Oral and Dental Health in Children with Chronic Liver Disease in the Turkey Northeast

O Baygin, M Cakır\(^1\), N Ucuncu\(^1\)

Department of Pediatric Dentistry, Faculty of Dentistry, Karadeniz Technical University, \(^1\)Department of Pediatric Gastroenterology Hepatology and Nutrition, Karadeniz Technical University, Trabzon, Turkey

**Background:** It is important to be aware of oral and dental problems in the early period in children with chronic liver disease (CLD) to prevent late complications. Therefore, we aimed to analyze the oral and dental health status in children with CLD.

**Methods:** The three groups of children (3–18 years old); Group 1 (disease group, \(n = 31\)) patients with CLD, Group 2 (disease control group, \(n = 17\)) patients with chronic renal failure, and Group 3 healthy children (control group, \(n = 35\)). Examination of oral and dental structures were made, and then salivary parameters were analyzed. Antegonial index were calculated from panoramic X-rays.

**Results:** Enamel hypoplasia was found in 54.8%, 41.1%, and 31.4% of the children in the Groups 1, 2, and 3, respectively (\(P_{1-3} < 0.05\)). High salivary buffer capacity was found in 45.2% and 70.6% of the patients in Groups 1 and 2, respectively, and 45.7% of the children in healthy group, (\(P_{1-2}\) and \(P_{2-3} < 0.05\)). Factors associated with enamel hypoplasia in patients with CLD were male gender (64.7% vs. 21.4%, \(P < 0.05\)) and the presence of malnutrition (41.1% vs. 7.1%, \(P < 0.05\)).

**Conclusion:** Pediatric hepatologists must be aware of the dental problems in children with CLD. Enamel hypoplasia is common in children with CLD, and it may predispose to dental caries.

**Keywords:** Chronic liver disease, dental health, enamel hypoplasia

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**INTRODUCTION**

Chronic liver disease (CLD) in children may cause a number of local and systemic complications and pathologies within other organs and systems. Some of these complications such as variceal bleeding or encephalopathy are life-threatening, whereas others are subclinical and may manifest in long-term period.\(^1\) Oral and dental health are important in children with CLD, because most of the physicians do not pay attention to oral examination during the routine outpatient visits, and poor oral hygiene and dental problems may cause serious problems, especially in the posttransplant period.

Children with end-stage liver disease may avoid tooth brushing due to bleeding tendency. In addition, nutritional deficiencies, cholestasis, metabolic problems (hypocalcemia and hypophosphatemia), and gastroesophageal reflux due to abdominal ascites may influence oral and dental health.\(^2\)

Systemic or local infections are the frequent cause of morbidity and mortality among the children with CLD. Oral infections are the potential risk of systemic infections. Damaged mucocutaneous barriers and colonization of pathogenic microorganisms in the oral mucosa may cause septicemia, especially in the end-stage disease.\(^3,4\)

We thought that it is important to be aware of oral and dental problems in the early period in children with CLD for to prevent late complications. Therefore, we aimed to analyze the oral health status in children with CLD in detail, (i) oral examination including caries formation, enamel hypoplasia and other oral lesions, and periodontal structures, (ii) salivary parameters including buffer...
capacity (SBC), salivary flow rate (SFR), and bacterial colonization including mutants streptococci (MS) and lactobacilli (LB), and (iii) oral bone health by calculation of antegonial index (AI) from panoramic X-rays, and its relation with calcium (Ca), alkaline phosphates (ALPs), and 25-OH Vitamin D levels.

**Methods**

**Study group**

This is a prospective study and included the three groups of children (3–18 years old); Group 1 (disease group, \(n = 31\)) patients with CLD, Group 2 (disease control group, \(n = 17\)) patients with chronic renal failure, and Group 3 (healthy control group, \(n = 35\)) children who attended the Pediatric Dentistry Department in the Faculty of Dental Medicine of Karadeniz Technical University without history or known chronic diseases.

Demographic features of the children in the groups are shown in Table 1. Etiology of the CLD was metabolic liver disease \((n = 17, 54.8\%)\) including Wilson’s disease, tyrosinemia and glycogen storage disease, congenital hepatic fibrosis \((n = 4, 12.9\%)\), biliary disease \((n = 5, 16.1\%)\) including biliary atresia and Alagille syndrome, and autoimmune hepatitis \((n = 5, 16.1\%)\) in Group 1. Etiology of chronic renal failure was congenital anomalies \((n = 8, 47\%)\) including renal hypoplasia, poly-cystic renal disease and posterior urethral valve, secondary to urinary infections \((n = 7, 41.1\%)\), chronic glomerulonephritis \((n = 1, 5.8\%)\), and secondary to systemic diseases \((n = 1, 5.8\%)\) in Group 2. None of the patients in Group 2 was receiving dialysis. Creatine clearance \((mean \pm standard deviation [SD])\) of the patients were \(27.6 \pm 14.9 \text{ ml/min/1.73 m}^2\). None of the participants was receiving any medications that affect the oral and dental health status during the study. No statistically significant difference was found between the groups in terms of age and gender.

Chronic malnutrition (height Z score \(\leq -2\text{SD})\) was found in 25.8% of the patients in Group 1 and 29.4% of the patients in Group 2. Six patients (19.3%) had cholestasis and seven patients (22%) had ascites in Group 1. Anemia was found in 35% and 58.8% of the patients in Groups 1 and 2, respectively.

**Questionnaire form**

After informed consent from the parents, a questionnaire form including the items about tooth brushing (never: 1, once a day: 2, more than 1/day: 3 points) and nutritional habits (cariogenic foods including sugary and starchy foods, sticky foods, and beverages consumption, more than once per each 1/week: 1, once or none per each/week: 2 points), prolonged feeding bottle use (more than 6 months) (yes: 1, no: 2 points), and milk and milk products use (i.e., yogurt, cheese) (not or less than twice/week: 1, 2–3/week: 2, >3/week: 3 points) was filled.

**Dental examination**

Oral examination of the patients and healthy children was done by the same pediatric dentist. The presence of enamel hypoplasia, malocclusion, staining, or other oral lesions was recorded using dental mirrors and explorers under daylight. Decayed, missing, or filled teeth (DMFT for permanent teeth/DMFT for deciduous teeth) index was established in accordance with the criteria suggested by the World Health Organization.[5]

Enamel hypoplasia was defined as a defect involving the enamel surface associated with a reduced localized thickness of enamel (that may be translucent or opaque).[6]

Periodontal structures were analyzed using plaque and gingival index.[7] Plaque; the visible plaque index (VPI) was recorded as “1” for visible plaque and “0” for nonvisible plaque on the mesiobuccal surface of every bonded tooth after rinsing and drying the tooth surface. The number of surfaces with plaque was divided by the total number of examined surfaces. Gingivitis; the gingival bleeding index (GBI) was assessed with a 0.5-mm-diameter periodontal probe. The gingiva was lightly air-dried, and the probe was gently inserted into the gingival crevice parallel to the long axis of the tooth until slight pressure was felt. At this point, the probe was run along the crevice in contact with the sulcular epithelium. Minimum axial force was used to avoid undue penetration into the tissue, and the probe was moved around the crevice, gently stretching the epithelium. Only the gingival margin at the mesiolabial surfaces was evaluated for every tooth. Bleeding was recorded as “1,” and no bleeding was recorded as “0.” The number of elicited bleeding points was summed and divided by the number of sites probed.

**Saliva analysis**

Saliva analysis included SFR, SBC, MS, and LB colonization counting. Unstimulated saliva samples were collected between 8 and 12 a.m. for the SFR. The individuals were instructed not to eat and drink at least 2 h before collection. The saliva was collected in a calibrated collector for 15 min and recorded as millimetre per minute.

Buffer capacity was measured using CRT® Buffer Test (CRT® Buffer Test, Vivadent Inc., Lichtenstein). Patients were instructed not eat or drink anything, chew chewing gum, brush their teeth, or use any mouthwash for at least 1 h before the test was conducted. The patients sat upright in a relaxed position. Salivation
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was stimulated by having the patient chew a paraffin pellet. The saliva was collected in a calibrated container. The entire yellow test field was wetted with saliva using a pipette. To determine the buffer capacity of saliva, the color of the test field was compared with the color samples after exactly 5 min of reaction time. Blue indicated a high, green indicated a medium, and yellow indicated a low buffer capacity of saliva.

Bacterial counts in saliva were determined using the CRT® Bacteria (CRT® Bacteria, Vivadent Inc., Schaan, Liechtenstein) as follows: CRT determines the MS and LB count in the saliva by means of selective culture media (bright agar surface: LB count, blue agar surface: MS count). Salivary secretion was stimulated in the patients by chewing an enclosed paraffin pellet, and saliva specimens were collected in a suitable container. The agar was removed from the test vial. A NaHCO₃ tablet was placed at the bottom of the vial. The protective foils were carefully removed from the two agar surfaces. Both agar surfaces were wetted with saliva using a pipette without scratching the agar surface. The test vial was placed upright in the incubator (Cultura, Vivadent Inc., Schaan, Liechtenstein) and incubated at 37°C/99°F for 48 h. After removal of the vial from the incubator, the density of the MS and LB colonies was compared with the corresponding evaluation images in the enclosed model chart. Findings of 10⁵ colony-forming units (CFUs) or more for MS and LB per ml saliva indicated a high caries risk [Figure 1]. CFUs of MS and LB per ml <10⁵ was recorded as “0,” >10⁵ as “1.”

All of the abovementioned recordings and measurements were collected and/or measured by two experienced operators, and assessor blinding was ensured throughout the trial period. One of the examiners collected the saliva samples for the bacterial procedures. This examiner performed all of the procedures according to the instructions for CRT® bacterial counts for each individual patient.

Panoramic X-ray examination

AI was used for the assessment of mandibular bone status.[8] To achieve a standard, the panoramic radiographs were obtained by a single dentomaxillofacial radiologist and in full compliance with the reference points specified by the manufacturer of the device. The AI measurements were made separately on the right and left mandibular sides and their means were calculated as defined previously.[9] In addition, the correlation between AI and serum 25-OH Vitamin D, ALP, and Ca were also analyzed.

All of the patients required tooth extraction and restorative treatment and lacked the appropriate oral hygiene habits described by the Karadeniz Technical University Faculty of Dentistry Department of Pediatric Dentistry. Ethical approval was obtained from the Ethical Committee of Karadeniz Technical University Faculty of Medicine. Informed consent was obtained from the parents of the participating children.

Statistical analysis

All data were analyzed by using SPSS (SPSS Inc., Chicago, IL, USA) software program and presented as mean ± SD. Mann–Whitney U-test and Chi-square test were used to compare the proportional data and categorical data (gender etc.) between groups, respectively. Spearman rank correlation test was used for the determination of correlations. Significant level was set at P < 0.05.

RESULTS

All the participants’ parents respond the all items in the questionnaire form. No significant difference was found between the groups in items score and total score [Table 2].

Enamel hypoplasia was found in 54.8%, 41.1%, and 31.4% of the children in the Groups 1, 2, and 3, respectively (P=1.3 < 0.05, odds ratio [OR]: 2.6, 95% confidence interval [95% CI]: 0.8–8.2). Malocclusion was found in a patient with Alagille syndrome in

<p>| Table 1: Demographic and clinical findings of the patients with chronic liver disease (Group 1), chronic renal failure (Group 2) and healthy controls (Group 3) |</p>
<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group 1 (n=31)</th>
<th>Group 2 (n=17)</th>
<th>Group 3 (n=35)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean±SD, years</td>
<td>11.4±4.4</td>
<td>11.4±4.1</td>
<td>9.8±3.4</td>
</tr>
<tr>
<td>Gender, female n (%)</td>
<td>17 (55)</td>
<td>7 (41)</td>
<td>13 (37)</td>
</tr>
<tr>
<td>PELD score, median (range)</td>
<td>6 (<del>10</del>25)</td>
<td>70.9,16.2,12.9</td>
<td></td>
</tr>
<tr>
<td>Child-Pugh score, % A, B, C</td>
<td>70,9,16,2,12,9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ascites, n (%)</td>
<td>7 (22)</td>
<td>8 (25.8)</td>
<td>5 (29.4)</td>
</tr>
<tr>
<td>Chronic malnutrition, n (%)</td>
<td>6 (19.3)</td>
<td>11 (35)</td>
<td>10 (58.8)</td>
</tr>
<tr>
<td>Anemia, n (%)</td>
<td>11 (35)</td>
<td>10 (58.8)</td>
<td></td>
</tr>
<tr>
<td>SD=Standard deviation; PELD=Pediatric end-stage liver disease</td>
<td></td>
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</tr>
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| Table 2: Oral habits of groups |
| Items | Group 1 (n=31) | Group 2 (n=17) | Group 3 (n=35) |
| Tooth brushing habits | 1.9±0.6 | 2±0.5 | 2.1±0.5 |
| Nutritional habits | 1.5±0.5 | 1.7±0.4 | 1.4±0.5 |
| Prolonged bottle use | 1.7±0.4 | 1.5±0.5 | 1.4±0.5 |
| Milk and milk products use | 2.3±0.7 | 2.1±0.8 | 2.4±0.6 |
| Total | 7.5±1.4 | 7.5±1.1 | 7.4±1 |
| SD=Standard deviation |
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patients with CLD (3.2%) and in two patients with chronic renal failure (11.7%). Yellowish staining of the teeth was seen in three patients with CLD (9.6%, all were cholestatic) and one patient with chronic renal failure (5.8%). Missing teeth was found in 22.5% of the patients with CLD, 5.8% of the patients with chronic renal failure, and 11.4% of the healthy children. Oral mucosal lesions were found in five patients (16.1%) with CLD; three patients with thrombocytopenia had pinpoint hemorrhages and dilated vessels, one had cheilitis, and one had mucosal candidiasis. Atrophic mucosal lesions were seen in two patients (11.7%) with chronic renal failure. Healthy children did not have any mucosal lesions. The VPI and GBI did not differ among the groups, but 12.9% and 16.1% of the patients with CLD had Grade 3 VPI and GBI, respectively [Table 3].

DMFT and DMFT were analyzed in 25 (80.6%) and 18 (58%) patients in Group 1, 13 (76.4%) and 8 (47%) patients in Group 2 and 27 (77.1%) and 26 (74.2%) patients in Group 3. DMFT index (mean ± SD) of the groups were 0.11 ± 0.09, 0.2 ± 0.2, and 0.15 ± 0.08, respectively, and DMFT index (mean ± SD) were 0.16 ± 0.17, 0.08 ± 0.11, and 0.17 ± 0.13. No significant difference was found between the groups in terms of DMFT and DMFT index. However, number of patients with “DMFT index = 0” was significantly high in patients chronic renal failure than the patients with CLD and healthy control (30% vs. 16 and 7%, respectively, P within the groups were <0.05) [Table 4].

SBC of the patients and control group is shown in Figure 2. High buffer capacity was found in 45.2%, 70.6% of the patients in Groups 1 and 2, respectively,
and 45.7% of the children in healthy group, (P<0.05). SFR was 0.39 ± 0.1, 0.4 ± 0.11 and 0.38 ± 0.08 ml/min in patients with CLD, chronic renal failure and healthy group, respectively, and no significant difference was found between the groups.

Prevalence of ≥10⁵ CFU/ml of saliva *Streptococcus mutans* (SM) and LB in Group 1 was 74.1% and 70.9%, respectively. It was found 47% and 52.9% in Group 2 and 51.4% and 51.4% in Group 3. No significant difference was found between the groups in terms of prevalence of ≥10⁵ CFU/ml of saliva SM and LB.

AI was (mean ± SD) 2.8 ± 0.87, 3.04 ± 0.8, and 2.5 ± 0.77 in patients with CLD, chronic renal failure, and healthy children, respectively (P > 0.05 among the groups). No correlation were found between AI, serum Ca, ALP, and 25-OH Vitamin D levels. Twenty-three of the 31 patients (74.1%) in Group 1, 8 of the 17 patients in Group 2 (47%), and 21 of the 35 children (60%) had Vitamin D deficiency (Vitamin D levels <20 ng/ml) and AI did not differ in patients with and without Vitamin D deficiency among the groups.

Factors associated with enamel hypoplasia was analyzed in patients with CLD and found that enamel hypoplasia was more common in males (64.7% vs. %21.4, P < 0.05, OR: 6.7, 95% CI: 1.3–33.9) and in patients with malnutrition (41.1% vs. 7.1%, P < 0.05, OR: 9.1, 95% CI: 0.9–86.4). No association was found with the other factors such as age, PELD score, etiology, presence of ascites, cholestasis and anemia, VPI, GBI, SFR, SBC, presence of SM or LM colonization, AI, serum Ca, and ALP levels, and Vitamin D deficiency for enamel hypoplasia in children with CLD. DMFT index was high in patients with enamel hypoplasia (0.14 ± 0.08 vs. 0.08 ± 0.09, P < 0.05) [Table 5].

**DISCUSSION**

In this study, we found that enamel hypoplasia is more common in children with CLD than healthy children. Risk factors including demographic, clinical, and laboratory findings were extensively analyzed, and male gender and chronic malnutrition were associated with increased risk of enamel hypoplasia in children with CLD.

Enamel abnormalities are common finding in childhood ranges between 10% and 30% in different populations.[10,11] Risk factors associated with enamel hypoplasia in childhood are prenatal (maternal) malnutrition, prematurity or low birth weight, low socioeconomic status, mineral deficiency, parental smoking, postnatal infections, anemia, and failure to thrive.[11,12] In addition, it was well defined in children with chronic diseases such as chronic renal failure, celiac disease (40–66%), and gastroesophageal reflux disease (76%).[13-16] Hypocalcemia due to malabsorption and immunological factors was found to be associated with enamel hypoplasia in children with celiac disease. [14] It is related with gastric acid exposure in children with gastroesophageal reflux disease.[15] In our study, only chronic malnutrition was associated with the development of enamel hypoplasia. Other factors such as SFR, SBC, and bacterial colonization did not differ in patients with and without enamel hypoplasia. The association of chronic malnutrition with enamel hypoplasia was well defined in previous studies.[12] Early childhood malnutrition (prenatal and postnatal 2–6 years old) is associated with structural defects in primary teeth that are vulnerable to enamel hypoplasia and severe caries. Macro- (especially Vitamin A, Vitamin D, and Ca in children with CLD) and micro-nutrient deficiency in malnutrition may lead to decrease in mineralization of surface and subsurface of enamel and may cause to enamel hypoplasia.[12,14]

The association of enamel hypoplasia with dental caries was shown in population studies.[12,15] Enamel hypoplasia...
provides mechanical nidus for bacteria and foods that may cause to caries formation. Surface irregularities due to enamel hypoplasia may predispose to plaque retentions and decrease the clearance of carbohydrate. In Addition, malnutrition is a risk factor for both enamel hypoplasia and dental caries. All of these predisposing factors increase the risk of dental caries in children with enamel hypoplasia.\(^\text{[10]}\)

In our study, we found that patients with enamel hypoplasia had higher DMFT index, which is an indices of dental caries, than the patients without enamel hypoplasia.

In this study, we found that 9.6% of the patients with CLD (all of them had cholestatic liver diseases) had yellowish or green staining. In previous studies, it was shown that staining is associated with conjugated hyperbilirubinemia, especially in the neonatal period and correlated with the disease severity. Lin \textit{et al}\.\(^\text{[17]}\) showed green staining in 61.3% of the patients with biliary atresia. Apart from staining, oral mucosal lesions may be seen in children with CLD due to thrombocytopenia or coagulopathy, vitamin deficiencies, especially Vitamin B, iron, and zinc deficiency and local infectious agents such as candidiasis. We found 16.1% of the children with CLD had mucosal lesions. Mucosal lesions were found in 13% of adult patients with cirrhosis. There have been no pediatric data. Interestingly, no oral mucosal lesion was found in 37 children after liver transplantation in a previous study.\(^\text{[8]}\)

We did not find any significant difference in DMFT index values among the groups. Only patients with “DMFT index = 0” was more common in children with chronic renal failure. Factors associated with dental status such as dietary habits, SFR, and bacterial colonization were analyzed and did not find any significant difference among the groups. Decreased SFR may be expected in patients with ascites due to decreased effective intravascular volume. In addition, salivary flow may be decreased in some autoimmune diseases (autoimmune hepatitis) due to infiltration of salivary glands. Due to small number of the patients in the study group, we could not make any subgroup analysis about the SFR in patients with CLD. On the other hand, patients with chronic renal failure had better SBC. In previous studies, it was shown that patients with chronic renal failure had better SBC because they have elevated salivary ammonia levels due to hydrolysis of urea that raise the pH above the critical level. The elevated urea levels in saliva are a complication of the disease and negating the effect of any acid formation from cariogenic food intake.\(^\text{[18]}\) Elevated SBC may be expected in children with decompensated cirrhosis (encephalopathy) due to increased salivary ammonia, but as abovementioned, we could not make subgroup analysis in our patients with CLD.

Radiomorphometric measurement of mandibular bone was used for the screening of osteoporosis among the postmenopausal women, and especially AI and mandibular cortical index were correlated with bone mineral density.\(^\text{[8]}\) Othman and Ouda\(^\text{[9]}\) showed the usefulness of radiomorphometric measurement of mandibular bone for the assessment of osteoporosis in adult celiac patients. There have been no studies about the usefulness of radiomorphometric measurement of mandibular bone for the assessment of osteoporosis in children. We did not find any significant difference in AI among the groups, and also no association was found between AI and 25-OH Vitamin D, ALP, and Ca levels. It may be related with that changes in radiomorphometric indices of mandibular bone may be seen in long-term disease; therefore, no difference was found in the early childhood.

We did not find any significant difference among the groups in terms of VPI and GBI, but severe (Grade 3) VPI and GBI were found in patients with CLD. Severe GBI may be related with the increased tendency of bleeding due coagulopathy or thrombocytopenia in children with CLDs.

Bacteria colonization (SM and LB) was more common in children with CLD, but did not reach the significant difference. Oral microbiota of the children with CLD was extensively analyzed before the liver transplantation in a previous study and found that there was no significant difference between the patients and control group in total aerobic and anaerobic bacteria count per sample, but number of yeasts was significantly high in patients with CLD. In addition, they found that the number of anaerobic bacteria and total streptococcal count except \textit{Streptococcus oralis} and \textit{mitis} was immediately decreased after liver transplantation. They suggested using oral hygiene agents before liver transplantation such as chlorhexidine mouthwash, gel, or varnishing to decrease the risk of bacteremia after liver transplantation.\(^\text{[1]}\)

The limitations of our study include the following: (i) Small number of patients, (ii) number of patients with end-stage liver disease or decompensated cirrhosis was low, and (iii) etiologies of the liver diseases were heterogeneous.

\textbf{Conclusion}

The results of our study suggest a need for dental advice and supervision and indicate that dental and medical care should be closely integrated for children with CLD. Pediatric hepatologists must be aware of the dental problems of children with CLD. Further prospective studies with large number of patients with CLD are...
needed to analyze the effect of pretransplant oral and dental status on posttransplant morbidity and mortality.

**Bullet points**

- Oral and dental health are important in children with CLD, because most of the physicians do not pay attention to oral examination during the routine outpatient visits, and poor oral hygiene and dental problems may cause serious problems, especially in the posttransplant period
- Enamel hypoplasia is common in children with CLD
- Children with CLD must be consulted with pediatric dentists for the oral dental problems during routine outpatient clinic examination.

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**Conflicts of interest**

There are no conflicts of interest.

**REFERENCES**