Oral Health Status of Kuwaiti Children with a History of Chronic Liver Disease

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Significance of the Study

- The findings of this study add to the scant literature verifying the observation that caries plaque scores and the prevalence of enamel defects are high among pediatric patients with a history of chronic liver disease. Also, liver transplant patients on tacrolimus therapy tend to display less gingival overgrowth. Pediatric liver transplant patients should be monitored closely regarding their dental care during both the pretransplantation and the posttransplantation periods.

Keywords

Liver disease · Children · Dental caries · Oral health · Enamel defects · Gingival overgrowth

Abstract

Objective: To investigate the oral health status and dental manifestations of children with a history of chronic liver disease (CLD) compared to healthy children. **Subjects and Methods:** Twenty children (15 boys and 5 girls) with a history of CLD were compared to 20 healthy controls matched for age and gender. The clinical examination was carried out by the same dentist. Caries prevalence, using the decayed, missing, and filled primary and permanent teeth indices (dmft/DMFT), was recorded. Developmental enamel defects, plaque scores, and gingival overgrowth were also investigated. **Results:** No statistically significant differences were found in mean dmft scores for children with a history of CLD (4.9 ± 5.4) and for healthy individuals (3.9 ± 4.5). However, the mean DMFT score was significantly higher ($p = 0.025$) in children with CLD (4.2 ± 4.6) compared to controls (1.7 ± 1.6). The mean decayed teeth parameter (DT) was also significantly higher in children

with CLD ($p = 0.004$). All patients with CLD exhibited enamel defects compared to only 33% in the control group ($p < 0.05$). A higher mean plaque index was observed in children with a history of CLD ($p < 0.001$). Also, a positive correlation for gingival overgrowth was noted in patients with a history of CLD ($p < 0.05$). Green staining was evident only in the permanent dentition of 1 child with CLD. **Conclusion:** Children with a history of CLD exhibited a high caries prevalence, high plaque scores, and more enamel defects compared to healthy subjects. Gingival overgrowth is less prevalent among pediatric liver transplant patients on tacrolimus therapy.

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Introduction

Chronic liver disease (CLD) in children and adolescents is not uncommon [1]. CLD indicates long-standing irreversible damage in the hepatic structure that may result in fibrosis and cirrhosis. Liver cirrhosis is a severe and rapidly fatal disease in children [1].

Complications of CLD are primarily related to liver dysfunction. These include cholestasis, portal hypertension, ascites, variceal bleeding, impaired protein synthesis, coagulopathy, hepatic encephalopathy, and hepatorenal and hepatopulmonary syndromes [2]. Patients with CLD also suffer from nutritional and metabolic disturbances, as well as impaired immunity [3]. As a result, there is an increased risk of malnutrition and microbial infections. In addition, patients with CLD may have several oral manifestations including dental enamel defects, impaired saliva secretion, and oral mucosal lesions [3].

In children, CLD is often the result of persistent cholestasis caused by different factors, including infectious, metabolic, genetic, idiopathic, structural, and autoimmune diseases [1]. The most common causes of CLD in infants are biliary atresia and genetic-metabolic diseases, while in older children CLD is often caused by chronic viral hepatitis and autoimmune diseases. A specific etiology cannot be determined in many patients [3, 4].

Liver transplantation has been a successful treatment for children with end-stage liver disease, improving the survival rate and resulting in a long healthy life [5]. However, in order to prevent liver transplant rejection and promote normal growth, the majority of children are placed on immunosuppressive drugs. The introduction of tacrolimus and other new immunomodulatory agents has decreased the incidence of chronic rejection. Unfortunately, prolonged immunosuppressive treatment after liver transplantation can cause many oral and dental problems [6]. The most notable oral findings in children who receive liver transplants include green staining of the teeth and gingiva due to elevated serum bilirubin levels before transplantation [7], gingival enlargement, and gingivitis associated with cyclosporine therapy [7], poor oral hygiene [8], dental hypoplasia, and an increased incidence of dental caries [9].

Only a small number of studies and case reports have considered oral findings in children with a history of CLD, especially those with end-stage liver disease and those undergoing liver transplantation [3, 10, 11]. Therefore, the purpose of this study was to investigate the oral health status and dental manifestations of Kuwaiti children with a history of CLD.

Subjects and Methods

The research protocol was approved by Kuwait University Health Sciences Centre Ethical Committee. Informed consents were obtained from the parents and their children.

Table 1. Primary diagnoses of children with CLD

Primary diagnosis	Subjects, <i>n</i> (%)
Biliary atresia	6 (30)
Neonatal hepatitis	2 (10)
Familial cholestasis	6 (30)
Alagille syndrome	2 (10)
Hepatoblastoma	1 (5)
Primary hyperoxaluria	1 (5)
Crigler-Najjar syndrome	1 (5)
Sclerosing cholangitis	1 (5)

Study Group

All pediatric patients who underwent or were scheduled to undergo liver transplantation at Al-Amiri Hospital, Kuwait, were invited to participate in this study. Twenty children whose parents gave consent were included in this study. All enrolled pediatric patients were seen at a single, specialized referral liver unit in Kuwait for children with liver disease. The study group was compared to a control group comprised of children attending Kuwait University's Dental Clinics and matched for age and sex. The inclusion criteria for the subjects in the control group were children in good health (ASA I) with or without a history of dental care.

Questionnaire Data

A structured questionnaire was used to collect data including demographic information, oral hygiene habits, and dietary practices (e.g., frequency of tooth brushing, previous dental visits, and frequency of sugary food and beverages).

Clinical Examination

A calibrated examiner performed the clinical examination of the participants. Before the beginning of this study, the examiner (A.A.) was trained and calibrated according to the diagnostic criteria of the WHO [12] on 10 random pediatric patients who were not involved in this study. The intraexaminer reliability agreement was more than 90%. All clinical examinations in this study were conducted using a sterile mouth mirror and a fixed dental unit light (A-dec; Newberg, OR, USA) without an explorer or compressed air. Gross debris (if present) was removed from the pit and fissures of teeth using a straight probe. Dental caries experiences were assessed using the decayed, missing, and filled primary and permanent teeth (dmft/DMFT) indices [12].

Oral hygiene status was determined by the presence of visible plaque using the modified Quigley-Hein plaque index (PI) [13]. Plaque was evaluated visually on the buccal and lingual surfaces of all teeth. To obtain the PI for each child, plaque scores were summed and divided by the number of surfaces scores.

Gingival overgrowth was diagnosed visually using the semi-quantitative index developed by Aas [14] and modified by McGaw et al. [15]. The interdental papillae and gingiva were scored in 4 points around each tooth. The gingival overgrowth index (%) for each patient was determined by dividing the gingival quadrisections with overgrowth by the total number of gingival quadrisections.

Table 2. Demographic features, oral hygiene practices, and dietary habits of the participants in the study groups

	History of CLD	Control	<i>p</i>
Age	10±2.7	10±2.7	1.000
Gender			1.000
Male	15	15	
Female	5	5	
Frequency of tooth brushing			
Never/sometimes	3	0	0.241
1× a day	7	11	
≥2× a day	10	9	
Frequency of sugary foods			
≤1× a day	15	11	0.247
>1× a day	5	9	
Frequency of sugary drinks			
≤1× a day	7	8	0.410
>1× a day	13	12	
Previous dental visits			
Never	4	6	0.891
Once	5	4	
Twice	2	3	
Three and more	9	7	

Values are presented as means ± SD or numbers. *p* < 0.05 was considered statistically significant (χ^2 and *t* tests).

The presence of enamel defects was determined using the modified developmental defects of enamel (DDE) index [16], in which the type (demarcated opacity, diffuse opacity, and hypoplasia), number (single or multiple), and position of the defects on teeth surfaces were recorded. Staining of teeth for each participant was assessed visually on the buccal/labial surfaces of all teeth. It was recorded as “no stain” (normal) or “with stain” (e.g., yellow, orange, green, brown, grey, or black). Oral soft and hard tissues assessment was also performed to detect the absence or presence of any soft tissue pathosis (i.e., erythema, ulceration, vesicles, petechiae, or white patches) or osseous abnormality in the oral structures [12]. The lips, tongue, floor of the mouth, hard and soft palates, tonsils, vestibule, and buccal mucosa were all examined.

Statistical Analyses

All data were entered into the Statistical Package for the Social Science version 20 (SPSS Inc., Chicago, IL, USA). Descriptive statistics (means, SD, and percents) were calculated for baseline background variables. Differences between the pediatric patients with CLD and the controls were statistically tested using χ^2 and *t* tests as deemed necessary. *p* < 0.05 was considered statistically significant.

Results

A total of 40 children participated in this study; 20 (15 boys and 5 girls) children aged 6–12 years had a history of CLD, and 20 healthy children of matched age and gender

Table 3. Differences in mean dmft, mean DMFT, plaque index, and gingival overgrowth index among the study groups

	History of CLD	Control	<i>p</i> value
dmft index	4.85±5.4	3.90±4.5	0.552
dt	2.90±3.5	1.50±2.6	0.161
mt	1.40±2.2	0.90±2.0	0.455
ft	0.60±1.5	1.50±2.3	0.146
DMFT index	4.20±4.6	1.65±1.6	0.025*
DT	3.30±3.8	0.55±1.1	0.004*
MT	0.10±0.3	0.15±0.4	0.643
FT	0.80±1.3	0.95±1.4	0.729
Plaque index	1.21±0.3	0.86±0.3	0.001*
Gingival over-growth index	0.13±0.1	0	0.001*

Values are presented as means ± SD. * *p* < 0.05 (*t* test).

served as controls. There were 14 children with CLD who had received liver transplants and were on tacrolimus therapy. The primary diagnoses of the children with CLD are listed in Table 1; these were: biliary atresia, neonatal hepatitis, familial cholestasis, and Alagille syndrome. Other causes included 1 case each of hepatoblastoma, primary hyperoxaluria, Crigler-Najjar syndrome, and sclerosing cholangitis. No significant differences were found between the groups in terms of demographic features, oral hygiene practices, or dietary habits (Table 2).

The mean dmft for the children with CLD (4.9 ± 5.4) was higher than that for the children in the control group (3.9 ± 4.5), but the difference was not statistically significant (*p* = 0.552; Table 3). In contrast, the mean DMFT for the children with CLD was significantly higher (4.2 ± 4.6) compared with the healthy controls (1.7 ± 1.6 , *p* = 0.025). In addition, the decayed teeth (DT) component of the index was higher in children with CLD (*p* = 0.004). No other significant differences were found in the missing (MT) or filled (FT) teeth components between the groups. The children with CLD showed significantly higher mean PI (1.21 ± 0.3) compared to the healthy children (0.85 ± 0.3 , *p* < 0.001). No gingival growth was observed in the control group. However, 3 children (15%) with history of CLD had gingival overgrowth. Of the latter, 1 child (5%) had received a liver transplant.

Developmental enamel defects were observed in all of the participants with CLD compared to 6 (30%) children from the control group. This difference was statistically significant (*p* = 0.004). Table 4 shows the prevalence of different types of developmental enamel defects in the primary

Table 4. Types of developmental enamel defects observed in the study groups

Type of defect	History of CLD (primary teeth), <i>n</i>	Liver disease (permanent teeth), <i>n</i>	Control Primary teeth, <i>n</i>	Permanent teeth, <i>n</i>
None	8	0	19	14
Demarcated opacities	0	7	7	3
Diffuse opacities	9	14	0	2
Hypoplasia	3	10	0	0
Combination	0	3	0	1

and permanent dentitions of both study groups. An increased prevalence of enamel hypoplasia was demonstrated in the CLD patients compared with the healthy children. Diffuse opacities were recorded more frequently than demarcated opacities among the children with CLD. In the control group, 3 of the 6 children had apparent enamel opacities as seen in the affected incisors and molars of children with molar incisor hypomineralization. Green staining was evident only in the permanent dentition of 1 child with CLD. In addition, there was no abnormality detected in the oral mucosa of children with CLD.

Discussion

The impact of CLD on the general and oral health of children and their quality of life is quite high as compared to adults [1]. In recent years, liver transplantation in pediatric patients has been an acceptable treatment option, increasing the long-term survival of these individuals significantly [5]. Therefore, dental professionals can encounter such patients in the clinical dental setting. Few studies and case reports have investigated the oral and dental manifestations in children with a history of CLD, specifically those with end-stage liver impairment and those who have received a liver transplant. To our knowledge, this is the first study to evaluate the oral health status of Kuwaiti children with a history of CLD.

The results of our investigation show that the dental caries experience in children with a history of CLD was higher than that in healthy controls. However, no significant differences were noted in the dmft scores of the primary dentitions. The findings were consistent with previous studies [10, 11] but not in agreement with the results of Lin et al. [9], who found significantly higher mean dmft scores among children with liver impairment. Likewise, Ferrazzano et al. [17] described increased dmft scores in their liver transplant group. The differences seen in the prevalence of dental caries among these studies can be

explained by the fact that dental caries is a multifactorial disease and has been linked to many risk factors including poor oral hygiene, high counts of cariogenic bacteria, a high frequency of sugary intake, and night feeding [18]. On the other hand, the nonsignificant differences seen in dmft scores between the groups in this study could be attributed to the high dmft scores among Kuwait children. A previous study on the dental caries experience of Kuwaiti schoolchildren reported a dft score of 4.6 in the primary dentition [19].

In the present study a significantly increased mean DMFT score was observed for the permanent dentition of children with CLD. However, few studies have documented no difference in the mean DMFT scores of patients with CLD and those of healthy controls [1, 10]. When the parameters of the DMFT scores were further analyzed, a significant correlation was noted with the mean decayed permanent teeth (DT). Although about half of CLD patients claimed to have previous dental visits, they had an increased number of untreated carious teeth. There are 2 possible reasons to explain the high scores of untreated teeth among children with CLD, i.e., the lack of specialized dental care for those children and the focus of parents/caregivers of children with medical problems on the medical aspect of the child's health [20].

In the current study, the CLD group showed poor oral hygiene as compared to healthy the children. An increased PI among children with a history of liver impairment was similarly documented by Baygin et al. [11] and Olczak-Kowalczyk et al. [3]. Also, Wondimu et al. [21] found an increased visible PI among pediatric liver transplant recipients. The poor oral hygiene detected among children with a history of CLD indicates a need for improvement in preventive oral health care.

Gingival overgrowth has been commonly reported to be associated with CLD, particularly after liver transplantation [22]. Children who receive liver transplants are placed on immunosuppressive drugs to prevent organ rejection following transplantation. A commonly used immunosup-

pressant is cyclosporin A, which is known to be associated with gingival overgrowth. Some studies have reported prevalences of gingival overgrowth as high as 62–100% with the use of cyclosporin A [23]. In contrast, immunosuppressive regimens using tacrolimus, a relatively new innovative immunosuppressive drug with minimal gingival hyperplastic side effects, have been recommended in recent years [24]. In the present study, gingival overgrowth was seen in 1 out of 14 pediatric liver transplant patients (7%) and in 2 out of 6 patients with CLD and without a subsequent liver transplant. All of the liver transplant patients enrolled into the study were placed on tacrolimus therapy either exclusively or in combination with mycophenolate mofetil, which has not been associated with gingival hyperplasia. Although, some studies have concluded that a lack of gingival enlargement is associated with tacrolimus [10, 24], a finding similar to ours was reported by Sandoval et al. [25]. They identified gingival enlargement in 7 out of 40 pediatric patients (18%) taking tacrolimus [25]. Also, a slightly higher percentage (25%) was previously reported by Shiboski et al. [6]. However, Lin et al. [10] concluded that the gingival enlargement was mainly correlated with the presence of plaque and not the use of immunosuppressive medications.

In general, developmental enamel defects are common among children and their incidence ranges from 10 to 30% [26, 27]. Many risk factors are associated with enamel hypoplasia including: childhood malnutrition, premature birth, anemia, postnatal infections, and chronic diseases [27]. In the current study, enamel defects were significantly higher in children with history of CLD than in healthy controls. The results are in agreement with previous studies [11, 17, 21, 23]. Various etiologies, including genetic influences and environmental factors, have been proposed

for the causation of enamel defects [28]. Disruption of mineralization pathways and disturbances in calcium and phosphate metabolism, a result of CLD, put affected children at risk for enamel defects [29]. Early childhood malnutrition in patients with CLD has also been associated with the enamel defects in permanent teeth [11].

Oral mucosal lesions may be seen in children with CLD due to vitamin deficiencies, coagulopathy, iron deficiency, and local infections [11]. A recent study by Baygin et al. [11] observed mucosal lesions in 16% of the children with CLD. However, none of the mucosal lesions was reported in our sample groups. Similarly, no oral mucosal lesions were detected in a previous study which involved 37 pediatric liver transplant recipients [30].

Despite the fact that the present study demonstrated a high prevalence of dental caries and poor oral health among children with a history of CLD, there are some shortcomings. The number of total participants was small, and the number of patients with end-stage liver disease was low. Also, the causes of CLD were heterogeneous. The results of this study highlight the need for an early caries prevention program and routine dental care for children with CLD before and after liver transplantation.

Conclusion

Children with a history of CLD exhibited a high prevalence of caries, plaque scores, and enamel defects compared to healthy subjects. Gingival overgrowth is less prevalent among liver transplant patients with tacrolimus therapy. More emphasis should be placed on preventive oral care in children with liver impairment and children who have received a liver transplant.

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