

THE PREVALENCE AND RISK FACTORS OF ORAL SOFT TISSUE LESIONS IN KIDNEY
TRANSPLANT RECIPIENTS



A Thesis Submitted in Partial Fulfillment of the Requirements
for the Degree of Master of Science in Geriatric Dentistry and Special Patients Care

Common Course

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จุฬาลงกรณ์มหาวิทยาลัย
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ความชุกและปัจจัยเสี่ยงต่อการเกิดรอยโรคของเนื้อเยื่ออ่อนในช่องปาก ในผู้ป่วยปลูกถ่ายไต



วิทยานิพนธ์นี้เป็นส่วนหนึ่งของการศึกษาตามหลักสูตรปริญญาวิทยาศาสตรมหาบัณฑิต
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ชรินทร์น์ ศิริวิชัยกุล : ความชุกและปัจจัยเสี่ยงต่อการเกิดรอยโรคของเนื้อเยื่ออ่อนในช่องปาก ในผู้ป่วยปลูกถ่ายไต. (THE PREVALENCE AND RISK FACTORS OF ORAL SOFT TISSUE LESIONS IN KIDNEY TRANSPLANT RECIPIENTS) อ.ที่ปรึกษาหลัก : ผศ. ทพ.ดร.อรพินท์ โคมิน, อ.ที่ปรึกษาร่วม : ศ. นพ.ยิ่งยศ อวิหิงสานนท์, ผศ. ทพ.ดร.สรนันทร์ จันทรางศุ

การปลูกถ่ายไต เป็นวิธีการรักษาที่ดีที่สุดสำหรับผู้ป่วยโรคไตเรื้อรัง ซึ่งปัจจุบันได้รับการยอมรับอย่างแพร่หลาย โดยเฉพาะประเทศที่พัฒนาแล้ว เนื่องจากทำให้ผู้ป่วยมีคุณภาพชีวิตที่ดีขึ้น อย่างไรก็ตาม ผู้ป่วยปลูกถ่ายไต ต้องได้รับยากดภูมิในระยะยาว เพื่อป้องกันการปฏิเสธไตที่ได้รับ ทำให้ผู้ป่วยมีระบบภูมิคุ้มกันทำงานลดลง รอยโรคของเนื้อเยื่ออ่อนในช่องปากอาจเกิดขึ้นจากผลข้างเคียงของยาในระหว่างการรักษาด้วยยากดภูมิ จุดประสงค์ของการศึกษานี้ เพื่อศึกษาความชุกและปัจจัยเสี่ยงต่อการเกิดรอยโรคของเนื้อเยื่ออ่อนในช่องปากในผู้ป่วยปลูกถ่ายไต

การศึกษานี้ เป็น cross-sectional study ตั้งแต่เดือนเมษายน ถึง ตุลาคม 2562 โดยตรวจรอยโรคของเนื้อเยื่ออ่อนในช่องปาก อนามัยช่องปาก และภาวะเหงือกโต ในผู้ป่วยปลูกถ่ายไต 65 คน และ ผู้ป่วยล้างไต 65 คน เปรียบเทียบความแตกต่างความชุกของรอยโรคของเนื้อเยื่ออ่อนในช่องปากในผู้ป่วยปลูกถ่ายไตกับผู้ป่วยล้างไตโดยใช้ chi-square และ หาความสัมพันธ์ของ plaque index กับตัวแปรต่างๆโดยใช้ univariate และ multivariate linear regression

ตรวจพบรอยโรคของเนื้อเยื่ออ่อนในช่องปาก ในผู้ป่วยปลูกถ่ายไต 7 คน(10.8%) และ ผู้ป่วยล้างไต 6 คน(9.2%) Plaque index ในผู้ป่วยปลูกถ่ายไตไม่แตกต่างจากผู้ป่วยล้างไต แต่พบว่า Plaque index ในผู้ป่วยปลูกถ่ายไตเพิ่มขึ้นตามอายุ (regression coefficient (95% confidence interval) = 0.009 (0.001-0.016); p -value=0.025) ซึ่งไม่พบความสัมพันธ์นี้ในกลุ่มผู้ป่วยล้างไต

รอยโรคของเนื้อเยื่ออ่อนในช่องปากในผู้ป่วยปลูกถ่ายไต และผู้ป่วยล้างไต ไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติ โดยจากการศึกษานี้ พบรอยโรคของเนื้อเยื่ออ่อนในช่องปากในผู้ป่วยปลูกถ่ายไตน้อยกว่าการศึกษาในอดีต ผู้ป่วยที่ได้รับการปลูกถ่ายไตควรได้รับการตรวจสุขภาพช่องปากทุก 6 เดือน ตรวจรอยโรคหรือความผิดปกติในช่องปาก เพื่อจะได้รับการวินิจฉัย และการรักษาอย่างเหมาะสม

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จุฬาลงกรณ์มหาวิทยาลัย
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KEYWORD: Oral soft tissue lesions, Kidney transplant, Immunosuppressive drug

Charinrat Sirivichayakul : THE PREVALENCE AND RISK FACTORS OF ORAL SOFT TISSUE LESIONS IN KIDNEY TRANSPLANT RECIPIENTS. Advisor: Asst. Prof. ORAPIN KOMIN, D.D.S., Ph.D. Co-advisor: Prof. YINGYOS AVIHINGSANON, M.D.,Asst. Prof. SORANUN CHANTARANGSU, D.D.S., Ph.D.

Background: Kidney transplantation is considered to be the best treatment for end-stage renal disease patient, and widely accepted it improves quality and length of life. However, the kidney transplant recipient has to receive long-term immunosuppressive therapy in order to prevent kidney transplant rejection, causing the immune function system declined. Oral and dental problems also increase in these patients, which mostly develop as a result of side effects and drug interaction. This study aims to determine the prevalence and risk factors of oral soft tissue lesions in kidney transplant recipients. Methodology: The cross-sectional study was conducted in April to October 2019. Sixty-five kidney transplant recipients and 65 dialysis patients were examined for oral soft tissue lesion, oral hygiene and gingival enlargement. Difference on prevalence of oral soft tissue lesions between groups was tested by Chi-square. For the risk factors, categorical data was presented in frequencies and percentages. Continuous data was presented in means and standard deviations. Univariate and multivariate linear regression was used to assess association between plaque index and different variables. Results: Oral lesions were found in 7 (10.8%) kidney transplant recipients and 6 (9.2%) dialysis patients. Though plaque index in kidney transplant recipients was not significantly different from dialysis group, linear regression model revealed that plaque index was increasing by age (regression coefficient (95% confidence interval) = 0.009 (0.001-0.016); p -value=0.025). Conclusions: Prevalence of oral soft tissue lesions in both groups were not statistically significant different and prevalence in kidney transplant recipients was lower than most of previous studies. Regular dental examination is necessary for early detection, which allows consulting in medications adjustment and stops or relieves progression of oral lesion.

Field of Study: Geriatric Dentistry and Special Patients Care Student's Signature

Academic Year: 2019 Advisor's Signature

Co-advisor's Signature

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Charinrat Sirivichayakul



TABLE OF CONTENTS

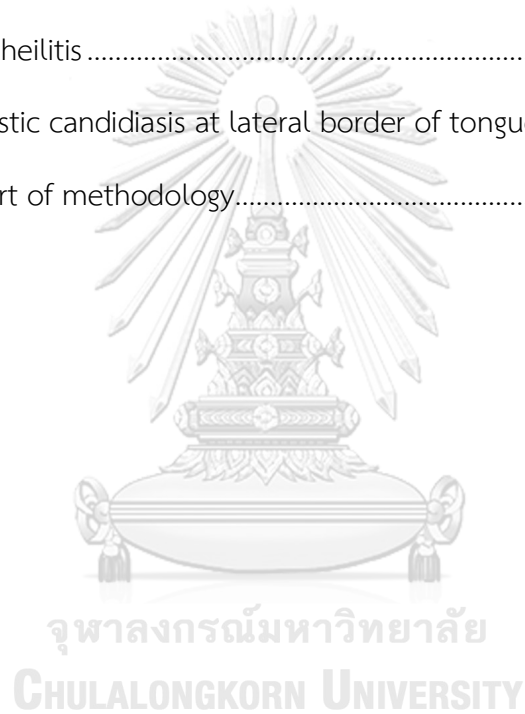
	Page
ABSTRACT (THAI).....	iii
ABSTRACT (ENGLISH).....	iv
ACKNOWLEDGEMENTS	v
TABLE OF CONTENTS.....	vi
LIST OF TABLES.....	vii
LIST OF FIGURES.....	viii
CHAPTER 1.....	1
INTRODUCTION.....	1
CHAPTER 2.....	4
LITERATURE REVIEW	4
CHAPTER 3.....	12
RESEARCH METHODOLOGY.....	12
CHAPTER 4.....	17
RESULTS.....	17
CHAPTER 5.....	25
DISCUSSION.....	25
CHAPTER 6.....	28
CONCLUSIONS	28
REFERENCES	29
VITA.....	51

LIST OF TABLES

	Page
Table 1 stage of chronic kidney disease	4
Table 2 Oral soft tissue lesions (WHO criteria).....	14
Table 3 Aas index.....	14
Table 4 Sillness and Loe index	15
Table 5 Basic characteristics of kidney transplant recipients and dialysis patients	17
Table 6 Oral soft tissue lesions following WHO criteria in kidney transplant recipients and dialysis patients.....	19
Table 7 The associations between immunosuppressive drug usage and the prevalence of oral lesions following WHO criteria in kidney transplant recipients.....	21
Table 8 Linear regression of Plaque index with different variables in kidney transplant recipients.	22
Table 9 Linear regression of Plaque index with different variables in dialysis patients.	23

LIST OF FIGURES

	Page
Figure 1 conceptual framework.....	2
Figure 2 Pseudomembranous candidiasis	8
Figure 3 Erythematous candidiasis.....	9
Figure 4 Median rhomboid glossitis.....	9
Figure 5 Angular cheilitis	10
Figure 6 Hyperplastic candidiasis at lateral border of tongue	10
Figure 7 Flow chart of methodology.....	16



CHAPTER 1

INTRODUCTION

Background and rationale

Chronic kidney disease is growing global public health problem since it is important risk factor of cardiovascular disease (1). Chronic kidney disease can progress and ultimately results in end-stage renal disease (ESRD). According to the nephrology society of Thailand, prevalence of chronic kidney disease stage1-5 is 17.5% of population. The prevalence increases by age. When chronic kidney disease develops into end-stage renal disease, there are substantial impact on patient's longevity and quality of life (2). End-stage renal disease (ESRD) is cessation of effective kidney function and needs kidney replacement therapy, including hemodialysis, peritoneal dialysis and kidney transplantation (1).

Kidney transplantation has become routine procedure in industrialized country owing to medically and economically effective (2). It is widely accepted that kidney transplantation improves quality and length of life (3). However, the kidney transplant recipient has to receive long-term immunosuppressive therapy in order to prevent kidney transplant rejection (4), the immune function system is declined.

Owing to increasing of life expectancy in kidney transplant recipients, there is an impact on oral and dental health services. Different oral and dental problems increase in these patients, which mostly develop as a result of drug-induced immunosuppression (5). Immunosuppressive therapy depresses the cell-mediated immune response, producing antibodies, neutrophils, monocytes, natural killer cells and complements (6). These cause greater risk of oral infection and other associated complications. So microbial agents of oral normal flora become opportunistic pathogens and cause oral tissue infection and destruction. Oral soft tissue lesions may also develop as a consequence of side effects and drug interactions during immunotherapy. These drugs reduce the general immune response of kidney

transplant recipients, increasing the susceptibility to infections and the potential of developing lesions. Since there is a high prevalence of oral manifestations after kidney transplantation, these kidney transplant recipients must undergo regular oral examination by dentist in order to diagnose and treat any suspicious lesion. Instruction of proper oral hygiene procedures in these patients may prevent oral lesions to some extent (7).

It is important to maintain good oral hygiene and care as well as regular professional control by the dentist. This approach can reduce the number and severity of oral lesions.

The aim of this study is to determine the prevalence and risk factors of soft tissue lesions in kidney transplant recipients

Keyword

Oral soft tissue lesions, kidney transplantation, immunosuppressive drug

Conceptual framework

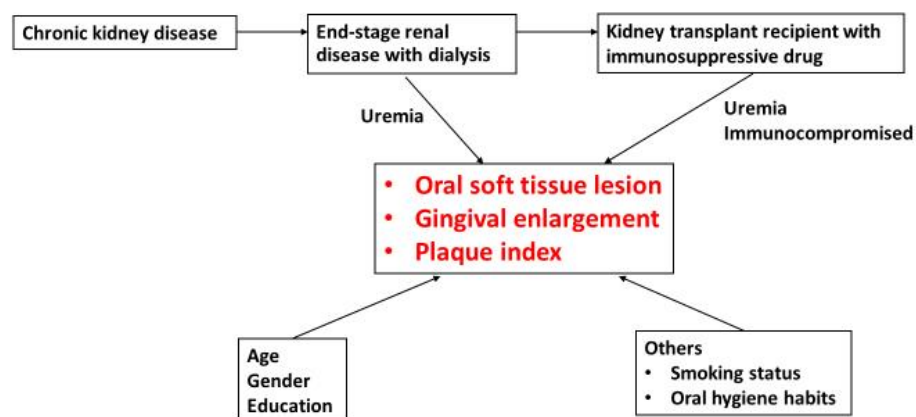


Figure 1 conceptual framework

Field of research

Clinical research

Type of research

Descriptive research

Research questions

1. Is the prevalence of oral soft tissue lesion in kidney transplant recipients different from in dialysis patients?
2. What are the risk factors that relate to oral soft tissue lesions in kidney transplant recipients?

Research objectives

1. To determine the prevalence of oral soft tissue lesions in kidney transplant recipients, compare with dialysis patients.
2. To identify the risk factors that related to oral soft tissue lesions in kidney transplant recipients.

Research hypothesis

The prevalence of oral soft tissue lesions in kidney transplant recipients is different from in dialysis patients.

Expected benefits

1. The result of this study will provide clinical evidence of oral soft tissue lesions in kidney transplant recipients.
2. The result of this study will provide benefit in oral care in kidney transplant recipients.

Scope of research

This study aims to determine the prevalence and risk factors of soft tissue lesions in kidney transplant recipients and dialysis patients at Division of Nephrology, Department of Medicine, Faculty of Medicine, Chulalongkorn University and Chulalongkorn Memorial hospital, Bangkok, Thailand.

CHAPTER 2

LITERATURE REVIEW

Chronic kidney disease

Chronic kidney disease is gradually irreversible loss of kidney function overtime. When GFR is decreased to less than 60mL/min/1.73m² for more than 3 months, patient is diagnosed as chronic kidney disease. (8) Staging of CKD is shown in Table 1.

Table 1 stage of chronic kidney disease

Stage	GFR (mL/min/1.73m ²)
1	>90
2	60-89
3a	45-59
3b	30-44
4	15-29
5	<15

As the disease progress, more nephrons are destroyed, normal homeostasis is inability to be maintained. Conservative care is not enough to control waste product, fluid balance and electrolyte level. Patient becomes end-stage renal disease (ESRD). They need kidney replacement therapy, consisting of hemodialysis, peritoneal dialysis and kidney transplantation (1).

Kidney transplantation

For the end-stage renal disease patient, kidney transplantation can be the kidney replacement therapy of choice unless there are comorbid conditions, including cannot perform surgery or receive long-term immunosuppressive therapy(4). It has become routine procedure in industrialized countries because of being medically and economically most effective (9).

Immunosuppressive drugs

Since the graft rejection is the major problem in transplantation. Long-term immunosuppressive therapy is required in order to pacify alloimmune response and allow long-term transplant survival (4). Though immunosuppressive drugs increase success rate of kidney transplant, transplant recipient is susceptible to infection due to being immunocompromised. The majority complication of kidney transplantation is sepsis. Acyclovir and Nystatin are always provided for first 3 months in order to prevent Herpes simplex virus, Cytomegalovirus and *Candida* infection (8).

Oral soft tissue lesions

Kidney transplantation recipients usually have significant comorbidities owing to being exposed to dialysis for long period, and permanent immunosuppression (10). Permanent immunosuppression after kidney transplantation may predispose patients to different conditions and diseases including oral lesions (10). The most common benign oral lesions in kidney transplantation are gingival enlargement, oral candidiasis, hairy leukoplakia, and saburral tongue.

Gingival enlargement

Gingival enlargement or gingival hyperplasia is the most common lesion in kidney transplantation recipients (11) and it is a well-known side effect of cyclosporine, calcium channel blockers, and anticonvulsants (12). The prevalence in kidney transplantation recipients ranges from 22 to 77%. According to Al-Mohaya et al study, the prevalence is 74% (11). The etiology of drug-induced gingival enlargement remains unknown and probably multiple factors, including inflammation, drug use, neoplasia, hormonal disturbance and ascorbic acid deficiency. Cyclosporine dose and serum level are significant risk factors, as well as gingival inflammation and tooth plaque. Lack of oral hygiene, abnormal relationship between adjacent and antagonist teeth, cervical caries, overhanged dental

restoration, food impaction and oral breathing may contribute to gingival enlargement.

Disorders affecting the gingival fibroblasts or the enzymes responsible for catabolism of the cellular matrix lead metabolic imbalance that favours the development of gingival enlargement. Chronic inflammation is the direct result of prolonged local irritation.

Gingival enlargement can be scored in three or better four grades. The most affected areas are usually labial aspects of both superior and inferior anterior teeth (13). At the beginning, interdental papilla become soft, red nodules, which can easily bleed. Progressive enlargement extends to labial, buccal, palatal, and lingual gingiva, later tissue becomes pink, firm and resilient to palpation because of fibrotic changes. Gingival enlargement can be aesthetic problems and painful, causing difficulties in eating and speaking. It also leads bleeding, friability of tissue, abnormal movement of teeth and enhances dental caries development and other periodontal disorders as well (14).

Oral candidiasis

Fungus infection in oral cavity is caused by several fungi species. Oropharyngeal candidiasis is an opportunistic infection which is resulted from *Candida* species (15), especially more than 87% in oral cavity are *Candida albicans* and *Candida glabrata* (16) that reside with normal flora. *Candida albicans* is the most prevalent species that can be isolated from human body as a commensal or an opportunistic pathogens (17). It can cause infection, varied from mild infection to severe mortality, especially in patients with underlying disease (18).

Candida albicans, a common opportunistic pathogen in oral cavity, is asexual diploid dimorphic fungus that was first found in the sputum of tuberculosis patient in 1844 (19). There are more than 150 *Candida* species that can grow on agar, at 20-40 °c pH 2-8. The characteristics of *Candida albicans* are opaque turbid. They can turn

into several forms, including yeast cell budding yeast cell, pseudohyphae, true hyphae, and chlamydozoospores (20).

In normal state, *Candida* can be found in oral cavity without any sign and symptom. These people are considered as *Candida* carriers.

In previous study (21), normal carriers were defined when they had colony counts of *Candida* less than 1000 colony-forming units (CFU) per 1 ml of saliva, whereas infected patients had 4000-20000 colony-forming units (CFU) per 1 ml of saliva, tested with periodic acid-Schiff (PAS) staining of a cytology smear of pseudomembrane.

One study in Thailand, from Oral Diagnostic Clinic, Chulalongkorn University, showed 1.8% candidiasis in the elderly whose ages were more than 60 years old (22). Another report in 20 to 60-year-old healthy people without any sign and symptom of candidiasis, by culture-based and molecular assays, found 55.1% candida carriage and 88.9% were *Candida albicans* (23).

Although, *Candida* species are normal flora and do not cause the disease in normal state, there can cause irritation taste alteration, dysphagia, and malnutrition. Especially in HIV patients, infection can spread through blood currency, causing septicemia that is virulent and mortal (24).

Categories of *Candida* infection (25)

1. Pseudomembranous candidiasis (Figure 2)

Lesions are covered by pseudo mucous membranes, consisting of hyphae of fungi desquamative cells, microorganisms, fibrins, and inflammatory cells. Clinical characteristic is white patch on the surface of tongue, lip, palate, gingiva, posterior pharyngeal wall that can be scraped off and may cause red lesions or bleeding beneath. The characteristic can be differential diagnosed *Candida* infection from other white lesions. The confirmation of *Candida* infection can be examined by

scraping white patch off in order to periodic acid-schiff (PAS). This infection can cause mortality especially when infection invades esophagus or trachea. The infection is usually found in neonate, immunosuppressed, HIV (26), elderly patients, uncontrolled diabetes mellitus patients, patients with psychotropic drugs, broad spectrum antibiotics, and terminal ill as well (27).



Figure 2 Pseudomembranous candidiasis

(28)

2. Erythematous candidiasis (Figure 3)

This type of lesions is classified into symptomatic and asymptomatic. In symptomatic lesions there are burning sensation. The diagnosis is difficult because lesions may be red, similar to vitamin B₁₂, folate, and iron deficiency. The lesions are commonly found in the elderly with dentures and antibiotics or steroid aerosol inhaler agents (27). For asymptomatic lesions, it frequently associated with poor oral hygiene and chronic use of prostheses (26). There may be red lesion on tissue under denture base, called denture-induced stomatitis. These may be confused with acrylic resin allergy. Most patients do not have any symptom, however ill-fitting denture promotes the growth of *Candida* (29). Severity of *Candida* lesions are categorized into 3 types (30), consisting of pinpoint hyperemia, diffuse hyperemia which is most common type, and papillary hyperplasia which is most severe type.



Figure 3 Erythematous candidiasis

(28)

3. Median rhomboid glossitis (27) (Figure 4)

This lesion is chronic inflammation, located in anterior tongue to the circumvallate papillae. The lesion is resulted from filiform papillae atrophy. Though etiology of the disease is unknown, *Candida* infections are found more than 85% in lesions when biopsy (31). Fig (28)

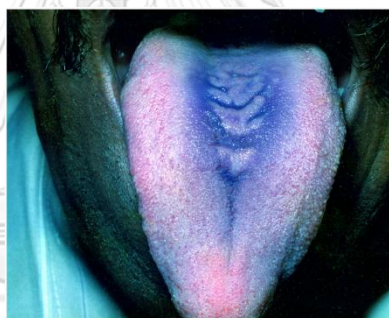


Figure 4 Median rhomboid glossitis

(28)

4. Angular cheilitis (Figure 5)

Red lesion at both corners of the mouth that is not only usually associated with oral *Candida* infection, but *Staphylococci* and *Streptococci* as well (27). *Staphylococci* from the nostril spread to the corners of mouth, especially in the elderly's wrinkles on the corners of mouth promote environment for these lesions (32). In patients with removable prostheses, bone resorption can cause loss of vertical dimension (33), promote more severe lesions. Besides, the lesions are related to iron (34) and vitamin B₁₂ deficiency (35).



Figure 5 Angular cheilitis

(25)

5. Hyperplastic candidiasis (Figure 6)

This lesion is related to chronic infection of oral epithelium. Clinical characteristic is white patch adhered to mucosa, located on buccal mucosa, corner of the mouth, palate, and tongue. It cannot be scraped off. The lesion is also associated with smoking (36). 15% of lesions can become severe dysplasia and develop to malignancy tumor (37). Biopsy is needed in order to confirm *Candida* infection and detect tissue abnormality as well.



Figure 6 Hyperplastic candidiasis at lateral border of tongue

(28)

Saburral tongue

Saburral tongue is clinically presented as a yellowish-white superficial layer on dorsum of the tongue, similar to pseudomembranous candidiasis, but cannot be scraped off (10). Filiform papillae can be enlarged. According to previous study, the lesion was found in 22% of kidney transplant recipients (7). Though the etiology remains unknown, some authors reported that saburral tongue associates with poor oral hygiene (38).

Hairy leukoplakia

Leukoplakia is defined as a white adherent patch or plaque that occur on oral mucosa. Oral hairy leukoplakia is a form of leukoplakia, displays as a white, hairy lesion on one or both lateral border of tongue that cannot be scraped off (10). Hairy leukoplakia was found in 8-11% in kidney transplant recipients (11) (39). The lesion is related to immune status and mostly presented in immunocompromised (40).

Aphthous ulcers

Aphthous ulcers have been shown to related to a high dose of immunosuppressive drugs, the withdrawal of corticosteroids or drug toxicity (41).

Malignancy tumour

Immunosuppressive therapy increases the risk of malignancy (11). The incidence ranges from 2.3 to 31% (42). The incidence of intraoral malignancy increases in patients with long-term immunosuppressive therapy as the time elapses. Lip cancer was shown to be more frequent in males and elderly patients in a lengthy post-transplant follow-up (42). Kidney transplant recipients also increase risk for other malignancies such as Kaposi's sarcoma, uterine cervix cancer, basal cell carcinoma, and non-Hodgkin's lymphoma (11).

CHAPTER 3

RESEARCH METHODOLOGY

Subjects and methods

Sample size calculation

The sample size was calculated using proportion of patients with oral lesions from the previous studies (42, 43) with an alpha of 0.05 and 0.8 power for testing two independent proportions (two-tailed test) using the following formula by n4Studies

$$n_1 = \left[\frac{z_{1-\frac{\alpha}{2}} \sqrt{\bar{p}\bar{q}(1+\frac{1}{r})} + z_{1-\beta} \sqrt{p_1 q_1 + \frac{p_2 q_2}{r}}}{\Delta} \right]^2$$

$$r = \frac{n_2}{n_1}, q_1 = 1 - p_1, q_2 = 1 - p_2$$

$$\bar{p} = \frac{p_1 + p_2 r}{1+r}, \bar{q} = 1 - \bar{p}$$

$$m_1 = \frac{n_1}{4} \left(1 + \sqrt{1 + \frac{2(r+1)}{n_1 r |p_2 - p_1|}} \right)^2$$

A sample size of n = 65 per group and n = 130 in total.

The population in this study were kidney transplant recipients and dialysis patients from Department of Medicine, Faculty of Medicine, Chulalongkorn University.

Inclusion criteria

1. Kidney transplant recipients who were adult 18 years old or over, post-transplanted at least 6 months and receiving immunosuppressive drugs.
2. Subjects who were on dialysis.
3. Subjects who were willing to undergo informed consent process and able to follow the study methods throughout the study.

Data collection

The cross-sectional study was conducted in the period of 6 months (April to October 2019) after approval by Research Ethics Committee, Institutional Review Board, Faculty of Medicine, Chulalongkorn University (IRB no.88/62). Seventy-one kidney transplant recipients who had received successful kidney transplantation at least 6 months earlier were included in this study. Seventy-one dialysis patients age-matched were also randomly recruited as a control group. The study was performed in follow-up visit at the Division of Nephrology, Department of Medicine, Faculty of Medicine, Chulalongkorn University and Chulalongkorn Memorial hospital.

The study protocol was explained to each patient. After signing informed consent, patients' demographic data and additional details regarding medical history and dental history were recorded.

Clinical oral examination, taking 15 minutes, consisted of oral soft tissue lesion, gingival hyperplasia and oral hygiene and was carried out by single investigator, using mouth mirror and dental explorer. Light weight portable examination light was provided as recommended by World Health Organization (WHO) (44). Results were calibrated in 10% by using photograph examination. Each photograph was examined 2 times and the same result was seen. The intraobserver agreement is equal to 0.99 when assessed by Cohen's kappa statistic.

Oral soft tissue lesion

Oral soft tissue lesions were clinically examined based on World Health Organization (WHO) criteria (44). The oral mucosa was evaluated in order to identify type of lesions and their locations. Lesions of oral mucosa were photographically documented and subjects were referred to Dental department for further diagnostic and treatment. Biopsy was performed in case with a doubtful diagnosis and for suspected malignancy. Oral lesions were recorded following WHO criteria in Table 2.

Table 2 Oral soft tissue lesions (WHO criteria)

Lesions	Locations
0 = no abnormal condition	0 = vermillion border
1 = malignant tumour (oral cancer)	1 = commissures
2 = leukoplakia	2 = lips
3 = lichen planus	3 = sulci
4 = ulceration (aphthous, herpetic, traumatic)	4 = buccal mucosa
5 = acute necrotizing ulcerative gingivitis (ANUG)	5 = floor of the mouth
6 = candidiasis	6 = tongue
7 = abscess	7 = hard and/ or soft palate
8 = other conditions (e.g. keratosis, Koplick spots)	8 = alveolar ridges/ gingiva
9 = not recorded	9 = not recorded

Gingival enlargement

Gingival enlargement was measured per sextant using Aas index (45), displaying in Table 3. Each sextant was graded according to most severe site. A subject was classified as having gingival enlargement when at least one interdental papilla with gingival enlargement grade presented in at least one sextant.

Table 3 Aas index

Grade	Criteria
0	No gingival enlargement
I	Slight or moderate gingival enlargement. The interdental papillae have assumed a more round, blunted form; the gingival margin is slightly thickened. The anatomic crowns are covered up to one-third of the vestibular surfaces.
II	Marked gingival enlargement. The papillae and the gingival margin cover

	from one-third to one-half of the vestibular surfaces. In most cases, the papillae are separated only by V-shaped cleft.
III	Severe gingival enlargement. The gingiva propria covers one-half to two-thirds of the vestibular surfaces and protrudes 3 to 4 mm from the surface of the teeth.
IV	Very severe gingival enlargement. The hyperplastic tissue covers from two-thirds to the whole of anatomic crowns in one or more regions, and occlusion is rendered difficult if not prevented.

Oral hygiene

Plaque index was determined by Silness-Loe index (Silness and Loe, 1964) (46). The measurement based on recording both soft debris and mineralized deposits on the following teeth: tooth 16 12 24 36 32 44. The sum of 4 surfaces (buccal, lingual, mesial and distal) of each tooth was divided by four, and then average plaque index of all investigated was calculated. Missing tooth was not substituted. The score of each surface is shown in Table 4.

Table 4 Silness and Loe index

Scores	Criteria
0	No plaque
1	A film of plaque adhering to the free gingival margin and adjacent area of the tooth. The plaque may be seen in situ only after application of disclosing solution or by using the probe on the tooth surface.
2	Moderate accumulation of soft deposit within the gingival pocket, or the tooth and gingival margin which can be seen with the naked eye.
3	Abundance of soft matter within the gingival pocket and/or on the tooth and gingival margin.

Statistical Analysis

The participants were divided into 2 groups (kidney transplant recipients and chronic kidney disease patients). Difference on prevalence of oral soft tissue lesions between groups was tested by Chi-square. For the risk factors, categorical data was presented in frequencies and percentages. Continuous data was presented in means and standard deviations. Data were analyzed using IBM SPSS Statistics for Windows, Version 22.0 (IBM, Armonk, NY). Univariate and multivariate linear regression were used to assess association between plaque index and different independent. Statistical significance was determined at p -value < 0.05 .

Ethical consideration

The project was approved by Research Ethics Committee, Institutional Review Board, Faculty of Medicine, Chulalongkorn University (IRB no.88/62).

Flow chart of methodology

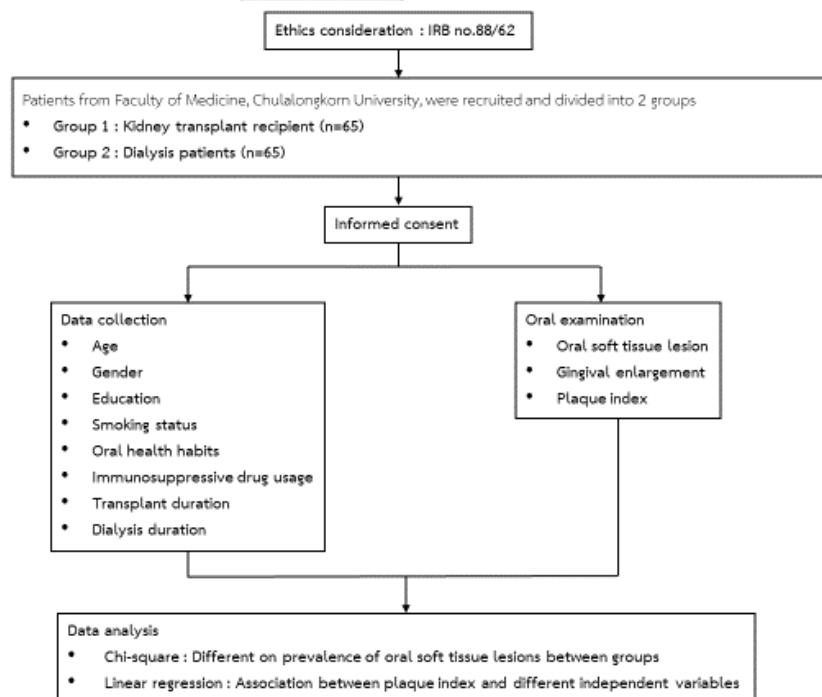


Figure 7 Flow chart of methodology

CHAPTER 4

RESULTS

One hundred and thirty participants were from the Division of Nephrology, Department of Medicine, Faculty of Medicine, Chulalongkorn University. All patients were Thai, 73 (56.2%) were male and 57 (43.8%) were female. Their age ranged from 22 to 81 years (average 49.1 ± 12.0).

Sixty-five kidney transplant recipients, of which 42 (64.6%) were male and 23 (32.3%) were female. The mean age of kidney transplant recipients was 50.3 ± 11.8 (range 22-79) years. The mean duration after kidney transplantation was 106.8 ± 82.0 (range 12 to 376) months.

Sixty-five dialysis patients were also examined as a control group. Thirty-one (47.7%) were male and 34 (52.3%) were female. The mean age of dialysis patients is 48.0 ± 12.2 (range 22-81) years. The duration of dialysis was 57.3 ± 37.7 (range 8-178) months. The demographic data of kidney transplant recipients and dialysis patients is displayed in Table 5.

Table 5 Basic characteristics of kidney transplant recipients and dialysis patients

Characteristics	Kidney transplant recipient	Dialysis patient	P-value
Gender, N (%)			
Male	42 (64.6%)	31 (47.7%)	0.052 ^a
Female	23 (32.3%)	34 (52.3%)	
Age, mean (S.D.)	50.3 (11.8)	48.0 (12.2)	0.273 ^b
Transplant duration, mean (S.D.)	106.8 (82.0)	-	
Dialysis duration, mean (S.D.)	-	57.3 (37.7)	

Education, N (%)			
None	0 (0%)	0 (0%)	0.658 ^a
Primary school	6 (9.2%)	9 (13.8%)	
High school	19 (29.2%)	20 (30.8%)	
University	40 (61.5%)	36 (55.4%)	
Smoking, N (%)			
Never	47 (72.3%)	47 (72.3%)	0.598 ^a
Former	17 (26.2%)	18 (27.7%)	
Smoking	1 (1.5%)	0 (0%)	
Frequency of teeth cleaning, N (%)			
0	0 (0%)	1 (1.5%)	0.574 ^a
1	6 (9.2%)	7 (10.8%)	
2	59 (90.8%)	57 (87.7%)	
Toothpaste, N (%)			
Fluoride	52 (80.0%)	53 (81.5%)	0.824 ^a
Non-fluoride	13 (20.0%)	12 (18.5%)	
Last visit to dentist, N (%)			
Within 6 months	17 (26.2%)	26 (40.0%)	0.730 ^a
Within 1 year	10 (15.4%)	14 (21.5%)	
More than 1 year	38 (58.5%)	25 (38.5%)	
Denture			
Yes	10 (15.4%)	8 (12.3%)	0.612 ^a
No	55 (84.6%)	57 (87.7%)	

^a chi-square test

^b independent t-test

Drug administration in kidney transplant recipients was in the following order: all patients were receiving immunosuppressive drugs, 40 (61.5%) were receiving tacrolimus, 18 (27.7%) were receiving cyclosporin, 47 (72.3%) were receiving prednisolone, 40 (61.5%) were receiving mycophenolate mofetil. Fourteen (21.5%) and 3 (4.6%) were receiving sirolimus and everolimus, respectively.

Oral lesions were found in both kidney transplant recipients and dialysis patients. Lesions in kidney transplant recipients were shown in higher prevalence than dialysis group. However, it was not significantly different from the control group (p -value 0.770). Lesions were found in 7 (10.8%) kidney transplant recipients and 6 (9.2%) dialysis patients. The most common oral manifestation was oral ulcer, 5 (7.7%) in kidney transplant recipients and 4 (6.2%) in dialysis patients. One (1.5%) median rhomboid glossitis and 1 (1.5%) fibroma on tongue were found in kidney transplant recipients. Gingival enlargement grade II was found in a kidney transplant recipient who was on CSA and calcium channel blocker. One (1.5%) geographic tongue and 2 (3.1%) fissure tongue were found in dialysis patients. Fifty-eight (89.2%) kidney transplant recipients and 59 (90.8%) dialysis patients did not show any oral manifestation. Oral lesions, follow WHO criteria, were displayed in their types and locations in the Table 6.

Table 6 Oral soft tissue lesions following WHO criteria in kidney transplant recipients and dialysis patients

Characteristics	Kidney transplant recipient (N = 65)	Dialysis patient (N = 65)	<i>P</i> -value
Lesions, N (%)			
Total lesions	7 (10.8%)	6 (9.2%)	0.770 ^a
0 = No abnormal condition	58 (89.2%)	59 (90.8%)	

1 = Malignant tumour (oral cancer)	0 (0%)	0 (0%)	
2 = Leukoplakia	0 (0%)	0 (0%)	
3 = Lichen planus	0 (0%)	0 (0%)	
4 = Ulceration (aphthous, herpetic, traumatic)	5 (7.7%)	4 (6.2%)	
5 = Acute necrotizing ulcerative gingivitis	0 (0%)	0 (0%)	
6 = Candidiasis	1 (1.5%)	0 (0%)	
7 = Abscess	0 (0%)	0 (0%)	
8 = Other conditions			
Fibroma	1 (1.5%)	0 (0%)	
Geographic tongue	0 (0%)	1 (1.5%)	
Fissure tongue	0 (0%)	2 (3.1%)	
9 = not recorded	0 (0%)	0 (0%)	
Location, N (%)			
None	58 (89.2%)	59 (90.8%)	0.411 ^a
0 = vermillion border	0 (0%)	0 (0%)	
1 = commissures	0 (0%)	0 (0%)	
2 = lips	2 (3.1%)	0 (0%)	
3 = sulci	0 (0%)	0 (0%)	
4 = buccal mucosa	2 (3.1%)	4 (6.2%)	
5 = floor of mouth	0 (0%)	0 (0%)	
6 = Tongue	3 (4.6%)	2 (3.1%)	
7 = Hard and/ or soft palate	0 (0%)	0 (0%)	
8 = Alveolar ridges/ gingiva	0 (0%)	0 (0%)	
9 = not recorded	0 (0%)	0 (0%)	

^a chi-square test

One patient can show more than one oral soft tissue lesion.

In kidney transplant recipients, there is no significant association between immunosuppressive drug usage and the prevalence of oral lesions following WHO criteria when assessed by Fisher's exact test (Table 7).

Table 7 The associations between immunosuppressive drug usage and the prevalence of oral lesions following WHO criteria in kidney transplant recipients

Immunosuppressive drug usage	Kidney transplant recipients without oral lesions, (N = 58)	Kidney transplant recipients with oral lesions, (N = 7)	P-value
Tacrolimus			0.415 ^a
Yes	37 (63.8%)	3 (42.9%)	
No	21 (36.2%)	4 (57.1%)	
Cyclosporine			0.385 ^a
Yes	15 (25.9%)	3 (42.9%)	
No	43 (74.1%)	4 (57.1%)	
Prednisolone			1.000 ^a
Yes	42 (72.4%)	5 (71.4%)	
No	16 (27.6%)	2 (28.6%)	
Sirolimus			0.638 ^a
Yes	12 (20.7%)	2 (28.6%)	
No	46 (79.3%)	5 (71.4%)	
Everolimus			0.294 ^a
Yes	2 (3.4%)	1 (14.3%)	
No	56 (96.6%)	6 (85.7%)	
Mycophenolate mofetil			0.698 ^a
Yes	35 (60.3%)	5 (71.4%)	
No	23 (39.7%)	2 (28.6%)	

^a Fisher's exact test

One patient received more than one immunosuppressive drug.

Plaque index was determined in both groups on tooth 16 12 24 36 32 44. In this study these representative teeth had not lost more than 2 in each patient, and they were not substituted. Plaque score (the sum of 4 surfaces of these teeth) was divided by the number of teeth.

In kidney transplant recipients, plaque index was ranging from 0.9 to 2.8 (average 1.4 ± 0.4) and this finding is not significantly different from the control group (p -value = 0.082) which plaque index was ranging from 0.9 to 2.3 (average 1.6 ± 0.3).

When relationship of plaque index with different variables was assessed by univariate and selected only variable with p -value < 0.05 to include in the multivariate model, the significant correlation was found in kidney transplant recipients that plaque index was increasing with age (regression coefficient (95% confidence interval) = 0.009 (0.001-0.016); p -value = 0.025), whereas this relationship was not found in dialysis patients. The significant correlation in dialysis patients was plaque index was increasing in patients who lesser performed teeth cleaning (regression coefficient (95% confidence interval) = -0.258 (-0.458--0.059); p -value = 0.012), who had not visited dentist within 1 year (regression coefficient (95% confidence interval) = 0.191 (0.032-0.350); p -value = 0.019) and who had higher hemoglobin (regression coefficient (95% confidence interval) = 0.050 (0.010-0.091); p -value = 0.016). Relationship between plaque index and different variables in kidney transplant recipients and dialysis patients were shown in Table 8 and 9, respectively.

Table 8 Linear regression of Plaque index with different variables in kidney transplant recipients.

Independent variables	Univariate linear regression		Multivariate linear regression	
	β (95% CI)	p -value	β (95% CI)	p -value
Age	0.010 (0.003, 0.017)	0.006	0.009 (0.001, 0.016)	0.025

Male	0.148 (-0.031, 0.328)	0.104	-	-
Education	0.001 (-0.132, 0.134)	0.990	-	-
Former/current smoking	-0.101 (-0.296, 0.093)	0.301	-	-
Transplant duration	0.001 (0.000, 0.002)	0.054	0.001 (0.000, 0.002)	0.266
Frequency of teeth cleaning	-0.210 (-0.508, 0.089)	0.165	-	-
Using fluoride toothpaste	0.090 (-0.128, 0.308)	0.410	-	-
More than 1 year last visiting to dentist (Reference: within 1 year visiting to dentist)	0.024 (-0.154, 0.202)	0.789	-	-
BUN	0.001 (-0.005, 0.006)	0.789	-	-
Creatinine	-0.017 (-0.078, 0.044)	0.578	-	-
Hb	-0.001 (-0.044, 0.043)	0.981	-	-
HbA1c	0.012 (-0.019, 0.043)	0.451	-	-
LDL	-0.001 (-0.003, 0.001)	0.248	-	-

Table 9 Linear regression of Plaque index with different variables in dialysis patients.

Independent variables	Univariate linear regression		Multivariate linear regression	
	β (95% CI)	<i>p</i> -value	β (95% CI)	<i>p</i> -value

Age	0.002 (-0.005, 0.009)	0.606	-	-
Male	0.023 (-0.151, 0.196)	0.795	-	-
Education	-0.041 (-0.161, 0.079)	0.495	-	-
Former/current smoking	0.069 (-0.123, 0.262)	0.476	-	-
Transplant duration	0.001 (-0.001, 0.004)	0.226	-	-
Frequency of teeth cleaning	-0.232 (-0.448, -0.017)	0.035	-0.258 (-0.458, -0.059)	0.012
Using fluoride toothpaste	0.101 (-0.121, 0.322)	0.368	-	-
More than 1 year last visiting to dentist (Reference: within 1 year visiting to dentist)	0.204 (0.033, 0.374)	0.020	0.191 (0.032, 0.350)	0.019
BUN	-0.001 (-0.005, 0.003)	0.586	-	-
Creatinine	-0.017 (-0.045, 0.011)	0.224	-	-
Hb	0.052 (0.008, 0.095)	0.020	0.050 (0.010, 0.091)	0.016
HbA1c	0.018 (-0.012, 0.048)	0.231	-	-
LDL	-0.002 (-0.004, 0.001)	0.121	-	-

CHAPTER 5

DISCUSSION

In current study, oral soft tissue lesion was determined in kidney transplant recipients and dialysis patients in Thai population, from Faculty of Medicine, Chulalongkorn University. The prevalence of oral lesions in kidney transplant recipients (10.8%) was not statistically significant different from dialysis patients (9.2%). In kidney transplant recipients. The prevalence of oral lesions was lower from most of previous reports, compared to the studies which determined the similar oral soft tissue lesions, the prevalence ranged from 10.7- 43.9% (42) (47) (48) (49).

The most common oral lesion in both groups was oral ulceration (7.7% in kidney transplant and 6.2% in dialysis patients), compared with previous studies (2.2- 7%) (42) (47) (48) (49). In patients with oral ulceration, they had received different combination of medicines: (tacrolimus, prednisolone, mycophenolate mofetil), (cyclosporin, prednisolone, mycophenolate mofetil), (tacrolimus, prednisolone, sirolimus), (everolimus and mycophenolate mofetil), (cyclosporin and mycophenolate mofetil). Oral ulcer might be related to high dose immunosuppressive drugs, the withdrawal of corticoids or pharmacologic problems (50) (41). There has been reports of oral ulcer in transplant recipients in relation to the immunosuppressants such as sirolimus (51) (52) (53), tacrolimus (50) (54) and mycophenolate mofetil (55) (56) (57).

Fibroma, benign tumor, was found in 1 (1.4%) kidney transplant recipients, compared to previous study (0.5-2.8%) (42) (49). Fibroma is a reactive hyperplasia of fibrous connective tissue in response to irritation or trauma (58). In this study, lesion was found on tongue and biopsy revealed that the lesion was fibroepithelial polyp. Sirolimus was just administered to this patient. This ulceration could be the result of the antiproliferative effect and the effect of sirolimus on growth factors (59) (60) that related to the greater prevalence of wound infection and delayed wound healing

(61). However, there is no evidence showed that the lesion could be related to any medication or patient's immune status.

Gingival enlargement grade II was found in a kidney transplant recipient which was caused by cyclosporin A and calcium channel blocker as reported in previous studies (62) (12) (63). In this study, 26.8% of kidney transplant recipients received cyclosporin A, but only 1.4% of gingival enlargement was found, showed much lower prevalence when compared with previous studies(ranged from 8 to 85%) (11) (12) (64). Though the mechanism of gingival enlargement remains unknown, some studies reported that cyclosporin affects different signaling molecules in gingival fibroblasts (65). Calcium channel blocker changes calcium ion flux which influences on collagenase, resulting in collagen production change and gingival fibroblast breakdown and finally collagen deposition in gingival tissue (11) (66).

Median rhomboid glossitis, one form of erythematous candidiasis, was found in kidney transplant recipients who was on tacrolimus. Candida species are normal flora in oral cavity can turn into opportunistic pathogens (15) when immune function is suppressed and it is possible when patient has received long-term immunosuppressive drugs. In previous studies oral candidiasis varied from 9.4 to 46.7% (11) (7) (67) (39) (68) (69).

Since the study of oral soft tissue lesions in kidney transplant recipients had just begun in Thailand. The limitation of this study is that the prevalence was determined in only single center, Faculty of Medicine, Chulalongkorn University, where all patients were referred to dentists for oral examination and they had received dental treatment before kidney transplantation. In addition to well-prepared oral care, medication level was monitored in order to control in appropriate level. Multidrug prescription not only allows synergistic effect, but also avoid drug toxicity. These might be the reasons which cause the influence of immunosuppressive level on oral soft tissue lesion was not found in current study.

The single center-based study might not represent prevalence of oral lesions in Thais. If population in other sites had been determined, the result would have been different. Sample size were relatively small when compared to previous reports and cross-sectional study had just observed in short duration. It might not display true prevalence.

When different variables were adjusted, plaque index in kidney transplant recipients was increasingly significant correlated with age as healthy people (70), while this relationship was not found in dialysis patients. This imply that after kidney transplantation immune system was restored by decreasing uremic toxin, causing the recovery of uremia in dialysis patients. And another reason is that kidney transplant recipient has much better quality of life (3). Dialysis patient had poor oral hygiene owing to impaction of chronic disease and prolonged hospitalization to lifestyle (62) (71) (72). This reason might also be the cause of higher plaque index in dialysis patients who performed lesser times of teeth cleaning and who had not seen dentist for more than 1 year. According to previous study, they found the relationship between the duration of dialysis and progression of periodontitis. Due to patients' uremic status, the more extent period of ESRD the patients had, the progression of periodontitis they would be (62). Then plaque index assessment and oral hygiene instruction could be beneficial to patients. Plaque index level in dialysis patients was found increasing in dialysis patients who had higher hemoglobin as well, though there was no previous study reported or mentioned this relationship.

CHAPTER 6

CONCLUSIONS

From Faculty of Medicine, Chulalongkorn University, oral soft tissue lesions were found (10.8%) in kidney transplant recipients and (9.2%) in dialysis patients. There was not statistically significant different between 2 groups. The lesions in kidney transplant recipients was found lower than most of previous studies. These might be the result of undergoing oral examination and dental treatment before transplantation and immunosuppressant level monitoring and adjusting in appropriate level after transplantation. The benefit of this study was that early detection allows consulting in medications adjustment and stops or relieves progression of oral lesion. Patients whose lesions was found in were received the suggestion to observe or were referred to dental department for additional examination and proper management in major or suspicious cases.

For the aspect of plaque index assessment, plaque index in kidney transplant recipients was not significantly different from the control group. However, oral hygiene instruction was given to all patients.

For further study, prevalence of oral soft tissue lesions in other areas in Thailand would be studied. Bone lesions in oral and maxillofacial regions and periodontal status should be determined.

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จุฬาลงกรณ์มหาวิทยาลัย
CHULALONGKORN UNIVERSITY

Appendices



จุฬาลงกรณ์มหาวิทยาลัย
CHULALONGKORN UNIVERSITY

Appendix A

Charting



จุฬาลงกรณ์มหาวิทยาลัย
CHULALONGKORN UNIVERSITY

Subject number		
Demographic information		
Age	Gender <input type="checkbox"/> Male <input type="checkbox"/> Female	Education <input type="checkbox"/> None <input type="checkbox"/> Primary school <input type="checkbox"/> High school <input type="checkbox"/> University
Smoking <input type="checkbox"/> never <input type="checkbox"/> former smoker <input type="checkbox"/> current smoker		
Medical history		
<input type="checkbox"/> Chronic kidney disease <input type="checkbox"/> BUN.....mg/dl <input type="checkbox"/> Creatinine.....mg/dl Hb..... Na..... K..... Cl..... HCO ₃ Ca..... PO ₄ Mg..... Alb.....		
<input type="checkbox"/> Hypertension		
<input type="checkbox"/> Diabetes mellitus FBS..... HbA1C.....		
<input type="checkbox"/> Others		
<input type="checkbox"/> Kidney transplantation Period after transplantation.....		
List of medications, dose, immunosuppressive drug level		
Dental history		
Frequency of teeth cleaning per day		
<input type="checkbox"/> none		
<input type="checkbox"/> once		
<input type="checkbox"/> twice or more		
Material used for cleaning		
<input type="checkbox"/> toothpaste		
<input type="checkbox"/> mouthwash		

Last visit to dentist

within 6 months

1 year

2 years

more than 2 years


Denture

yes

no

Oral examination

Oral soft tissue lesions (WHO criteria)



0 = no abnormal condition

1 = malignant tumour (oral cancer)

2 = leukoplakia

3 = lichen planus

4 = ulceration (aphthous, herpetic, traumatic)

5 = acute necrotizing ulcerative gingivitis (ANUG)

6 = candidiasis

7 = abscess

8 = other conditions (e.g. keratosis, Koplick spots)

9 = not recorded

0 = vermillion border

1 = commissures

2 = lips

3 = sulci

4 = buccal mucosa

5 = floor of the mouth

6 = tongue

7 = hard and/ or soft palate

8 = alveolar ridges/ gingiva

9 = not recorded

Plaque index (Silness and Loe, 1964)

16				12				24			
B	Li	M	D	La	Li	M	D	B	Li	M	D
44				32				36			
B	Li	M	D	La	Li	M	D	B	Li	M	D

0 = no plaque

1 = A film of plaque adhering to the free gingival margin and adjacent area of the tooth. The plaque may be seen in situ only after application of disclosing solution or by using the probe on the tooth surface.

2 = Moderate accumulation of soft deposit within the gingival pocket, or the tooth and gingival margin which can be seen with the naked eye.

3 = Abundance of soft matter within the gingival pocket and/or on the tooth and gingival margin.

Gingival hyperplasia

0 = No gingival enlargement

I = Slight or moderate gingival enlargement. The interdental papillae have assumed a more round, blunted form; the gingival margin is slightly thickened. The anatomic crowns are covered up to one-third of the vestibular surfaces.

II = Marked gingival enlargement. The papillae and the gingival margin cover from one-third to one-half of the vestibular surfaces. In most cases, the papillae are separated only by V-shaped cleft.

III = Severe gingival enlargement. The gingiva propria covers one-half to two-thirds of the vestibular surfaces and protrudes 3 to 4 mm from the surface of the teeth.

IV = Very severe gingival enlargement. The hyperplastic tissue covers from two-thirds to the whole of anatomic crowns in one or more regions, and occlusion is rendered difficult if not prevented.

Appendix B

Patients' data



จุฬาลงกรณ์มหาวิทยาลัย
CHULALONGKORN UNIVERSITY

Patients' demographic data



pt number	age	gender	education	smoking	F of cleaning	toothpaste	last visit to dentist	F check up	denture	time after KT (M)	oral lesion	hyperplasia	plaque index
kt1	47	1	4	1	2	2	2	2	2	252	0	0	1.1
kt3	39	1	4	1	2	2	3	3	2	18	1	0	1.7
kt4	36	2	4	1	2	2	1	1	2	28	0	0	1.083
kt5	38	1	4	1	2	1	3	2	1	133	0	0	1.6
kt6	63	1	4	2	2	1	3	2	1	17	0	0	1.05
kt7	29	2	4	1	2	2	1	1	2	16	0	0	1.167
kt8	22	1	3	1	2	1	1	1	2	170	0	0	1.542
kt9	52	2	2	1	1	1	3	3	2	22	0	0	1.583
kt10	56	1	4	1	2	2	3	3	2	111	0	0	1.375
k11	65	1	4	1	2	1	3	3	2	231	0	0	2.208
kt12	45	2	4	1	2	1	3	3	2	44	0	0	1.167
kt13	56	1	4	1	2	2	1	1	2	144	0	0	1.813
kt14	52	2	4	1	2	1	3	1	2	18	0	0	1.083
kt15	56	1	4	2	2	1	3	3	1	214	0	0	2.25
kt16	36	1	4	1	2	2	3	3	2	28	0	0	1.458
kt17	35	1	3	2	2	1	3	2	2	172	0	0	1
kt18	61	2	4	1	2	2	1	1	2	153	0	0	1.667
kt19	58	1	3	2	2	1	3	3	2	17	0	0	1.6
kt20	60	1	4	1	1	1	3	2	2	133	0	0	1.4
kt21	43	1	3	1	2	1	3	3	2	25	0	0	1.33
kt22	60	1	3	1	2	1	1	3	2	58	0	0	1.875
kt23	44	2	3	1	2	1	3	3	2	118	0	0	1.833
kt24	49	2	3	1	2	1	3	3	2	193	0	0	1.15
kt25	56	2	3	1	2	1	3	3	2	24	1	0	1.2
kt26	45	1	4	1	1	1	1	3	2	25	0	0	1.167
kt29	28	1	4	2	2	1	1	3	2	36	0	0	0.958
kt30	53	1	3	1	2	2	1	3	2	54	0	0	1.5
kt31	49	1	4	1	2	1	3	3	2	85	0	0	1.6
kt32	39	2	4	1	2	1	3	1	2	60	0	0	1.375
kt34	59	1	4	1	1	2	3	3	2	116	1	0	1.167
kt35	67	1	2	2	2	1	2	3	2	49	0	0	1.75
kt36	63	2	4	1	2	1	3	2	2	53	0	0	1.2
kt37	58	2	4	1	2	1	1	2	1	216	0	0	1.25
kt38	45	1	3	2	2	1	3	2	2	12	0	0	1.042
kt39	53	1	3	2	2	1	1	1	2	161	0	0	1
kt40	46	1	4	1	2	1	2	2	2	41	1	0	1.5
kt41	62	1	3	1	2	2	2	2	2	13	0	0	1.292
kt42	58	2	4	1	2	1	3	3	2	147	0	0	1.25

kt43	66	1	3	1	2	1	1	3	2	77	1	0	1.875
kt44	63	1	2	2	2	1	3	3	2	204	0	0	1.25
kt45	56	1	4	2	2	1	1	3	2	243	2	2	0.875
kt46	79	2	4	1	2	1	1	2	1	376	0	0	2.083
kt47	41	2	4	1	2	1	3	1	2	74	0	0	1.375
kt48	64	2	2	1	2	1	3	3	2	192	0	0	1.167
kt49	44	1	4	1	2	1	1	1	2	84	0	0	1.542
kt50	29	2	4	1	2	2	3	1	2	132	0	0	1.583
kt51	54	1	4	1	2	1	3	3	2	259	0	0	1.375
kt52	51	2	4	1	2	2	2	2	2	72	0	0	0.95
kt53	31	2	4	1	2	1	3	2	2	63	1	0	1.417
kt55	37	1	4	1	2	1	2	2	2	17	0	0	1.208
kt56	46	2	4	1	2	1	1	2	2	158	0	0	1.167
kt57	56	1	4	2	2	1	2	2	1	31	0	0	1.938
kt58	36	1	4	1	2	1	1	2	2	74	0	0	1.5
kt59	56	1	3	2	2	1	3	2	2	13	0	0	1.4
kt60	51	1	3	1	2	1	2	2	1	14	0	0	1.67
kt62	59	1	4	3	2	1	3	3	1	138	0	0	1.33
kt63	59	1	4	2	1	1	3	3	2	230	0	0	1.75
kt64	50	1	3	2	2	1	3	3	2	218	0	0	1.542
kt65	77	1	4	1	1	1	3	3	1	198	0	0	2.75
kt66	37	1	3	2	2	1	3	3	2	143	0	0	1.458
kt67	49	1	3	2	2	1	2	2	2	56	0	0	1.313
kt68	49	2	4	1	2	1	3	3	2	99	0	0	1.4
kt69	51	2	2	2	2	1	3	3	2	96	0	0	1.2
kt70	36	1	3	1	2	1	2	2	2	86	0	0	1.875
kt71	59	2	2	1	2	1	3	2	1	190	0	0	1.7

pt number	age	gender	education	smoking	F of cleaning	toothpaste	last visit to dentist	F check up	denture	time after DL	oral lesion	hyperplasia	plaque index
ckd1	22	2	4	1	2	1	2	1	2	8	0	0	1.167
ckd2	43	1	4	1	2	1	3	3	2	41	0	0	1.875
ckd3	23	1	4	1	2	1	1	1	2	82	0	0	1.125
ckd4	50	2	3	1	2	1	2	2	2	80	0	0	1.15
ckd6	33	2	4	1	2	1	1	1	2	18	0	0	1.33
ckd7	58	2	2	1	2	2	2	2	2	86	0	0	1.79
ckd8	60	2	2	1	2	1	1	2	2	145	0	0	1.83
ckd9	58	2	2	1	2	1	3	3	2	37	0	0	1.85
ckd10	39	1	4	2	2	1	3	2	2	48	0	0	1.375
ckd11	63	1	2	2	2	1	1	3	1	73	2	0	1.33
ckd12	48	2	3	1	0	1	1	3	2	34	0	0	1.542
ckd13	30	1	3	2	1	1	1	2	2	156	0	0	2
ckd14	26	1	3	1	1	1	1	3	2	25	0	0	1.792
ckd15	42	1	3	2	2	1	3	3	2	99	0	0	1.708
ckd16	61	2	4	1	2	1	1	2	2	37	0	0	1.45
ckd17	35	2	4	1	2	2	3	3	2	22	0	0	1.458
ckd18	49	2	3	1	2	1	3	3	2	75	0	0	2.125
ckd19	31	2	4	1	2	1	3	2	2	22	0	0	1.916
ckd20	55	2	4	1	2	1	1	1	2	21	0	0	1.625
ckd22	44	1	3	1	2	1	1	2	2	52	0	0	1.25
ckd23	32	1	4	1	2	1	2	2	2	24	1	0	1.83
ckd24	38	2	4	1	2	1	3	2	2	11	0	0	1.125
ckd25	53	2	3	1	2	1	2	2	2	31	0	0	1.313
ckd26	30	2	4	1	2	2	1	1	2	37	0	0	1.375
ckd27	52	1	4	2	2	1	1	1	2	80	0	0	1.45
ckd28	46	2	4	1	2	1	1	1	2	119	0	0	0.9
ckd30	46	1	4	2	1	1	3	3	1	71	1	0	1.95
ckd31	42	2	4	1	2	1	3	2	2	178	0	0	2.33
ckd32	41	2	4	1	2	1	3	3	1	72	0	0	1.792
ckd33	48	1	4	2	2	1	3	3	2	177	0	0	1.2
ckd34	50	1	3	2	2	1	1	2	2	59	0	0	1.292
ckd35	53	1	4	1	2	2	2	1	2	42	0	0	1.1
ckd36	62	1	4	1	2	1	1	1	2	63	1	0	1.33
ckd37	52	2	4	2	2	1	3	1	2	56	0	0	1.5
ckd38	50	1	4	1	2	1	2	2	2	59	0	0	1.542
ckd39	27	2	4	1	2	1	1	2	2	18	0	0	1.708
ckd40	62	2	2	1	2	2	2	2	2	49	0	0	1.33
ckd41	57	2	3	2	2	1	3	3	2	16	1	0	1.35

ckd42	48	1	4	1	2	1	1	1	2	28	0	0	1.25
ckd43	53	2	4	1	2	2	2	2	2	48	0	0	1.292
ckd44	55	1	3	1	2	2	3	2	2	45	0	0	1.65
ckd45	81	2	2	1	2	1	1	1	1	13	1	0	1.85
ckd46	47	2	3	1	2	1	1	1	2	73	0	0	1.75
ckd47	55	1	3	2	2	1	3	3	2	38	0	0	1.417
ckd49	31	2	4	1	2	1	2	2	2	43	0	0	1.167
ckd51	40	2	4	1	2	1	3	3	2	57	0	0	1.5
ckd52	61	1	3	2	2	2	1	1	2	53	0	0	1
ckd53	36	1	4	1	2	1	3	2	2	61	0	0	1.8125
ckd54	59	1	3	2	2	2	3	3	2	33	0	0	2.25
ckd55	62	2	2	1	2	1	1	3	2	24	0	0	1.5625
ckd56	56	2	4	1	2	1	3	2	1	72	0	0	1.4375
ckd57	53	1	3	2	2	1	2	2	1	73	0	0	1.95
ckd58	62	1	3	1	2	1	1	1	2	34	0	0	1
ckd59	57	1	4	2	2	1	2	2	1	87	0	0	1.75
ckd61	61	1	4	2	1	1	1	1	2	62	0	0	2.042
ckd62	48	1	2	1	2	2	2	2	2	78	0	0	1.2
ckd63	54	2	4	1	2	1	3	2	2	31	0	0	1.667
ckd64	62	1	3	2	2	1	2	3	1	47	0	0	1.667
ckd65	57	1	4	2	1	1	3	3	2	67	0	0	1.625
ckd66	51	2	3	1	2	1	3	3	2	61	0	0	2.3
ckd67	70	1	4	1	1	2	3	3	2	68	0	0	1.5
ckd68	42	2	3	1	2	1	1	1	2	45	0	0	1
ckd69	45	1	4	1	1	1	1	1	2	13	0	0	2.25
ckd70	42	2	2	1	2	2	1	2	2	126	0	0	1.708
ckd71	40	2	4	1	2	1	3	3	2	22	0	0	1.25

Data of kidney transplantation



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pt number	cadKT0 /livKT1	HAAA	HLAB	HLADR	PRA (%)	TAC or CSA	TAC	TAC dose	CSA	CSA dose	SRL or EVL	SRL	SRL dose	EVL	EVL dose
kt1	0	NA			19	1	0	0	1	50	1	0	0	1	3.5
kt3	1	1	2	2	0	1	0	0	1	200	0	0	0	0	0
kt4	0	0	0	0	7	1	1	4.5	0	0	0	0	0	0	0
kt5	0	2	1	1	0	1	1	6.5	0	0	0	0	0	0	0
kt6	0	1	1	1	7bcell	1	1	1.5	0	0	1	1	1	0	0
kt7	1	1	1	1	0	1	1	5	0	0	0	0	0	0	0
kt8	1	0	1	1	0	1	1	2	0	0	0	0	0	0	0
kt9	0	1	1	1	54	1	1	4	0	0	0	0	0	0	0
kt10	1	1	1	1	5tcell	1	1	2	0	0	0	0	0	0	0
kt11	1	NA	NA	NA	NA	1	0	0	1	100	0	0	0	0	0
kt12	0	1	1	0	0	1	1	5.5	0	0	0	0	0	0	0
kt13	0	1	1	1	0	1	1	2	0	0	0	0	0	0	0
kt14	0	1	1	2	0	1	1	6	0	0	0	0	0	0	0
kt15	1	0	0	0	NA	1	1	2.5	0	0	0	0	0	0	0
kt16	0	1	2	1	0	1	1	4	0	0	0	0	0	0	0
kt17	0	1	1	0	0	1	1	10	0	0	0	0	0	0	0
kt18	1	0	1	1	NA	0	0	0	0	0	1	1	1	0	0
kt19	1	2	2	2	0	1	1	4.5	0	0	0	0	0	0	0
kt20	0	1	1	1	0	1	0	0	1	100	0	0	0	0	0
kt21	0	1	2	1	27tcell	1	1	3.5	0	0	0	0	0	0	0
kt22	0	1	1	1	0	1	1	1.5	0	0	1	1	1.5	0	0
kt23	0	1	2	1	0	0	0	0	0	0	1	1	2	0	0
kt24	0	1	1	0	0	1	1	2	0	0	0	0	0	0	0
kt25	0	1	1	1	8	1	0	0	1	25	1	1	1	0	0
kt26	0	1	2	0	0	1	1	5	0	0	0	0	0	0	0
kt29	0	0	0	0	0	1	1	4.5	0	0	0	0	0	0	0
kt30	0	1	0	0	0	1	1	2.5	0	0	0	0	0	0	0
kt31	0	0	0	0	0	1	1	6	0	0	1	1	3	0	0
kt32	0	1	2	1	89bcell 38tcell	1	1	5	0	0	0	0	0	0	0
kt34	1	0	1	0	0	0	0	0	0	0	1	0	0	1	2.5
kt35	0	0	1	0	0	0	0	0	0	0	1	1	1.5	0	0
kt36	0	1	1	0	0	1	1	2.5	0	0	1	1	1.5	0	0
kt37	1	2	2	1	NA	1	1	3.5	0	0	1	1	2.5	0	0
kt38	1	2	2	2	0	1	1	2.5	0	0	0	0	0	0	0
kt39	1	0	0	0	0	0	0	0	0	0	1	1	2	0	0
kt40	0	1	0	1	0	1	1	5.5	0	0	0	0	0	0	0
kt41	0	1	1	1	0	1	1	2	0	0	0	0	0	0	0

kt42	0	1	0	1	NA	1	0	0	1	150	0	0	0	0	0
kt43	0	1	0	1	0	1	1	2.5	0	0	1	1	1	0	0
kt44	0	2	2	1	0	1	0	0	1	100	0	0	0	0	0
kt45	0	2	1	0	0	1	0	0	1	150	0	0	0	0	0
kt46	0	NA	NA	NA	NA	1	0	0	1	50	0	0	0	0	0
kt47	0	1	1	2	89bcell	1	1	2.5	0	0	0	0	0	0	0
kt48	1	1	2	2	0	1	0	0	1	100	0	0	0	0	0
kt49	0	1	1	2	4	1	1	4.5	0	0	0	0	0	0	0
kt50	0	0	2	1	0	1	1	5	0	0	0	0	0	0	0
k51	0	NA	NA	NA	NA	1	0	0	1	275	0	0	0	0	0
kt52	1	2	2	2	0	1	1	2	0	0	1	1	1.5	0	0
kt53	0	2	1	2	0	1	1	4.5	0	0	0	0	0	0	0
kt55	1	1	1	1	0	1	1	6.5	0	0	0	0	0	0	0
kt56	1	1	1	1	0	1	0	0	1	100	0	0	0	0	0
kt57	0	1	1	1	0	1	1	5	0	0	0	0	0	0	0
kt58	1	1	1	1	1	1	1	5.5	0	0	0	0	0	0	0
kt59	0	0	0	0	0	1	1	3	0	0	0	0	0	0	0
kt60	0	0	0	0	0	1	0	0	1	125	0	0	0	0	0
kt62	1	2	2	2	0	0	0	0	0	0	1	1	2	0	0
kt63	1	0	0	0	0	1	0	0	1	100	0	0	0	0	0
kt64	0	2	2	1	0	1	0	0	1	125	0	0	0	0	0
kt65	0	2	0	0	0	1	0	0	1	100	0	0	0	0	0
kt66	1	1	1	1	43tcell	1	0	0	1	100	0	0	0	0	0
kt67	0	1	1	1	0	1	1	1	0	0	1	0	0	1	2
kt68	0	1	2	1	58	1	1	4	0	0	0	0	0	0	0
kt69	0	0	0	1	51	0	0	0	0	0	1	1	1.5	0	0
kt70	1	1	0	2	0	1	1	1.5	0	0	0	0	0	0	0
kt71	0	1	1	0	0	1	0	0	1	150	0	0	0	0	0



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