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

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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

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 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**

**Ethics**

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 inter-vs. 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)

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).

**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 ± 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

<table>
<thead>
<tr>
<th>Enamel defect</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>70</td>
<td>72.2</td>
</tr>
<tr>
<td>Demarcated opacities</td>
<td>13</td>
<td>13.4</td>
</tr>
<tr>
<td>Diffuse opacities</td>
<td>8</td>
<td>8.2</td>
</tr>
<tr>
<td>Hypoplasia</td>
<td>3</td>
<td>3.1</td>
</tr>
<tr>
<td>Mixed</td>
<td>3</td>
<td>3.1</td>
</tr>
<tr>
<td>Total</td>
<td>97</td>
<td>100.0</td>
</tr>
</tbody>
</table>

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\(^{(2,14)}\). 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 experience enamel defect\(^{(17,18)}\). Renal tubular acidosis (RTA) is a form of metabolic acidosis arising from a lack of urine excretion of \(\text{H}^+\) ions or loss of bicarbonate (\(\text{HCO}_3^-\)) 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
Table 2. Prevalence of gingival enlargement

<table>
<thead>
<tr>
<th>Gingival enlargement</th>
<th>Number</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>81</td>
<td>83.5</td>
</tr>
<tr>
<td>Less than 1/3 of clinical crown</td>
<td>10</td>
<td>10.3</td>
</tr>
<tr>
<td>Middle 1/3 of the crown</td>
<td>4</td>
<td>4.1</td>
</tr>
<tr>
<td>More than 2/3 of clinical crown</td>
<td>2</td>
<td>2.1</td>
</tr>
<tr>
<td>Total</td>
<td>97</td>
<td>100.0</td>
</tr>
</tbody>
</table>

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

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

Table 4. Percentage of gingival enlargement by taking any medicine

<table>
<thead>
<tr>
<th>Medicine taken</th>
<th>Number</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium channel blocker</td>
<td>10</td>
<td>9 (90.0)</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>3</td>
<td>3 (100.0)</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>3</td>
<td>0 (0.0)</td>
</tr>
</tbody>
</table>

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 English-language presentation.

Potential conflicts of interest

None.

References

ร้อยวิถิาระบบคลื่นพื้นและเหลือกโดในผู้ป่วยเด็กโรคโคโรนาร์ที่โรงพยาบาลศรีนครินทร์ มาดาของอัตราแนวคิด
ประเทศไทย

วิวัฒน์ วิโรจน์กุล, วัลภา วิโรจน์กุล, สุวรรณี วิวัฒน์โต, มานัส ประณามา

คุณสมบัติ: ที่ได้รับการประมวลผลของวิธีการโดยการขยายงานและวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผลของวิธีการโดยการประมวลผล

วัสดุและวิธีการ: การศึกษาแบบคัดกรองที่กับเก็บข้อมูลในช่วงสัปดาห์แรกของเดือนสิงหาคม พ.ศ. 2556 ที่โรงพยาบาลศรีนครินทร์ มาดามของเสนอเก็บ

ผลการศึกษา: ค่าคิวแอลขอผู้ป่วยเด็กโรคโคโรนาร์ 11.53±3.7 ปี (4-17 ปี) ผู้ป่วยในกลุ่มวาระจะมีพยาบาลตามหน้าที่ (ร้อยละ 97.9) กลุ่มวาระที่ส่งกลับต่อสังกัด (ร้อยละ 93.8) และเก็บคลื่นการวิเคราะห์การที่ตามแนวทางของศูนย์ควบคุมโรค (ร้อยละ 84.5) พบว่าการเคลื่อนที่

สรุป: การศึกษาแสดงให้เห็นว่าความสูงของระดับการเคลื่อนที่ในผู้ป่วยโรคโคโรนาร์ 27.8 และพยาบาลที่มีโรคโคโรนาร์ 16.5