total impact score ranging from 0–200. To get a percentage score, the total impact score was then divided by 2 (74). In addition, the severity of impact was described as the OIDP intensity level. It was classified with the highest performance score into 5 groups: very little (1-2), little (3-5), moderate (6-12), severe (15-16) and very severe (20-25) were also displayed (74). OIDP scores were reported with mean ± SD, 95% confidence interval (CI), median, minimum and maximum. In addition, the extent of impact was described as percentage of performances with impacts (PWI).

3.4.2 Association of variables

3.4.2.1 Association of the Thongprasom sign score and the OIDP score

Spearman‘s correlation was used to test the relationship between the percentage score (0-100), the OIDP intensity level (0-5) and

Thongprasom sign score (0-5). The OIDP scores were stratified for each Thongprasom sign score and compared to one step lower category with the Mann-Whitney U test.

3.4.2.2 Association of the Thongprasom sign score and the NRS score

Spearman's correlation was used to test the relationship between the NRS score (0-10) and Thongprasom sign score (0-5). The NRS score were rated in relation to the Thongprasom sign score. The Mann-Whitney U test was used to evaluate the difference between one step lower category.

3.4.2.3 Association of the NRS score and the OIDP score

Spearman's correlation was used to test the relationship between the NRS score (0-10) and the OIDP intensity level (0-5).

3.5 Ethical consideration

This study had been approved by the Ethics Committee of the Faculty of Dentistry Chulalongkorn University with the study code HREC-DCU 2019-044 (Appendix D, E). Participant information sheet was in an appendix F. The patients were verbally informed about the aims and methods of this study and invited to participate in the study. Then, they were informed about their oral conditions and health education was provided.

3.6 Significance of research

This research provided information with scientific rationale addressing the OLP problems in QoL aspect. Considered the QoL impairment as an outcome in this study may add the information in which clinical status best predict QoL deterioration. The obtained data may help to set the modified OLP index. This may serve the purpose of patient assessment, treatment plan and monitoring

disease activity as well as observing for treatment response both in clinical settings and research studies. Cumulatively, these obtained findings were supported the construct validity of using OIDP inventory in clinical settings.

CHAPTER 4
RESULTS

This chapter presents the descriptive results of the research study with regard to the patient, the OLP clinical characteristics and the OHRQoL. In addition, the associations between the OLP clinical characteristics, the OHRQoL and the pain intensity were explored.

4.1 Patient characteristics

Estimated total sample size was 70 patients. One participant failed to meet the inclusion criteria and was excluded from the analysis. Therefore, a total of 69 patients (63 OLP and 6 OLDR) were enrolled in the study. Data was shown in Table 2. Most patients were female, 55 women (79.7%) and 14 men (20.3%). The female and male ratio was 4:1. About 82.6 percent of the participants were the recall patients. The mean age was 55.08 ± 13.85 years. The mean duration was 44.96 ± 49.61 months. Forty-three of them (62.3%) have had OLP lesion for 1–5 years followed by more than 5 years (20.3%) and less than 1 year (17.4%). Almost all of patients (95%) complained of pain with the mean NRS pain scores were 2.56 ± 2.32 (ranged 0–8). Average pain intensity perception was mostly mild pain (59.4%) followed by moderate pain (34.8%) and severe pain (1.4%). Three patients (4.4%) reported of no pain.

Patient's self-symptom perception comprised of the negative effect. All patients perceived about the presence of "burning sensation". The second most common symptom were having the "roughness sensation" in the oral cavity (62.3%), followed by having the "abrasion" or the "ulceration" (44.9%). In addition, patients had the "blister" about 8.7%. Others 3 patients (4.3%) complained of noticing the red and white lesions in the mouth, having numbness at the buccal mucosa and the tongue.

Table 2 Distribution of sociodemographic, clinical status and pain perception variables in OLP patients

Characteristics		Total n=69 (%)
Sociodemographic		
Gender	Female	55 (79.7)
	Male	14 (20.3)
Age	Mean ± SD: 55.08 ± 13.85 years, range 21-86 years	
	-15-32 years	5 (7.2)
	-33-85 years	64 (92.8)
Clinical status		
Diagnosis	Oral Lichen planus (OLP)	63 (91.3)
	Oral lichenoid drug reaction (OLDR)	6 (8.7)
Patient type	New patient	12 (17.4)
	Recall patient	57 (82.6)
Disease duration	Mean ± SD: 44.96 ± 49.61 months, range 1-264 months	
	< 1 year	12 (17.4)
	1-5 years	43 (62.3)
	> 5 years	14 (20.3)
Pain perception		
Pain intensity	Mean ± SD: 2.56 ± 2.32, range 0-8	
	No pain	3 (4.4)
	Mild	41 (59.4)
	Moderate	24 (34.8)
	Severe	1 (1.4)
Patient's self-symptom perception		
Burning sensation		69 (100)
Roughness		43 (62.3)
Abrasion/ulceration		31 (44.9)
Blister		6 (8.7)
Others		3 (4.3)

4.2 Oral health related quality of life (OHRQoL)

Prevalence, intensity and score of oral impacts among OLP patients were demonstrated in Table 3. About 97% of the patients had the impact of OLP disease to the daily activities. Although the overall prevalence of oral impacts was high, mean overall percentage score was low (maximum score is 100) with the value of 12.11 ± 13.26, 95%CI = 8.93-15.30, range = 0-77.50. The prevalence consistent with the performance score, higher scores indicate a greater number of impacts on QoL. Among patients, 88.4% had impact on eating with mean eating performance score of 8.08 ± 6.80, followed by cleaning teeth (65.2%) with mean cleaning teeth performance score of 6.58 ± 7.48 and mood stabilizing (62.3%) with mean mood stabilizing performance score of 5.24 ± 7.20. In addition, there were also impact to the social activities (17.4%) and smiling or aesthetic concerns (14.5%). For extent of oral impacts, about 70% of the affected impacts were reported between 1-3 daily performances.

For intensity level of oral impacts, more than one-third (37.6%) had the impact in “severe” to “very severe” intensity, followed by 33.3% with “moderate” intensity and 26% with “very little” to “little” intensity, respectively.

Table 3 Prevalence, intensity and impact score of Oral Impacts on Daily Performances in OLP patients (n=69)

Total	Overall impact	Daily performances n (%)							
		Eating	Speaking	Cleaning	Relaxing Sleeping	Mood stabilizing	Smiling	Working	Social activities
- Prevalence	97.1	88.4	7.2	65.2	5.8	62.3	14.5	8.7	17.4
- Intensity level n (%)									
No	2 (2.9)	8 (11.6)	64 (92.8)	24 (34.8)	65 (94.2)	26 (37.7)	59 (85.5)	63 (91.3)	57 (82.6)
Very little	9 (13)	10 (14.5)	1 (1.4)	9 (13)	0 (0)	17 (24.6)	1 (1.4)	3 (4.3)	8 (11.6)
Little	9 (13)	11 (15.9)	1 (1.4)	7 (10.1)	0 (0)	2 (2.9)	4 (5.8)	0 (0)	1 (1.4)
Moderate	23 (33.3)	23 (33.3)	2 (2.9)	11 (15.9)	0 (0)	12 (17.4)	3 (4.3)	3 (4.3)	1 (1.4)
Severe	13 (18.8)	7 (10.1)	0 (0)	12 (17.4)	1 (1.4)	5 (7.2)	0 (0)	0 (0)	1 (1.4)
Very severe	13 (18.8)	10 (14.5)	1 (1.4)	6 (8.7)	3 (4.3)	7 (10.1)	2 (2.9)	0 (0)	1 (1.4)
- OIDP score	Percentage score*	Daily performance score**							
Mean (SD)	12.11 ± 13.26	8.08 ± 6.80	0.63 ± 2.90	6.58 ± 7.48	1.17 ± 4.82	5.24 ± 7.20	1.33 ± 4.54	0.31 ± 1.25	0.85 ± 3.17
95% Confidence interval	8.93 - 15.30	6.45 - 9.72	-0.06 - 1.33	4.78 - 8.37	0.01 - 2.33	3.51 - 6.97	0.24 - 2.42	0.01 - 0.62	0.09 - 1.61
Median	8	6	0	4	0	2	0	0	0
Min-Max	0-77.5	0-25	0-20	0-25	0-25	0-25	0-25	0-6	0-20
Performances with impacts (PWI) n (%)									
No affected activities	2 (2.9)	-	-	-	-	-	-	-	-
1 activity	16 (23.2)	-	-	-	-	-	-	-	-
2 activities	16 (23.2)	-	-	-	-	-	-	-	-
3 activities	16 (23.2)	-	-	-	-	-	-	-	-
4 activities	11 (15.9)	-	-	-	-	-	-	-	-
5 activities	4 (5.8)	-	-	-	-	-	-	-	-
6 activities	2 (2.9)	-	-	-	-	-	-	-	-
7 activities	2 (2.9)	-	-	-	-	-	-	-	-

Maximum possible percentage score = 100, **Maximum possible daily performance score = 25

4.3 OLP clinical characteristics

4.3.1 OLP localization

OLP clinical characteristics were shown in Table 4. The three most common sites of involvement in our study were buccal mucosa (88.4%), followed by gingiva (60.9%), tongue and lip (14.5%), respectively. The small number of patients with OLP involvement at floor of the mouth (4.3%) and soft palate (2.9%) were reported.

4.3.2 OLP type

All patients had the reticular type. The second most common form was the atrophic (95.7%), followed by the ulceration (26.1%) and the bullous variant (2.9%) (Table 4).

4.3.3 Number of OLP affected side

Regarding the number of OLP affected side, about 40% had affected two sides followed by four and three affected sides (21.7% and 18.8%), respectively (Table 4).

4.3.4 OLP clinical severity according to The Thongprasom sign score

Mostly OLP clinical severity according to the Thongprasom criteria score was score 3 (39.1%), score 2 (31.9) followed by score 4 (17.4%) and score 5 (7.2%). Only 3 patients with score 1 (4.3%) were reported (Table 4).

Table 4 Distribution of clinical characteristics in OLP patients (n=69)

Variable	n (%)
OLP localization	
Buccal mucosa	61 (88.4)
Tongue	10 (14.5)
Lip	10 (14.5)
Gingiva	42 (60.9)
Floor of the mouth	3 (4.3)
Soft palate	2 (2.9)
Hard palate	0 (0)
OLP type	
Reticular	69 (100)
Atrophic	66 (95.7)
Ulcer	18 (26.1)
Bullous	2 (2.9)
Number of OLP affected side*	
1 affected side	5 (7.2)
2 affected sides	28 (40.6)
3 affected sides	13 (18.8)
4 affected sides	15 (21.7)
5 affected sides	4 (5.8)
6 affected sides	4 (5.8)
OLP clinical severity (Thongprasom sign score)	
Score 1	3 (4.3)
Score 2	22 (31.9)
Score 3	27 (39.1)
Score 4	12 (17.4)
Score 5	5 (7.2)

* Maximum possible affected sides = 11 sides

4.4 Association between OLP clinical variables and OHRQoL (OIDP) as well as pain perception (NRS)

4.4.1 OLP clinical severity according to the Thongprasom sign score

Table 5 exhibited positive correlation between the level of OLP clinical severity and the QoL impairment. There was a significant correlation between the clinical severity according to the Thongprasom sign score and the percentage score (r_s = 0.444, p <0.001) as well as the intensity of oral impacts (r_s = 0.490, p < 0.001). These indicated the more severity of OLP clinical sign associated with the poorer QoL.

When the OIDP scores were rated in relation to the Thongprasom sign scores (Table 5). Both of the percentage scores and the intensity level of oral impacts were step increased in relation to the clinical severity of Thongprasom sign score 2 to score 5. The mean percentage scores rose from 4.77 ± 4.67 at score 2 to 32.00 ± 26.95 at score 5. Besides, the intensity of oral impacts acted accordingly in the same way with significantly increasing from the little intensity level at score 2 to very severe intensity level at score 5. Although the mean percentage score and the median intensity of oral impacts were step increased in consistent with the clinical severity from clinical score 2 to score 5. Compared to 1 step lower category, a statistically significant difference was observed from clinical score 1 to score 4 with the intensity of oral impacts (p < 0.001). The difference of the intensity of oral impacts was statistically significant between score 2 and 3 (p = 0.002) and between score 3 and 4 (p = 0.030). That means clinical score from score 2 to score 4 could identify logical change and discriminate between each score of OLP condition. Each of OLP clinical score changed consistent with the change of OHRQoL measured by the OIDP index. For example, OLP clinical score changed from score 2 to score 3 means increasing of

atrophic area deteriorate the QoL and vice versa. The changing from score 3 to score 4 indicated that having OLP ulcer would be the worst deterioration in term of QoL. In contrast, the transition from score 4 to score 5 did not get statistically significant (p = 0.604). The greater size of ulcer did not represent with the more QoL impairment. Unexpectedly, 3 patients with score 1 (4.3%) showed the severe intensity level, which was higher than patients with score 2 that had little intensity level (p = 0.010).

In pain perception aspect, the Thongprasom sign scoring system had associated with the NRS score (r_s = 0.298, p = 0.013). There was no statistically significant when compared to 1 step lower category. Compared to the QoL measurement concept, the strength of association with the NRS was less than that of the intensity of oral impacts, indicated a trend favoring the usefulness of the QoL measurement.

As above result indicated higher strength of association with the intensity of oral impacts than that of the percentage score (Table 5). The intensity of oral impacts was selected for exploring the following association with other variables.

Table 5 Association and distribution of the OIDP score and NRS by the OLP clinical severity according to the Thongprasom sign score (n=69)

Thongprasom sign score	n (%)	Percentage score (Mean ± SD)	Correlation coefficient, *P*-value	Intensity level (Median)	Correlation coefficient, *P*-value	NRS (Mean ± SD)	Correlation coefficient, *P*-value
1	3 (4.3)	14.83 ± 7.02	$r_s = 0.444^{**}$ $p < 0.001$	Severe	$r_s = 0.490^{**}$ $p < 0.001$	3.66 ± 1.52	$r_s = 0.298^{*}$ $p = 0.013$
2	22 (31.9)	4.77 ± 4.67‡		Little‡		1.54 ± 2.04	
3	27 (39.1)	10.85 ± 9.67‡		Moderate‡‡		2.48 ± 2.40	
4	12 (17.4)	19.45 ± 14.09		Severe - Very severe‡		3.75 ± 2.45	
5	5 (7.2)	32.00 ± 26.95		Very severe		4.00 ± 1.00	
Total	69 (100)	12.11 ± 13.26		Moderate		2.56 ± 2.32	

r_s= Spearman 's correlation coefficient

* Correlation is significant at the 0.01 level (2-tailed), ** Correlation is significant at the 0.001 level (2-tailed)

‡ $p < 0.05$, ‡‡ $p < 0.01$ (Mann–Whitney U test) compare to 1 step lower category

4.4.2 OLP location

These findings provided QoL analysis with regards to the OLP localization (Table 6). Our study highlighted the OLP involvement at the soft palate was statistically significant impacts on QoL. Although those patients had not presented with their life suffering in aspect of pain perception (p = 0.636), they showed of more suffering to QoL with very severe intensity level (p = 0.039).

4.4.3 OLP type

Regarding the clinical subtypes of OLP, presence of the ulcer exhibited worsening QoL (Table 6). Patients with the ulcerative OLP reported of the severe to very severe intensity level, which was significantly worse than the other types (p < 0.001). Furthermore, those patients had significantly higher mean NRS scores (3.88 ± 2.05) compared to the others (2.09 ± 2.24) (p = 0.004).

4.4.4 Number of OLP involvement

There was no significant difference between the number of OLP side involvement and OHRQoL (p = 0.316) as well as pain perception (p = 0.284) (Table 6). The QoL impairment did not depend on the number of affected lesion sides. Given these associations, only one maximum OLP sign score that presented OLP status pictorially was selected.

Table 6 Distribution of the OLP localization, type, number of OLP involvement and their association with OHRQoL and pain perception in OLP patients (n=69)

Variables		n (%)	Intensity level (Median)	*P*-value	NRS (Mean ± SD)	*P*-value
OLP Localization						
Buccal mucosa	No	8 (11.6)	Moderate	$p = 0.729$	3.87 ± 2.47	$p = 0.082$
	Yes	61 (88.4)	Moderate		2.39 ± 2.26	
Tongue	No	59 (85.5)	Moderate	$p = 0.086$	2.66 ± 2.27	$p = 0.348$
	Yes	10 (14.5)	Severe		2.00 ± 2.62	
Lip	No	59 (85.5)	Moderate	$p = 0.425$	2.39 ± 2.20	$p = 0.205$
	Yes	10 (14.5)	Severe		3.60 ± 2.83	
Gingiva	No	27 (39.1)	Moderate	$p = 0.591$	2.25 ± 2.62	$p = 0.199$
	Yes	42 (60.9)	Moderate		2.76 ± 2.11	
Floor of the mouth	No	66 (95.7)	Moderate	$p = 0.506$	2.60 ± 2.31	$p = 0.401$
	Yes	3 (4.3)	Moderate		1.66 ± 2.88	
Soft palate	No	67 (97.1)	Moderate	$p = 0.039^{*}$	2.55 ± 2.35	$p = 0.636$
	Yes	2 (2.9)	Very severe		3.00 ± 0	
OLP type						
Reticular	No	0	-	-	-	-
	Yes	69 (100)	Moderate		2.56 ± 2.32	
Atrophic	No	3 (4.3)	Severe	$p = 0.173$	3.67 ± 1.52	$p = 0.337$
	Yes	66 (95.7)	Moderate		2.51 ± 2.34	
Ulcerative	No	51 (73.9)	Moderate	$p < 0.001^{***}$	2.09 ± 2.24	$p = 0.004^{**}$
	Yes	18 (26.1)	Severe-Very severe		3.88 ± 2.05	
Bullous	No	67 (97.1)	Moderate	$p = 0.358$	2.59 ± 2.33	$p = 0.512$
	Yes	2 (2.9)	Severe		1.50 ± 2.12	
Number of OLP involvement						
1 affected side		5 (7.2)	Moderate	$p = 0.316$	4.20 ± 3.42	$p = 0.284$
2 affected sides		28 (40.6)	Moderate		1.96 ± 2.09	
3 affected sides		13 (18.8)	Severe		2.61 ± 2.21	
4 affected sides		15 (21.7)	Moderate		3.40 ± 2.29	
5 affected sides		4 (5.8)	Very severe		2.25 ± 2.21	
6 affected sides		4 (5.8)	Moderate-severe		1.75 ± 2.36	

*$p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ (Mann–Whitney U test)

4.4.5 The OLP clinical severity at the soft palate in relation to the OHRQoL

As above mentioned, the presence of OLP at the soft palate revealed worsening QoL. Figure 1 illustrated the intensity of oral impacts to OHRQoL in relation to OLP clinical severity according to the Thongprasom sign score and clustered in group of soft palate involvement. Interestingly, graph showed substantial higher values of the intensity level of oral impacts at the soft palate involvement particularly of Thongprasom sign score 3 and slightly higher intensity level of oral impacts than that of Thongprasom sign score 5.

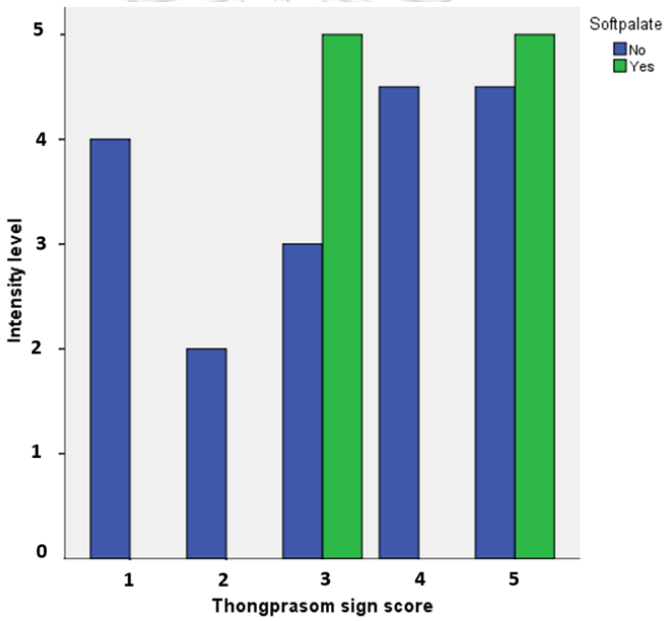

Figure 1 Association of the intensity of oral impacts to OHRQoL and the OLP clinical severity according to the Thongprasom sign score with the soft palate involvement.

4.5 Association between the pain perception (NRS) and the OHRQoL (OIDP)

Subjective pain assessment is considered to be the gold standard for the OLP criterion measurement. To evaluate OIDP performance being

checked against a criterion, the bivariate correlation between OLP pain and the intensity of oral impacts revealed a statistically significant correlation. The Spearman's correlation coefficient indicated a moderate positive correlation (r_s= 0.400, p = 0.001) which means more severe of pain perception indicating worsen QoL.

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CHAPTER 5
DISCUSSION

Our study exhibited OLP affected women more often than men with a ratio of 4:1. Although the ratio was slightly higher than majority studies, it was in agreement with those studies which reported from 1.6:1 to 3.3:1 (4, 136). The mean age in this current study was 55.08 ± 13.85 years which was similar to numerous published studies reported in the fifth or sixth decade of life (4, 136).

5.1 Association between OLP clinical severity according to Thongprasom sign score and OHRQoL

Our evidence supported the validity of generic OHRQoL measures to assess the effects of OLP. It was statistically proved the ability to detect QoL impairment in OLP patients. Current finding showed stronger correlation between the intensity of oral impacts and the OLP clinical severity than the overall OIDP scores. This corroborated with the findings of Krisdapong et al. in 2014. They pointed out the intensity level better reveal degrees of oral impacts than aggregated scores and supported it used in the OIDP/Child-OIDP indices (75). As well, our study supported the validation of the Thongprasom scale to measure OLP clinical severity. The result revealed a significantly positive association between OLP clinical severity according to the Thongprasom sign scoring system and QoL. Both OIDP scores and intensity level were associated step increase with OLP clinical severity from clinical score 2 to score 5. That means this clinical scoring system could reflect not only from the clinician points of view but also patients' perspective of their life's dimension. The intensity of oral impacts was higher in consistent with the clinical severity. Clinical scores from score 2 to score 4 could identify logical change and discriminate between each score of OLP

condition. Surprisingly, the transition from score 4 to score 5 did not get statistically significant. It was not along with the thought of the greater size of ulcer, the more effect to the QoL score. The patients might value the effects of the ulcer to their daily activities by irrespective of the OLP ulcer size.

In addition to clinician's decision, this finding suggested of integrating the patient's perspectives to quantify the treatment response. This implied that the transition from score 5 or 4 to score 3 or 2 would be judged the successful clinical outcome. This finding was supported by the concept which proposed by Gonzalez-Moles et al. in 2018 (137). Instead of achieving the complete remission, they suggested of considering the effective OLP treatment if an erosive/ulcerative lesion was improved into an atrophic one or erosive/ulcerative lesion was healed.

Turn to the reticular OLP topic, there was a clinician's impression that reticular OLP lesion might not have symptom. In contrast, 3 patients with only white reticular lesion (score 1) reported of more substantial impacts to QoL than that of patients with clinical score 2. In addition, the patients with clinical score 1 also reported of higher pain level, although no statistical significance was found when compared among patients with higher clinical scores. This unexpected finding was supported by other studies (138-140). Adamo et al. in 2017 reported higher level of anxiety and depression in patients with symptomatic reticular type compared to patients with non-symptomatic reticular OLP (138). Their result were confirmed with the following study of Vilar-Villanueva et al. in 2019 (139).

The finding of clinical severity with score 1 revealed that they still got pain and QoL burden. Clinicians should include insights to seeking the information whether pain bothered them or impeded any aspects of daily life. This

implied that setting the recall program does not depend only from the clinician's finding of the OLP severity but also from patient's perceptions. The importance of regularly recall visit throughout their life should be emphasized because the OLP nature is a dynamic disease and could be transformed to malignant lesion even from a previous hyperkeratotic lesion (141).

5.2 Association between OLP clinical severity according to Thongprasom sign score and pain perception

To the best of our knowledge, no previous study has investigated the association between the NRS and the Thongprasom sign score. Our data demonstrated the construct validity of the NRS in OLP patients. In case of OLP related pain measurement, our data exhibited the correlation between OLP clinical severity according to Thongprasom grading system and OLP pain perception with the NRS which was similar to the other OLP sign scoring system (20, 66). The NRS was proved to be of value in assessing pain perception in OLP patients.

However, the data showed the trend favor of using the OHRQoL measurement in preference to using the pain perception scale. This might be explained by the way of OLP patients described their bothersome symptoms. They usually expressed of the "soreness" instead of having "pain". This challenged concept was supported by the study of Burke et al. that confirmed the soreness sensation was the suitable approach to describe their OLP symptoms (142). In addition, the study of Niissalo et al. showed affected OLP was not promoted by sympathetic denervation or hyperalgesia pain in oral mucosa (143).

Our data suggested that there was a limited value in OLP related pain measurement in OLP clinical trial. The current result was in agreement with the concept of involving the QoL measurement. It would be more beneficial to

measure OHRQoL because it might reflect multidimensional concept of the patient's perception.

5.3 Association between OLP pain perception and OHRQoL

So far, our data demonstrated the construct validity of the OIDP index when using with OLP patients. There was a correlation of OLP pain perception assessed with the NRS and the intensity of oral impacts to OHRQoL valued with the OIDP index. The present finding was in agreement with the study of Hergaty et al. in 2002. They reported the OHIP-14 scores, another generic OHRQoL measure, were correlated with the severity of pain measured by the VAS scores. Our finding supported the value of using the OIDP scale in OLP patients.

Our finding revealed that the OIDP was better than pain measure since it reflected difficulties in daily life activities which might not totally caused by pain. For example, the patients with OLP lesion at soft palate were not related to pain; however, related to difficulties in eating and maintaining their emotional state without being irritable, leading to substantial OHRQoL impairment. Therefore, OIDP measure could capture the impacts of OLP while pain scale could not detect.

5.4 Association between OLP characteristics, pain perception and OHRQoL

Our finding showed that most frequently involved OLP lesion were the buccal mucosa followed by gingiva, tongue and lip (4). These results matched those observed in the study of Kaomongkolgit et al. in 2019 which was retrospectively reviewed study of Thai patients in the northern Thailand (144). However the reported prevalence of OLP at hard palate, floor of the mouth and soft palate was quite low (136).

Our study showed an QoL analysis and pain assessment in OLP patients to better understand the anatomic localization in Thai patients. In aspect of pain assessment, a number of studies have found that OLP at tongue was the most painful lesion (140). Although our result differs from some published studies in which there was no difference in the OLP related pain regarding the location. Interestingly, this study has demonstrated, for the first time, that OLP involving soft palate significantly impacted QoL. Although those patients did not present with their life suffering in aspect of pain perception, they showed of more suffering to QoL. A possible explanation for this finding were, first, they were new patients who did not receive any treatment. Second, individuals with OLP at soft palate reported the difficulty during eating and kept worrying about their lesional condition which contributed to a lower QoL. This might be the soft palate located in the deep oral cavity region and has an important role in speech and swallowing. Otherwise, the limitation of this finding was relatively small numbers of patients with soft palate involvement.

Regarding OLP type, our data showed the ulcerative OLP were observed to be a significant factor for poor QoL. This result was matched those observed in the Thongprasom sign score 4 and score 5 that the ulcerative lesion had high OIDP scores and the intensity of oral impacts to OHRQoL. This confirmed with other studies that reported of more painful symptoms and greater QoL burden in patients with erosive and/or ulcerative OLP (17, 134, 140). Additionally, our results confirmed with the report of Sullliman et al. in which ulcerative oral mucosal lesions were statistically significantly impacts to daily activities (134).

According to the QoL impairment, the majority of OLP patients had reported of daily activities relevant of worsening QoL, predominantly with eating,

cleaning and mood stabilizing activities. Also, some of those experienced of social impairment. Therefore, there might be the benefit of individual behaviour modification to promote healing of the ulcer and controlling of the pain. For example, the dentist should provide oral hygiene instruction to modify the patient's cleaning abilities or inform them to avoid some types of food that evoked symptoms. Also, they should be assessed if the psychological support or psychological reassuring would be needed. These strategies would be the benefit for OLP patients to recover from the ulcer and would return their capacities for basic daily activities.

The QoL impairment and pain perception did not depend upon the number of OLP involvement but upon the most severity of the clinical severity. These findings were identical instances to the concept of the intensity of oral impacts which could provide more detailed picture of impacts than the single score (75). The most severe of OLP clearly mirrored the intensity of oral impacts. In addition, the number of affected OLP was similar to the number of performances with impacts (PWI) or the extent of impacts. While the sum of affected OLP lesion were comparable to the aggregated OIDP scores.

5.5 The modified OLP clinical severity according to the Thongprasom sign score and OHRQoL

Findings of the association between OLP clinical severity and worsening QoL had important implications for developing the modified OLP clinical severity index. Initially, whereas the Thongprasom sign score 5 referred to the greater ulcerative area as compared with that of score 4. This study had been unable to demonstrate the significance difference of the QoL burden between these two clinical scores. Clinically relevant findings suggested that the ulcerative OLP would be graded, irrespective of the ulcer size, with the maximum clinical

score 4. Interestingly, OLP lesion at the soft palate presented worse QoL than that found among other areas. The finding of substantial QoL impairment of OLP lesion at the soft palate raised the issue to adjust OLP clinical severity index. Although the appearance of the OLP lesions at soft palate were white striae with atrophic, corresponding to the clinical score 3, it should be appointed the OLP clinical severity score almost to the ulcerative score (score 4). Last, it was somewhat surprising that the patients with reticular OLP lesion still had pain and QoL burden. Although these evidence remained inconclusive, it was also worth asking patients about pain related burdens or worsening QoL. In summary, these findings suggested the clinical ranking system for OLP, modified from Thongprasom sign scoring criteria and were demonstrated as

score 0: no lesions or normal mucosa

score 1: mild white striae (but if patients still have symptoms, the score should be adjusted to score 2 or score 3)

score 2: white striae with atrophic area <1 cm^2

score 3: white striae with atrophic area ≥ 1cm^2

score 4: white striae with erosive area or lesion at soft palate

Finally, this chapter had described a discussion of the main findings and also the implications. Findings from this study had extended our understanding of the OLP impacts to OHRQoL which was the key strength of this study. However, there were also some limitations. Firstly, the numbers of participants were relatively small. Secondly, the data were mostly derived from recall patients who had been treated. The findings might, therefore, not be generalizable to those patients who had not received treatment. Future research with larger and approximately equal numbers of patients in the different groups are required to corroborate these findings.

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CHAPTER 6
CONCLUSION

In summary, this study had showed the association between OLP pain perception and OHRQoL. This supported the construct validity of the OIDP scale when using with OLP patients. Additionally, there were association between OLP clinical signs and OHRQoL as well as pain symptom perception. The intensity of oral impacts to OHRQoL and pain intensities were increased along with OLP clinical severity, except for the OLP lesion corresponding to clinical score 1. Furthermore, the ulcerative OLP lesions, equivalent to clinical score 4 and 5, were the most painful symptom and had substantial impacts to OHRQoL. Presence of OLP at soft palate had considerable deterioration in OHRQoL. In addition, the worsening QoL did not depend upon the number of affected OLP lesion.

The current result demonstrated that the OIDP index was valid somehow, against Thongprasom sign scoring system. However, clinical grading measures were restricted to record clinical appearances of the lesions. With this discrepancy based on its measurement, using merely OLP sign scoring index or others clinical indicators would be insufficient. The results supported the application of OHRQoL assessment to complement OLP clinical measures.

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APPENDIX A

PATIENT PERCEPTION RECORD FORM

วันที่ .....

ชื่อ-นามสกุล.....**อายุ**.....**เพศ**.....

เลขประจำตัวคนไข้ (HN.).....**ระยะเวลาที่พบรอยโรคไลเคนแพลนัส** .....**ปี**..... **เดือน**

☐ **ผู้ป่วยใหม่** ☐ **ผู้ป่วยเก่า** ☐ **ใช้ยาสม่ำเสมอตามทันตแพทย์สั่ง**

☐ **ใช้ยาไม่สม่ำเสมอตามทันตแพทย์สั่ง**

ใน 6 เดือน ที่ผ่านมา ตั้งแต่เดือน..... **หรือตั้งแต่ช่วง**.....**จนถึงวันนี้**

ปัญหาจากรอยโรคในช่องปาก ทำให้เกิดปัญหาตามข้อข้างล่างนี้หรือไม่

มิติที่ 1 : **อาการสำคัญ** (Chief complaint)

อาการสำคัญ (Chief complaint)	**มี** (Presence)	**ไม่มี** (Absence)
- **อาการปวดแสบปวดร้อนหรือเจ็บในช่องปาก** (Burning sensation or pain)		
- **ความขรุขระของเนื้อเยื่ออ่อนในช่องปาก** (Roughness of the oral mucosa)		
- **การถลอกของเนื้อเยื่ออ่อนหรือมีแผลที่เนื้อเยื่ออ่อนในช่องปากในช่องปาก** (Abrasion of the oral mucosa or Ulceration)		
- **การเกิดตุ่มน้ำเกิดขึ้นในเนื้อเยื่ออ่อนในช่องปาก** (Blisters in the oral mucosa)		
- **อาการอื่น ๆ** (Others)		

มิติที่ 2 : **อาการเจ็บปวด** (Pain)

Numerical rating scale (NRS) ...../10

APPENDIX B

ORAL IMPACTS ON DAILY PERFORMANCES (OIDP)

RECORD FORM

ชื่อ-นามสกุล.....**อายุ**.....**เพศ**.....
ใน 6 เดือนที่ผ่านมาตั้งแต่เดือน..... **หรือ ตั้งแต่ช่วง**..... **จนถึงวันนี้ปัญหาจากรอยโรคในช่องปาก ทำให้เกิดปัญหาตามข้อข้างล่างนี้ แต่ละข้อหรือไม่**

Performance (กิจกรรม)	Frequency (ความถี่)	Severity (ความรุนแรง)	Performance Score (คะแนนกิจกรรม)
1. การกินอาหาร เช่น อาหารรสเผ็ด รสเปรี้ยว อาหารแข็ง (Eating)			
2. การพูดได้ตามปกติ ชัดเจน การออกเสียงได้ตามปกติ (Speaking)			
3. การทำความสะอาดช่องปาก เช่น การแปรงฟัน แสบเวลาแปรงฟัน การใช้ไหมขัดฟัน (Cleaning abilities)			
4. การพักผ่อน นอนหลับ (Relaxing and sleeping)			
5. การรักษาอารมณ์ตามปกติ โดยไม่หงุดหงิด รำคาญใจ (Demonstrating in emotional stability) เช่น กังวลใจ ไม่สบายใจ ว่าสามารถรักษาให้หายได้หรือไม่ หรือ มีความวิตกกังวลว่ารอยโรคจะเป็นมะเร็ง			
6. การยิ้ม หัวเราะ หรือให้คนอื่นเห็นริมฝีปากและเหงือก โดยไม่รู้สึกอาย (Smiling without feeling embarrassment) เช่น มีปัญหาในการทาลิปสติกในสุภาพสตรี			
7. การทำงาน เช่น การประกอบอาชีพ (ที่เกิดปัญหาข้างต้น เช่น การลางานเพราะต้องมาพบทันตแพทย์) หรือ การประกอบกิจกรรมทั่วไป เช่น การทำความสะอาดบ้าน เป็นต้น (Carrying out major work or social role)			
8. การออกไปพบผู้คน การออกไปรับประทานอาหารนอกบ้านกับเพื่อน เช่น กลัวสังคมรังเกียจ เนื่องจากความเข้าใจว่าเป็นโรคติดต่อ (Socialisation)			
ผลคะแนนรวม			

คะแนนความถี่	
0 = ไม่กระทบกระเทือน	0 = ไม่กระทบกระเทือน
1 = น้อยกว่า1 ครั้งต่อเดือน	1 = 1 - 5 วัน
2 = 1 -2 ครั้งต่อเดือน	2 = 6 - 15 วัน
3 = 1 -2 ครั้งต่อสัปดาห์	3 = 16 - 30 วัน
4 = 3 -4 ครั้งต่อสัปดาห์	4 = 1 - 3 เดือน
5 = ทุกวันหรือเกือบทุกวัน	5 = มากกว่าสามเดือน

คะแนนความรุนแรง
0 = ไม่กระทบกระเทือน
1 = เล็กน้อยมาก
2 = เล็กน้อย
3 = ปานกลาง
4 = รุนแรง
5 = รุนแรงมาก

APPENDIX C

ORAL EXAMINATION RECORD FORM

ชื่อ-นามสกุล.....

อายุ.....**เพศ**.....**เลขประจำตัวคนไข้** (HN.).....

หมายเลขทางพยาธิ (Histological report).....

Lesion site	Thongprasom sign score	Lesion distribution	Lesion type					
			R	A	U	B	P	Pa
Buccal mucosa		Uninvolved						
		Right side						
		Left side						
Tongue		Uninvolved						
		Dorsal						
		Ventral						
Lip		Uninvolved						
		Upper						
		Lower						
Gingiva		Uninvolved						
		Upper						
		Lower						
Palate		Uninvolved						
		Involved						
Floor of the mouth		Uninvolved						
		Involved						
Soft palate		Uninvolved						
		Involved						

R = Reticular, A = Atrophic, U = Erosive/ulcerative, B = Bullous, P = Pigmented, Pa = Plaque

Thongprasom sign score

Score 0 = no lesions or normal mucosa.

Score 1 = mild white striae only

Score 2 = white striae with atrophic area < 1 cm^2

Score 3 = white striae with atrophic area ≥ 1 cm^2

Score 4 = white striae with erosive area < 1 cm^2

Score 5 = white striae with erosive area ≥ 1 cm^2

APPENDIX D

ETHICAL APPROVAL FORM

No. 059/2019

Study Protocol and Consent Form Approval

The Human Research Ethics Committee of the Faculty of Dentistry, Chulalongkorn University, Bangkok, Thailand has approved the following study to be carried out according to the protocol and patient/participant information sheet dated and/or amended as follows in compliance with the **ICH/GCP**

Study Title	:	Association between clinical signs and quality of life in Thai patients with oral lichen planus
Study Code	:	HREC-DCU **2019-044**
Study Center	:	Chulalongkorn University
Principle Investigator	:	Lieutenant colonel Sasirin Yiemstan
Protocol Date	:	June 27, 2019
Date of Approval	:	July 5, 2019
Date of Expiration	:	July 4, 2021

K. Bhalang

.....

(Assistant Professor Dr. Kanokporn Bhalang)
Chairman of Ethics Committee
Associate Dean for Research

*A list of the Ethics Committee members (names and positions) present at the Ethics Committee meeting on the date of approval of this study has been attached (upon requested). This Study Protocol Approval Form will be forwarded to the Principal Investigator.

Approval is granted subject to the following conditions: (see back of the approval)

APPENDIX E

ETHICAL APPROVAL FORM

บันทึกข้อความ

ส่วนงาน งานบริการวิจัยและพัฒนา คณะทันตแพทยศาสตร์ จุฬาฯ โทร. 02-2188866 โทรสาร 02-2188810
ที่ จธ. 149/2562 **วันที่** 4 กรกฎาคม 2562
เรื่อง ผลการพิจารณาจริยธรรมการวิจัยในมนุษย์

เรียน รองคณบดีฝ่ายวิจัย

ตามที่คณะกรรมการพิจารณาจริยธรรมการศึกษาวิจัยในมนุษย์ได้พิจารณาโครงการวิจัยเรื่อง "ความสัมพันธ์ระหว่างอาการแสดงทางคลินิกและคุณภาพชีวิตในผู้ป่วยไทยโรคไลเคนแพลนัสช่องปาก (Association between clinical signs and quality of life in Thai patients with oral lichen planus)" HREC-DCU 2019-044 **ผู้วิจัยหลัก** พ.ท.หญิง ศศิรินทร์ เยี่ยมสถาน

คณะกรรมการฯ มีมติ อนุมัติโดยไม่มีเงื่อนไข โดยมีระยะเวลาการรับรองการทำวิจัยตั้งแต่ 5 กรกฎาคม 2562 ถึง 4 กรกฎาคม 2564 และให้ผู้วิจัยปฏิบัติดังนี้คือ

- ดำเนินการวิจัยตามขั้นตอนที่ปรากฏในเอกสารโครงการที่ได้รับการรับรองอย่างเคร่งครัด หากมีการเปลี่ยนแปลงหรือเพิ่มขั้นตอนของการวิจัยจะต้องส่งเอกสารขออนุมัติต่อคณะกรรมการฯ
- รายงานต่อคณะกรรมการฯทันทีกรณีที่มีความผิดพลาดหรือเหตุการณ์อันไม่พึงประสงค์เกิดขึ้นในการวิจัย
- ส่งรายงานสรุปผลการดำเนินการ (จธ. 5) ภายใน 1 เดือน หลังสิ้นสุดโครงการ

ทั้งนี้ คณะกรรมการฯจะออกเอกสารรับรองด้านจริยธรรม ซึ่งลงนามกำกับโดยประธานคณะกรรมการฯ และ รองคณบดีฝ่ายวิจัย ให้แก่ผู้วิจัยต่อไป

จึงเรียนมาเพื่อโปรดดำเนินการต่อไปด้วย จักขอบคุณยิ่ง

(รองศาสตราจารย์ ทันตแพทย์ ดร. ชาญวิทย์ ประพิณจำรูญ)
กรรมการและเลขานุการ

แจ้งผลให้ผู้วิจัยทราบ

(ผศ.ทญ.ดร. กนกพร พะลัง)

APPENDIX F

PARTICIPANT INFORMATION SHEET

1.**โครงการเรื่อง** ความสัมพันธ์ระหว่างอาการแสดงทางคลินิกและคุณภาพชีวิตในผู้ป่วยไทยโรคไลเคนแพลนัสช่องปาก

2. **ชื่อผู้วิจัยหลัก** พ.ท.หญิง ศศิรินทร์ เยี่ยมสถาน

ชื่อผู้วิจัยร่วมหรืออาจารย์ที่ปรึกษา ร.ศ.ทพญ.ดร.พรพรรณ พิบูลย์รัตนกิจ

ศ.ทพญ.ดร.สุดาดวง กฤษฎาพงษ์

สถาบันที่สังกัด คณะทันตแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

แหล่งทุนวิจัย ทุนส่วนตัว

3. **วัตถุประสงค์ของโครงการ**

เพื่อศึกษาความสัมพันธ์ระหว่างดัชนีวัดโรคทางคลินิกในผู้ป่วยไลเคนแพลนัสกับดัชนีคุณภาพชีวิตในมิติสุขภาพช่องปาก และศึกษาความสัมพันธ์ระหว่างดัชนีวัดความเจ็บปวดในผู้ป่วยไลเคนแพลนัสกับดัชนีคุณภาพชีวิตในมิติสุขภาพช่องปาก

4. **สถานที่ดำเนินการวิจัย**

คลินิกบัณฑิตศึกษา ภาควิชาเวชศาสตร์ช่องปาก คณะทันตแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย

5. **วิธีการที่ใช้ในการวิจัย**

อาสาสมัครเป็นผู้ป่วยที่คลินิกบัณฑิตศึกษา ภาควิชาเวชศาสตร์ช่องปาก คณะทันตแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย ทั้งประเภทคนไข้ใหม่และคนไข้เก่าที่ได้รับการรักษาต่อเนื่อง เป็นผู้ป่วยที่ได้รับการวินิจฉัยเป็นโรคไลเคนพลานัส หรือโรคไลเคนอยด์สาเหตุจากยาอยู่แล้ว โดยอาสาสมัครจะได้รับการตรวจโดยทันตแพทย์ด้วยอุปกรณ์ที่ปราศจากเชื้อ และบันทึกข้อมูลตามแบบบันทึกลักษณะทางคลินิก อาสาสมัครได้รับรู้สภาวะโรคช่องปากของตน และได้รับการรักษาตามมาตรฐานปกติ หลังจากนั้นมีการสัมภาษณ์ตามแบบสอบถามในส่วนของอาการที่เป็นและระดับของความเจ็บปวด ตลอดจนผลกระทบของสภาวะโรคไลเคนแพลนัสต่อกิจกรรมในการดำเนินชีวิตปกติ ได้แก่ 1) การรับประทานอาหาร 2) การพูดหรือการออกเสียงให้ชัดเจน 3) การทำความสะอาดช่องปาก 4) การดำเนินชีวิตทั่วๆ ไป เช่น การทำงานบ้าน การประกอบอาชีพ 5) การนอนหลับพักผ่อน 6) การยิ้ม หัวเราะอวดฟันได้โดยไม่อายใคร 7) การรักษาอารมณ์และจิตใจให้เป็นปกติ ไม่หงุดหงิดรำคาญ 8) การได้ออกไปพบญาติสนิทมิตรสหาย โดยใช้การสัมภาษณ์เพื่อให้ทราบถึงปัญหา ปริมาณความถี่ของการเกิดปัญหาและความรุนแรงของผลกระทบจากปัญหา โดยอาสาสมัครจะได้รับการสัมภาษณ์ด้วยน้ำเสียงที่นุ่มนวล และไม่มีถ้อยคำที่สื่อไปในเชิงคุกคาม แต่อย่างใด ข้อมูลจากการสัมภาษณ์จะถูกเก็บเป็นความลับ หลังจากนั้นจะถูกทำลายเมื่อสิ้นสุดโครงการ

6. **เหตุผลที่เชิญเข้าร่วมเป็นอาสาสมัครในโครงการ**

เนื่องจากท่านเป็นผู้ป่วยโรคไลเคนแพลนัสช่องปาก หรือผู้ป่วยรอยโรคไลเคนอยด์ช่องปากสาเหตุจากยา โดยมีคุณสมบัติข้อกำหนดดังนี้

6.1 มีอายุตั้งแต่18 ปีขึ้นไป

6.2 มีรอยโรคไลเคนแพลนัสช่องปาก

6.3 สามารถสื่อสารด้วยการพูดได้

6.4 สามารถให้คำยินยอมในการเข้าร่วมโครงการ

7. **ความรับผิดชอบของอาสาสมัคร และระยะเวลาที่อาสาสมัครจะอยู่ในโครงการ**

คณะผู้วิจัยขอให้ท่านปฏิบัติตามที่ผู้วิจัยแนะนำ โดยอาสาสมัครแต่ละคนจะอยู่ในโครงการเป็นเวลาไม่เกิน 1 วัน

8. **ประโยชน์ของการวิจัยที่อาสาสมัครและ/หรือผู้อื่นอาจได้รับ**

ท่านจะไม่ได้รับประโยชน์โดยตรงจากการเข้าร่วมโครงการวิจัยนี้ แต่ผลการวิจัยที่ได้จากการศึกษาในครั้งนี้จะทำให้เกิดความเข้าใจในเรื่องอาการแสดงทางคลินิก และ ระดับความเจ็บปวด ในรอยโรคไลเคนแพลนัสและรอยโรคไลเคนแพลนัสสาเหตุจากยา กับคุณภาพชีวิตในมิติสุขภาพช่องปาก และอาจเป็นประโยชน์ในการพัฒนาดัชนีวัดโรคไลเคนแพลนัสทางคลินิก ซึ่งอาจนำมาใช้ในการปฏิบัติงานทางคลินิก และงานวิจัยทางคลินิกต่อไป

9. **ความเสี่ยงหรือความไม่สะดวกที่อาจจะเกิดขึ้นแก่อาสาสมัคร และในบางกรณีแก่ทารกในครรภ์หรือทารกที่ดื่มนมมารดา**

การเข้าร่วมโครงการวิจัยนี้ ท่านจะไม่ได้รับความเสี่ยงใดๆ แต่ท่านอาจไม่ได้รับความสะดวกเนื่องจากสัมภาษณ์ ซึ่งจะใช้เวลาไม่เกิน 15 นาที ซึ่งอาจทำให้เสียเวลาเพิ่มมากขึ้นจากมาตรฐานการรักษาตามปกติ

10. **ค่าใช้จ่ายที่อาสาสมัครจะต้องจ่าย หรืออาจจะต้องจ่าย**

เนื่องจากโครงการวิจัยนี้เป็นการสัมภาษณ์ข้อมูล ในระหว่างที่ท่านได้รับการรักษาปกติตามมาตรฐานการรักษา ซึ่งจะไม่มีการจัดเก็บค่าใช้จ่ายใดๆ เพิ่มเติมจากท่าน นอกเหนือจากการชำระค่ารักษาพยาบาลและค่ายาปกติ

11.**การชดเชยใดๆ และการรักษาที่จะจัดให้แก่อาสาสมัครในกรณีที่ได้รับอันตรายซึ่งเกี่ยวข้องกับการวิจัย**

หากท่านได้รับอันตรายใดๆ ที่เป็นผลจากการทำวิจัย ผู้วิจัยจะเป็นผู้รับผิดชอบค่าใช้จ่ายของการรักษาที่เกิดขึ้นทั้งหมด

12.**การจ่ายค่าเดินทาง ค่าเสียเวลา แก่อาสาสมัครที่เข้าร่วมในการวิจัย**

ไม่มี แต่อาสาสมัครจะได้รับอุปกรณ์ดูแลสุขภาพช่องปากตนเอง คนละ 1 ชุด

13.**เหตุการณ์ที่อาจจะเกิดขึ้น หรือเหตุผลซึ่งผู้วิจัยจะต้องยกเลิกการเข้าร่วมในโครงการวิจัยของอาสาสมัคร**

อาสาสมัครไม่สะดวกกะทันหันระหว่างการดำเนินการเก็บข้อมูล หรืออาสาสมัครไม่สามารถให้ข้อมูลได้

14.**มีการเก็บชิ้นตัวอย่างที่ได้มาจากอาสาสมัครเอาไว้ใช้ในโครงการวิจัยในอนาคตหรือไม่ เก็บจำนวนเท่าไหร่ อย่างไร และที่ไหน**

ไม่มี

15. **การกำกับดูแลและควบคุมการดำเนินโครงการ**

ผู้กำกับดูแลการวิจัย ผู้ตรวจสอบ คณะกรรมการพิจารณาจริยธรรม และคณะกรรมการที่เกี่ยวข้อง สามารถเข้าไปตรวจสอบการดำเนินโครงการ รวมทั้ง ตรวจสอบบันทึกข้อมูลของอาสาสมัคร เพื่อเป็นการยืนยันถึงขั้นตอนในการวิจัยทางคลินิกและข้อมูลอื่นๆ โดยไม่ล่วงละเมิดเอกสิทธิ์ในการปิดบังข้อมูลของอาสาสมัครตามกรอบที่กฎหมายและกฎระเบียบได้อนุญาตไว้ นอกจากนี้ โดยการลงนามให้ความยินยอม อาสาสมัครหรือผู้แทนตามกฎหมายจะมีสิทธิตรวจสอบและมีสิทธิที่จะได้รับข้อมูลด้วยเช่นกัน

16. **จริยธรรมการวิจัย**

การดำเนินการโครงการวิจัยนี้ ผู้วิจัยคำนึงถึงหลักจริยธรรมการวิจัย โดย

1. หลักความเคารพในบุคคล (Respect for person) โดยการให้ข้อมูลจนอาสาสมัครเข้าใจเป็นอย่างดีและตัดสินใจอย่างอิสระในการให้ความยินยอมเข้าร่วมในการวิจัย รวมทั้งการเก็บรักษาความลับของอาสาสมัคร
2. หลักการให้ประโยชน์ไม่ก่อให้เกิดอันตราย (Beneficence/Non-Maleficence) ซึ่งได้ระบุในข้อ 8 และ 9 ว่า จะมีประโยชน์หรือความเสี่ยงกับอาสาสมัครหรือไม่
3. หลักความยุติธรรม (Justice) คือมีเกณฑ์คัดเข้าและคัดออกชัดเจน มีการกระจายความเสี่ยงและผลประโยชน์อย่างเท่าเทียมกัน โดยวิธีสุ่มเข้ากลุ่มศึกษา

17. ข้อมูลที่อาจนำไปสู่การเปิดเผยตัวของอาสาสมัครจะได้รับการปกปิด ยกเว้นว่าได้รับคำยินยอมไว้โดยกฎระเบียบและกฎหมายที่เกี่ยวข้องเท่านั้น จึงจะเปิดเผยข้อมูลแก่สาธารณชนได้ ในกรณีที่ผลการวิจัยได้รับการตีพิมพ์ ชื่อและที่อยู่ของอาสาสมัครจะต้องได้รับการปกปิดอยู่เสมอ และอาสาสมัครหรือผู้แทนตามกฎหมายจะได้รับแจ้งโดยทันท่วงที ในกรณีที่มีข้อมูลใหม่ซึ่งอาจใช้ประกอบการตัดสินใจของอาสาสมัครว่าจะยังคงเข้าร่วมในโครงการวิจัยต่อไปได้หรือไม่

18. หากท่านมีข้อสงสัยต้องการสอบถามเกี่ยวกับสิทธิของท่านหรือผู้วิจัยไม่ปฏิบัติตามที่เขียนไว้ในเอกสารข้อมูลคำอธิบายสำหรับผู้เข้าร่วมในการวิจัย ท่านสามารถติดต่อหรือร้องเรียนได้ที่ ฝ่ายวิจัย คณะทันตแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย ตึกสมเด็จย่า 93 ชั้น 10 หรือที่หมายเลขโทรศัพท์ 02-218-8866 ในเวลาทำการ

19. **หากท่านต้องการยกเลิกการเข้าร่วมเป็นอาสาสมัครในโครงการนี้ ให้ท่านกรอกและส่งเอกสารขอยกเลิกมาที่**

พ.ท.หญิง ศศิรินทร์ เยี่ยมสถาน

ที่อยู่ปัจจุบัน 136/83 ถ. วิภาวดีรังสิต 41 แขวงสนามบิน เขตดอนเมือง จ. กรุงเทพ 10210

โทรศัพท์ 02-533-5562 โทรศัพท์มือถือ 081-829-3129

20. **อาสาสมัครสามารถติดต่อผู้วิจัยได้ตลอด 24 ชั่วโมง ที่**:

พ.ท.หญิง ศศิรินทร์ เยี่ยมสถาน ภาควิชาเวชศาสตร์ช่องปาก คณะทันตแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย ถ. อังรีดูนังต์ เขตปทุมวัน แขวงวังใหม่ กรุงเทพฯ 10330 เบอร์โทรศัพท์ 081-829-3129

ร.ศ.ทพญ.ดร.พรพรรณ พิบูลย์รัตนกิจ ภาควิชาเวชศาสตร์ช่องปาก คณะทันตแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย ถ. อังรีดูนังต์ เขตปทุมวัน แขวงวังใหม่ กรุงเทพฯ 10330 เบอร์โทรศัพท์ 0-2218-8942

ศ.ทพญ.ดร.สุดาดวง กฤษฎาพงษ์ ภาควิชาทันตกรรมชุมชน คณะทันตแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย ถ. อังรีดูนังต์ เขตปทุมวัน แขวงวังใหม่ กรุงเทพฯ 10330 เบอร์โทรศัพท์ 0-2218-8543-5

ลงนาม พ.ท.หญิง .....

(ศศิรินทร์ เยี่ยมสถาน)

ผู้วิจัยหลัก

วันที่

...../...../.....

หมายเหตุ - ให้พิมพ์ข้อความโดยละเอียดลงในช่องว่าง โดยใช้ตัวอักษร TH SarabunPKS ขนาด 16

- หลังจากกรอกข้อความครบถ้วน พิมพ์เอกสารทั้งหมด แล้วให้ผู้วิจัยหลักลงนาม
- ทำสำเนาเอกสารข้อมูลคำอธิบายสำหรับอาสาสมัครที่เข้าร่วมในการวิจัย (Patient/Participant Information Sheet) มอบให้อาสาสมัครแต่ละคนๆ ละ 1 ชุด

VITA

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PUBLICATION	-
AWARD RECEIVED	-