Enamel Defect and Gingival Enlargement in Pediatric Patients with Kidney Disease at Srinagarind Hospital, Khon Kaen University, Thailand

Wiboon Weraarchakul MD*, Wilawan Weraarchakul DDS**, Suwannee Wisanuyotin MD*, Manat Panamonta MD*

*Department of Pediatrics, Faculty of Medicine, Khon Kaen University, Khon Kaen, Thailand **Department of Community Dentistry, Faculty of Dentistry, Khon Kaen University, Khon Kaen, Thailand

Background: Although many complications from kidney disease therapy can be prevented or effectively treated, oral health problems are nevertheless a consequence.

Objective: The objective of this study was to explore the prevalence of enamel defect and gingival enlargement in pediatric patients with kidney disease at Srinagarind Hospital, Khon Kaen University, Thailand.

Material and Method: This cross-sectional study was conducted between January and August 2013, at Srinagarind Hospital, Khon Kaen University. Ninety-seven pediatric patients with kidney disease were allowed by their parents to participate in this study. Data were collected from medical records, questionnaires and oral examination records. The enamel defect was recorded using the Developmental Defects of Enamel Index. Gingival enlargement was recorded using the Gingival Enlargement Index. An oral examination was conducted using a mouth mirror, explorer and periodontal probe.

Results: The average age of the pediatric patients with kidney disease was 11.53 ± 3.7 years (range, 4-17). The majority of subjects were able to (a) come for an appointment (97.9%), (b) take medication according to the medical directions (93.8%) and (c) avoid inappropriate foods for those suffering kidney disease (84.5%). The prevalence of enamel defect was 27.8%. The most common enamel defects were demarcated opacities (13.4%) or diffuse opacities (9.3%). The prevalence of gingival enlargement was 16.5%.

Conclusion: This study revealed that the prevalence of enamel defect was 27.8% and the prevalence of gingival enlargement was 16.5%.

Keywords: Enamel defect, Gingival enlargement, Pediatric patients, Kidney disease

J Med Assoc Thai 2014; 97 (Suppl. 10): S75-S81 Full text. e-Journal: http://www.jmatonline.com

Most patients with renal insufficiency present with oral signs and symptoms in the soft and hard tissues; some of these are the result of the disease while others are from its treatment. Enamel is the hardest tissue in the body (>98% mineral and <2% organic matrix and water): it is produced by specialized end-differentiated cells known as ameloblasts. The formation of enamel can be separated into (a) initial stages, which involve secretion of matrix proteins (i.e. amelogenin, ameloblastin and enamelin) and (b) later stages of mineralization and maturation. Both of which can be concurrent in any developing tooth⁽¹⁾.

Abnormalities in the enamel are usually

Correspondence to:

Weraarchakul WB, Department of Pediatrics, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand. Phone: 08-1873-1659

E-mail: wibwer@kku.ac.th

expressed as: (a) hypoplasia (reduction in the quantity of tissue formed), (b) opacity (altered translucency) and (c) hypomaturation (reduction in the deposition of mineral at the maturation end stage of mineralization)⁽²⁾. Enamel hypoplasia is frequently seen in patients with renal disease. One factor responsible for the disruption is abnormal calcium-phosphorous (Ca-P) metabolism, which causes an elevation in serum P and a reduction of plasma Ca. The enamel defects noted in such patients are typical of those observed in children with Ca deficiency⁽³⁾.

Gingival enlargement is the painless enlargement of buccal and lingual gingiva⁽⁴⁾ and it is prevalent (13-85%) in children undergoing treatment with nifedipine and/or cyclosporine A, following kidney transplantation⁽⁵⁻⁷⁾. Enamel defect and gingival enlargement affects a patient's lifestyle by impairing the appearance and function of the masticatory tract.

Due to oral health concerns of such patients, and since there has been no such study in Thailand, our objective was to explore the prevalence of enamel defect and gingival enlargement in pediatric patients with kidney disease at Srinagarind hospital, Khon Kaen University, Thailand.

Material and Method *Ethic*

The current study was approved by the Khon Kaen University Ethics Committee for Human Research, based on the stipulations of the Declaration of Helsinki and the ICH Good Clinical Practice Guidelines (HE551355). Written informed consent was obtained from the parents of the pediatric patients and assent from the children.

Subjects

This cross-sectional study was conducted between January and August 2013, at Srinagarind Hospital, Khon Kaen University. Ninety-seven pediatric patients with kidney disease were allowed by their parents to participate in the study. The subjects were between 4 and 17 years of age with renal diseases, followed-up at Division of Pediatric Nephrology Srinagarind Hospital. Data were collected from medical records, questionnaires and oral examination records.

Reproducibility of oral indices

Two researchers trained to examine oral status performed collecting the status of any enamel defects and/or gingival enlargements. Our study was done in order to assess the reproducibility of recording indices for enamel defect and gingival enlargement. The intervs. intra-examiner kappa value for enamel defect and gingival enlargement was 0.84 and 0.89 vs. 0.86 and 0.95, respectively.

Oral examination and definitions

An oral examination was performed using a mouth mirror, an explorer and a periodontal probe. Enamel defect was assessed using the Developmental Defects of Enamel Index, considering: (a) demarcated opacities (a defect involving the translucency of the enamel that can appear white, yellow or brown with a clear boundary); (b) diffuse opacities (involving an alteration in enamel translucency, but the defect can appear as lines or patchy or irregular cloudy areas confluent with the adjacent normal enamel); and, (c) hypoplasia (a defect associated with a reduced local thickness of the surface enamel presenting as pits or

grooves or larger sheets of missing enamel)(8).

The Gingival Enlargement Index includes measurements of overgrowth/height of the gingival tissue vertically in the apex-crown direction from the cemento-enamel line to the free gingival margin. Using a periodontal probe, the dentist grades the height of the enlarged gingiva covering the clinical crown and the non-visible crown surface at six points around each tooth (0 = normal gingiva; 1 = slight, <2 mm increase and gingiva covering the cervical 1/3 or less of the anatomic crown; 2 = moderate, 2-4 mm increase and/or gingiva extending into the middle 1/3 of the clinical crown; and 3 = severe, >4 mm and/or gingiva covered more than 2/3 of the clinical crown)⁽⁹⁾.

Medical records and questionnaires

The diagnosis of kidney disease and the drugs administrated were gathered from medical records. A questionnaire was designed to collect information on (a) socio-demographic characteristics, (b) oral and general healthcare and (c) dental care over the previous 6-month period.

Data analysis

A descriptive analysis was performed. Results are hereafter presented as percentages or means \pm SD.

Results

The average age of the pediatric patients with kidney disease was 11.53 ± 3.7 years (range, 4-17). Among the 97 patients, boys represented 44.3% and girls 55.7%. The education level completed by parents was: primary school or below (44.3%), secondary school (21.6%), diploma (8.2%) and bachelor degree (23.8%). The distribution of family income (baht/month) was: <5,000 (34.0%); 5,100-10,000 (26.8%); 10,001-20,000 (21.6%); and, 20,001-50,000 (17.6%).

A respective 97.9%, 93.8% and 84.5% of subjects were able to go for a doctor's appointment, take their medications as prescribed and avoid inappropriate foods for sufferers of kidney disease. A majority of subjects brushed their teeth 2 times/day (77.3%), visited a dentist when they had symptoms (79.4%) and had not visited a dentist in the last six months (73.2%).

The prevalence of enamel defect was 27.8% and the most common presentations were demarcated opacities (13.4%) and diffuse opacities (8.2%) (Table 1). The current study revealed that the deciduous teeth number 51, 61, 62, and 63 and the permanent teeth number 11, 13, 23, 21, 12, and 22 had enamel defects

Table 1. Prevalence of enamel defect

Enamel defect	Number	%
Normal	70	72.2
Demarcated opacities	13	13.4
Diffuse opacities	8	8.2
Hypoplasia	3	3.1
Mixed	3	3.1
Total	97	100.0

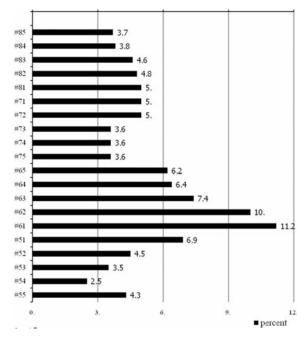
more than other teeth (Fig. 1, 2). The prevalence of gingival enlargement was 16.5% (Table 2). All of the patients with renal tubular acidosis and periodic hypokalemia had enamel defect. Patients with renal failure had more gingival enlargement than any other oral condition (Table 3). Patients taking calcium channel blockers and cyclosporine presented gingival enlargement respectively, 90.0% and 100.0% of the cases (Table 4).

Discussion

The current study represents a preliminary report on Thai children demonstrating that renal disease in children is associated with enamel defect and gingival enlargement. In our study, enamel defect occurred in 27.8% of pediatric patients with renal disease. The prevalence of developmental defects of the enamel was lower in our study than in previous reports for children with renal disease^(10,11), perhaps because most of our patients received early management of their renal disease prior to renal transplantation, minimizing any metabolic disturbances and dental calcification anomalies.

In our patients, demarcated opacities were the most common defect, followed by diffuse opacities and hypoplasia. The defect pattern was different from a study of patients between 2 and 16 years attending the regional Children's Kidney Unit Outpatient Clinic in Newcastle, where diffuse opacities were the most common defect⁽¹⁰⁾. The current study revealed that upper incisor and canine teeth presented with problems more often than other teeth, which agrees with epidemiological studies in healthy children in whom the maxillary central incisors most often presented an enamel defect⁽¹²⁻¹⁴⁾. Other studies, however, reported that second primary molars were the most affected primary teeth^(15,16).

All patients with renal tubular acidosis in our study had enamel defect. It has been suggested elsewhere that children with renal tubular acidosis will



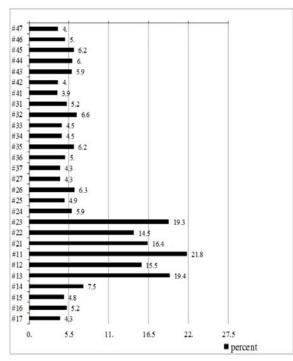
Type of teeth*

*#55 = Upper right 2nd molar, #54 = Upper right 1st molar, #53 = Upper right cuspid, #52 = Upper right lateral incisor, #51 = Upper right central incisor, #61 = Upper left central incisor, #62 = Upper left lateral incisor, #63 = Upper left cuspid, #64 = Upper left 1st molar, #65 = Upper left 2nd molar, #75 = Lower left 2nd molar, #74 = Lower left 1st molar, #73 = Lower left cuspid, #72 = Lower left lateral incisor, #71 = Lower left central incisor, #81 = Lower right central incisor, #82 = Lower right lateral incisor, #85 = Lower right 2nd molar

Fig. 1 Prevalence of enamel defect in each deciduous tooth.

experience enamel defect^(17,18). Renal tubular acidosis (RTA) is a form of metabolic acidosis arising from a lack of urine excretion of H⁺ ions or loss of bicarbonate (HCO3") ions due to a variety of renal tubular disorders. Acid-base disturbances can interfere with the development of dental structures⁽¹⁹⁾. Backman et al reported that the odontoblasts were partly under the same metabolic regulation as the osteoblasts and that the formation of the bone and enamel were probably regulated by similar factors. Thus, changes in the acid-base balance likely affect dentine metabolism as they do bone. It has been observed that chronic metabolic acidosis slows the rate of dentine formation and general body growth in young rats⁽²⁰⁾.

The prevalence of gingival enlargement in the current study was 16.5%, which is lower than previous reports^(7,21,22). But it is higher than the study in normal



Type of teeth*

*#17 = Upper right 2nd molar, #16 = Upper right 1st molar, #15 = Upper right 2nd bicuspid, #14 = Upper right 1st bicuspid, #13 = Upper right cuspid, #12 = Upper right lateral incisor, #11 = Upper right central incisor, #21 = Upper left central incisor, #22 = Upper left lateral incisor, #23 = Upper left cuspid, #24 = Upper left 1st bicuspid, #25 = Upper left 2nd bicuspid, #26 = Upper left 1st molar, #27 = Upper left 2nd molar, #47 = Lower right 2nd molar, #46 = Lower right 1st molar, #45 = Lower right 2nd bicuspid, #44 = Lower right 1st bicuspid, #43 = Lower right central incisor, #31 = Lower left central incisor, #32 = Lower left lateral incisor, #33 = Lower left cuspid, #34 = Lower left 1st bicuspid, #35 = Lower left 2nd bicuspid, #36 = Lower left 1st molar, #37 = Lower left 2nd molar

Fig. 2 Prevalence of enamel defect in each permanent

children in India⁽²³⁾. Nine of 10 patients in our study received calcium channel blockers and had gingival enlargement. Only two patients received cyclosporine; all of whom had gingival enlargement. In 1997, Seymour et al reported gingival enlargement secondary to drug therapy is the most-reported oral manifestation of patients with renal disease-an estimated 30% of dentate patients medicated with cyclosporine alone experienced clinically significant gingival enlargement⁽²⁴⁾. When patients were medicated with a combination of cyclosporine and calcium channel

Table 2. Prevalence of gingival enlargement

Gingival enlargement	Number	%
Normal	81	83.5
Less than 1/3 of clinical crown	10	10.3
Middle 1/3 of the crown	4	4.1
More than 2/3 of clinical crown	2	2.1
Total	97	100.0

blockers (i.e. nifedipine, verapamil, diltiazem, oxodipine, amlodipine), the prevalence of gingival enlargement increased to 50%. This effect occurred within 3 months of treatment. The pathogenesis of this disorder was multifactorial, but it was thought that the key factors were drug variables, plaque-induced inflammation, the susceptibility of gingival fibroblasts and other genetic factors⁽²⁴⁾. In 2008, Lima et al countered that not all patients treated with cyclosporine had gingival enlargement⁽²⁵⁾.

Investigations into enamel defect and gingival enlargement in pediatric patients with kidney disease are needed for improving patient quality of life. Parents and patients need to be informed that teeth with enamel defects are highly susceptible to decay and erosion from acids in foods and drinks. Preventive advice given to parents should include replacing cariogenic snacks with healthy foods, twice daily tooth-brushing and topical fluoride application. To reduce sensitivity from tooth-brushing, a very soft toothbrush and lukewarm water for mouth-rinsing may be suggested(26). With regard to gingival enlargement, when it is severe, a surgical treatment should be performed (gingivectomy). The clinical decision for performing the surgery is generally based on the presence of functional discomfort and esthetic alteration. This treatment is not, however, definitive and a change in the immunosuppressive therapy is an alternative treatment, albeit not always practicable. Tacrolimus is also an alternative for reducing gingival enlargement⁽²⁵⁾.

Limitations

This cross-sectional study was conducted between January and August 2013. The study had a small number of subjects, which represents a fraction of the total cases of pediatric patients with kidney disease. Further study is needed, therefore, to increase the numbers of children being treated at other centers. Furthermore, a longitudinal study is needed to: (a) explore the epidemiology of enamel defect and gingival enlargement among this patient group; (b) make more

Table 3. Percentage of enamel defect and gingival enlargement by condition

Condition	Number	Enamel defect frequency (Row percent)	Gingival enlargement frequency (Row percent)
Glomerulonephritis	8	2 (25.0)	3 (33.3)
Nephrotic syndrome	34	9 (26.4)	5 (15.1)
Vesicoureteral reflux	3	1 (33.3)	0 (0.0)
Systemic lupus erythematosus	32	6 (26.2)	4 (12.5)
Renal failure	8	2 (25.0)	3 (37.5)
Renal tubular acidosis	4	4 (100.0)	0 (0.0)
Bartter syndrome	1	0 (0.0)	0 (0.0)
Renal transplantation	3	1 (33.3)	1(33.3)
Periodic hypokalemia	2	2 (100.0)	0 (0.0)
Urinary tract infection	2	0 (0.0)	0 (0.0)
Total	97	27 (27.8)	16 (16.5)

 Table 4. Percentage of gingival enlargement by taking any medicine

Medicine taken	Number	Frequency (%)
Calcium channel blocker	10	9 (90.0)
Cyclosporine	3	3 (100.0)
Tacrolimus	3	0 (0.0)

accurate and early diagnosis; (c) identify preventable or reversible causes of progression; and, (d) predict prognosis of these oral lesions.

Conclusion

Based on our findings, the respective prevalence of enamel defect and gingival enlargement among pediatric patients with kidney disease (at Srinagarind Hospital, Khon Kaen University, Thailand) was 27.8% and 16.5%. It would be prudent, therefore, to establish a periodic dental-checking protocol for these patients in order to improve their oral health status.

Acknowledgement

The authors thank (a) the children and their families for participating in the study, (b) the Center of Cleft lip-Cleft palate and Craniofacial Deformities, Khon Kaen University, in association with Tawanchai Project for supporting this publication and (c) Mr. Bryan Roderick Hamman for assistance with the Englishlanguage presentation.

Potential conflicts of interest

None.

References

- 1. Nanci A. Enamel: composition, formation, and structure. In: Nanci A, editor. Ten Cate's oral histology development, structure, and function. St Louis: Mosby; 2008: 141-90.
- 2. Suckling GW. Developmental defects of enamel—historical and present-day perspectives of their pathogenesis. Adv Dent Res 1989; 3: 87-94.
- 3. Davidovich E, Davidovits M, Peretz B, Shapira J, Aframian DJ. The correlation between dental calculus and disturbed mineral metabolism in paediatric patients with chronic kidney disease. Nephrol Dial Transplant 2009; 24: 2439-45.
- 4. Carranza FA, Hogan EL. Gingival enlargement. In: Carranza FA, Newman M, Takei H, editors. Clinical periodontology. Philadelphia: WB Saunders; 2002: 279-96
- 5. Seymour RA, Jacobs DJ. Cyclosporin and the gingival tissues. J Clin Periodontol 1992; 19: 1-11.
- Lucas VS, Roberts GJ. Oro-dental health in children with chronic renal failure and after renal transplantation: a clinical review. Pediatr Nephrol 2005; 20: 1388-94.
- 7. Farge P, Ranchin B, Cochat P. Four-year follow-up of oral health surveillance in renal transplant children. Pediatr Nephrol 2006; 21: 851-5.
- A review of the developmental defects of enamel index (DDE Index). Commission on Oral Health, Research & Epidemiology. Report of an FDI Working Group. Int Dent J 1992; 42: 411-26.
- Miranda J, Brunet L, Roset P, Farre M, Mendieta C. Reliability of two measurement indices for gingival enlargement. J Periodontal Res 2012; 47: 776-82.

- Nunn JH, Sharp J, Lambert HJ, Plant ND, Coulthard MG. Oral health in children with renal disease. Pediatr Nephrol 2000; 14: 997-1001.
- Koch MJ, Buhrer R, Pioch T, Scharer K. Enamel hypoplasia of primary teeth in chronic renal failure. Pediatr Nephrol 1999; 13: 68-72.
- 12. Seow WK, Ford D, Kazoullis S, Newman B, Holcombe T. Comparison of enamel defects in the primary and permanent dentitions of children from a low-fluoride District in Australia. Pediatr Dent 2011; 33: 207-12.
- Montero MJ, Douglass JM, Mathieu GM. Prevalence of dental caries and enamel defects in Connecticut Head Start children. Pediatr Dent 2003; 25: 235-9.
- Farsi N. Developmental enamel defects and their association with dental caries in preschoolers in Jeddah, Saudi Arabia. Oral Health Prev Dent 2010; 8: 85-92.
- Slayton RL, Warren JJ, Kanellis MJ, Levy SM, Islam M. Prevalence of enamel hypoplasia and isolated opacities in the primary dentition. Pediatr Dent 2001; 23: 32-6.
- Lunardelli SE, Peres MA. Prevalence and distribution of developmental enamel defects in the primary dentition of pre-school children. Braz Oral Res 2005; 19: 144-9.
- Sandhyarani B, Huddar D, Patil A, Sankeshwari B. The dental management of troublesome twos: renal tubular acidosis and rampant caries. BMJ Case Rep 2013; 2013 May 10; 2013. pii: bcr-2013-009224. doi: 10.1136/bcr-2013-009224.
- 18. Bahadure RN, Thosar N, Kriplani R, Baliga S, Fulzele P. Dental aspect of distal tubular renal acidosis with genu valgum secondary to rickets: a

- case report. Case Rep Dent 2012; 2012: 374945.
- 19. Krishnan B, Krishnamurthy S, Daniel MJ. Distal renal tubular acidosis An uncommon cause of enamel hypoplasia in siblings. Int J Stomatol Occlusion Med 2012; 5: 183-7.
- Backman T, Pajari U, Larmas M. Effect of metabolic acidosis on dentinogenesis in rat. In: Shimano M, Maeda T, Suda H, Takahashi K, editors. Dentin pulp complex. Tokyo: Quintessence; 1999: 291-2.
- 21. Shiboski CH, Krishnan S, Besten PD, Golinveaux M, Kawada P, Tornabene A, et al. Gingival enlargement in pediatric organ transplant recipients in relation to tacrolimus-based immunosuppressive regimens. Pediatr Dent 2009; 31: 38-46.
- 22. David-Neto E, Lemos FB, Furusawa EA, Schwartzman BS, Cavalcante JS, Yagyu EM, et al. Impact of cyclosporin A pharmacokinetics on the presence of side effects in pediatric renal transplantation. J Am Soc Nephrol 2000; 11: 343-9.
- 23. Krishna KB, Raju PK, Chitturi RR, Smitha G, Vijai S, Srinivas BV. Prevalence of gingival enlargement in Karnataka school going children. J Int Oral Health 2014; 6: 106-10.
- 24. Seymour RA, Thomason JM, Nolan A. Oral lesions in organ transplant patients. J Oral Pathol Med 1997; 26: 297-304.
- 25. Lima RB, Benini V, Sens YA. Gingival overgrowth in renal transplant recipients: a study concerning prevalence, severity, periodontal, and predisposing factors. Transplant Proc 2008; 40: 1425-8.
- Kazoullis S, Seow WK, Holcombe T, Newman B, Ford D. Common dental conditions associated with dental erosion in schoolchildren in Australia. Pediatr Dent 2007; 29: 33-9.

รอยวิการของเคลือบฟันและเหงือกโตในผู้ป่วยเด็กโรคไตที่รับการรักษาที่โรงพยาบาลศรีนครินทร[์] มหาวิทยาลัยขอนแก[่]น ประเทศไทย

วิบูลย ์วีระอาชากุล, วิลาวัลย ์วีระอาชากุล, สุวรรณี วิษณุโยธิน, มนัส ปะนะมณฑา

ภูมิหลัง: ถึงแม้วาภาวะแทรกซอนของการรักษาโรคไตสามารถป้องกันและรักษาได้อย่างมีประสิทธิภาพ แต่การรักษาเหล่านี้ทำให้เกิดปัญหาสุขภาพชองปาก วัตถุประสงค์: เพื่อสำรวจความชุกของรอยวิการของเคลือบพ้นและเหงือกโตในผู้ป่วยเด็กโรคไตที่รับการรักษาที่โรงพยาบาลศรีนครินทร์ มหาวิทยาลัยขอนแก่น ประเทศไทย

วัสดุและวิธีการ: การศึกษาแบบตัดขวางนี้คำเนินการในช่วงเดือนมกราคมถึงสิงหาคม พ.ศ. 2556 ที่โรงพยาบาลศรีนครินทร มหาวิทยาลัยขอนแก่น มีผู้ป่วยเด็กโรคไตทั้งหมด 97 ราย ที่ผู้ปกครองสมัครใจให้เข้าร่วมในการศึกษานี้ เก็บรวบรวมข้อมูลจากแบบบันทึกการแพทย แบบสอบถาม และ แบบตรวจสุขภาพช่องปาก บันทึกรอยวิการของเคลือบพื้นโดยใช้คัชนีวัดรอยวิการของเคลือบพื้น บันทึกเหงือกโตโดยใช้คัชนีวัดเหงือกโต การตรวจสุขภาพ ช่องปากใช้กระจกตรวจช่องปาก เครื่องมือตรวจพ้น และเครื่องมือตรวจเนื้อเยื่อปริทันต์

ผลการศึกษา: อายุเฉลี่ยของผู้ป่วยเด็กโรคไตเท่ากับ 11.53±3.7 ปี (4-17 ปี) ผู้ป่วยส่วนใหญ่สะดวกที่จะมาพบแพทย์ตามนัดหมาย (ร้อยละ 97.9)
กินยาตามแพทย์สั่งอย่างเคร่งครัด (ร้อยละ 93.8) และหลีกเลี่ยงการรับประทานอาหารที่ไม่เหมาะสมต่อโรคไต (ร้อยละ 84.5) พบรอยวิการของเคลือบพ้น
ในผู้ป่วยร้อยละ 27.8 โดยส่วนใหญ่รอยวิการที่พบจะมีลักษณะเคลือบพ้นขาวขุ่นเป็นจุดๆ มีขอบเขตชัดเจน (ร้อยละ 13.4) และเคลือบพ้นขาวขุ่น
กระจายไปทั่วผิวเคลือบพ้นไม่มีขอบเขตชัดเจน (ร้อยละ 9.3) พบเหงือกโตในผู้ป่วยร้อยละ 16.5

สรุป: การศึกษานี้แสดงใหเ้ห็นวาพบความชุกของรอยวิการของเคลือบฟันในผู้ป่วยร้อยละ 27.8 และพบความชุกของเหงือกโตร้อยละ 16.5