Oral health status in liver transplant Italian children

ABSTRACT

Aim The aim of this study was to assess the oral health status in children submitted to liver transplantation in order to evaluate the need to promote suitable dental caries prevention programmes.

Methods Thirty-eight children submitted to liver transplantation (4-5 years) were selected and their data were compared to those of an age-matched control healthy group of 78 children. Clinical examinations were carried out and X-ray bitewings were taken, in order to record caries prevalence, caries experience, periodontal health and dental enamel defects. A questionnaire investigating demographic and oral health behaviour data was completed by parents.

Results Caries prevalence was 78.9% in the liver transplantation group and 39.7% in the healthy control group. The dmft mean value was 2.26±2.25 in the liver transplantation group and 0.69±1.51 in the healthy group. The difference in the mean dmft between the two groups was statistically significant (p<0.0001). From the elaboration of the data on periodontal health it resulted that 23.7% of the liver transplantation subjects and 48.7% of controls had a healthy periodontal status, respectively; 39.5% of the liver transplantation children and 23.6% of the controls had plaque and calculus. In addition, 44.7% of the liver transplantation patients and 28.2% of the control subjects showed bleeding on probing. In the liver transplantation subjects there was a higher prevalence (65.8%) of dental enamel defects with respect to the healthy group (21.8%).

Conclusions The high prevalence of caries and gingival diseases showed the need to promote specific dental caries prevention programmes in liver transplant children.

Introduction

Liver transplantation is the treatment of choice for end-stage liver disease in both adult and paediatric patients [Burra et al., 2000]. In the last years, the success rates have improved significantly as a result of advances in surgical techniques and improved postoperative care. The main indications for the procedure were biliary atresia, inborn metabolic disorders, liver cirrhosis, liver neoplasms, Alagille syndrome, and fulminant hepatic failure. The cumulative survival rate was 77%, 76%, 73%, and 71 at 1, 3, 5, and 7 years, respectively [Pompli et al., 2002], although 1- and 10-years survival appears to be even higher in more recent data from European registries [Spada et al., 2009].

The main causes of death were primary non-function of the graft and sepsis. In fact, infection can compromise the survival of any organ transplant recipient [Holt and Winston, 2005]. Among the multiple causes of post-transplantation infection cited in the literature, dental sources, although rare, have been implicated [Wilson et al., 1982; Reyna et al., 1982]. Therefore, infections of the oral cavity could have serious consequences in liver transplantation children, whereas preoperative sanitation could be difficult for the high rate of complication linked to coagulopathy and the postoperative course might be worsened by immunosuppression [Niederhagen et al., 2003]. Furthermore, it is not uncommon to see green-stained teeth in the oral cavity of liver transplantation children [Lin et al., 2003; Seow et al., 1991; Herbert and Delcambre, 1987; Morisaki et al., 1990; Morimoto et al., 1998; Funakoshi et al., 1992; Allman et al., 1994; Uemoto et al., 1993]. In fact, scientific literature shows that the risk of dental enamel defects is higher in children with poor health (due to conditions like severe malnutrition, hyperbilirubinemia, thyroid and parathyroid disturbances, neonatal hypocalcemia, liver neoplasms, maternal diabetes, asthma, genetic disorders such as amelogenesis imperfecta, tuberous sclerosis and cystic fibrosis) during the first three years of life because this period of time is critical for tooth development [Mathu-Muju and Wright, 2006].

Developmental enamel defects have important clinical significance, since they are responsible for aesthetic problems, dental sensitivity, dentofacial anomalies, as well as predisposition to dental caries [Rosenthal et al., 1986; Seow, 1991].

For these reasons, the aim of this study was to assess the oral health status of children after liver transplantation in order to evaluate the need to

Keywords Caries experience; Dental enamel defects; Liver transplantation; Periodontal health.
promote specific dental caries prevention programmes for these patients.

**Material and methods**

**Participants**

Thirty-eight children (22 males and 16 females; mean age 4.63±0.49) submitted to liver transplantation were selected from volunteer patients in the “Federico II” Hospital, Department of Paediatrics, Naples, Italy, and compared with 78 healthy children (35 males and 43 females; mean age 4.66±0.47) randomly selected from 5 public schools of the Regional Campania district, in order to avoid socioeconomic bias.

All the enrolled liver transplantation patients were observed at a single paediatric liver unit that was the only referral center for liver transplanted children living in the Campania region. Inclusion criteria for the liver transplantation group required that children were submitted to liver transplantation between 3 years and 9 months before the start of study, with or without history of therapeutic dental care.

Inclusion criteria for the control group required that children were from single live births, in good health (ASA I) with or without history of therapeutic dental care.

Exclusion criteria for both groups were systemic fluoride assumption during growth.

At the time of the study (dental evaluation), all liver transplantation patients were in treatment with tacrolimus as immunosuppressant drug and none of them was receiving steroids. Prednisone (2.5-5 mg/die) was given only in the first 6-12 months after liver transplantation and thereafter discontinued. None of the studied patients had significant alterations in either bone density or calcium-phosphate metabolism. Hyperglycemia was not present in any case.

**Questionnaire data**

A questionnaire investigating demographic and oral health behaviour data was completed by their parents. The fist part of the questionnaire included questions on demographic and social factors such as children’s age, gender, date and place of birth, family income, ect.

Oral health questions were administered to obtain data on children’s oral hygiene habits like onset of tooth-brushing habits, frequency of tooth-brushing at the time of the interview and frequency of use of extra cleaning devices such as dental floss or use of fluoridate toothpaste.

**Clinical examination**

All subjects were visited in the Paediatric Dentistry Department of the “Federico II” University, Naples (Italy). Clinical examinations were carried out by three calibrated examiners, in the same room, using a plane buccal mirror and the WHO CPITN ballpoint, with air drying when necessary. The presence of tooth decay was assessed by systematic evaluation of each child’s caries experience using the dmft index (sum of decayed, missing and filled teeth in the deciduous dentition).

A bitewing x-ray was also taken. A thyroid collar and lead apron for children and for the accompanying person if assisting during x-ray exposures were used. Pointing cone and dental films (Kodak Ultraspeed, Speed group D) were placed using a paediatric x-ray positioner. Bitewings radiographs were made for each child according to the EAPD guidelines for use of radiographs in children [Espelid et al., 2003].

Gingival inflammation was diagnosed as ‘bleeding’ or ‘no bleeding’ after gentle probing, according to Loe and Silness in all primary tooth surfaces (80 surfaces) [Loe and Silness, 1963].

Plaque was measured after drying the teeth with air, and classified as ‘visible’ or ‘no visible’ plaque, according to Silness and Loe [1964]. Plaque was registered buccally on primary upper incisors (four surfaces).

The enamel defects were recorded using the modified Developmental Defects of Enamel (DDE) index, in which the type (opacity, hypoplasia, discoloration), number (single and multiple), demarcation (demarcated and diffuse), and location of defects on the buccal and lingual surface of teeth could be recorded [Clarkson and Mullane, 1989] (Table 1).

**Statistical analysis**

All statistical procedures were performed using the Statistical Package for the Social Sciences (SPSS 10.0 for Windows). For all statistical tests, a confidence interval of 95% and significance level of 5% (p <0.05) were adopted. The kappa statistic was used to evaluate inter-examiner calibration. The comparison of mean dmft among groups was carried out using one-way analysis of variance (ANOVA). The comparison of gingival inflammation and DDE score between the two groups was carried out using logistic regression analysis, respectively.

<table>
<thead>
<tr>
<th>MODIFIED DDE INDEX</th>
<th>0 Normal</th>
<th>1 Demarcated opacities white/cream</th>
<th>2 Demarcated opacities yellow/brown</th>
<th>3 Diffuse lines opacities</th>
<th>4 Diffuse patchy opacities</th>
<th>5 Diffuse confluent opacities</th>
<th>6 Diffuse confluent/patchy opacities with hypoplasia missing enamel</th>
<th>7 Hypoplasia pits</th>
<th>8 Hypoplasia missing enamel</th>
<th>9 Any other defects</th>
</tr>
</thead>
</table>
| TABLE 1 Classification of dental enamel defects.
Ethics committee approval
The ethical principles expressed in the World Medical Association Declaration of Helsinki were followed in this study and all parents of the children, after receiving verbal and written explanations of the experimental protocol and the study aims, gave written informed consent. Furthermore, the approval for this study has been asked and obtained by the ethical committee of the University of Naples “Federico II” (Italy).

Results
Inter-examiner calibration
For dmft/dfs index, the kappa was 0.85 when comparing examiners 1 and 2, 0.79 when comparing examiners 2 and 3, and 0.82 when comparing examiners 1 and 3. For the gingival inflammation, there was perfect concordance between examiners with a kappa of 1. The kappa score for DDE index was 0.76 when comparing examiners 1 and 2, 0.73 when comparing examiners 2 and 3, and 0.81 when comparing examiners 1 and 3.

Clinical examination
Caries prevalence was 78.95% in the liver transplantation group and 39.7% in the healthy control group. In the liver transplantation group the dmft mean value was 2.26±2.25 (Table 2). In the healthy group the dmft mean value was 0.69±1.51 (Table 2). The difference in the mean dmft between the two groups was statistically significant (p<0.0001). The distribution of the dmft index components is showed in table 2. The values for decayed teeth, missing teeth and filled teeth were 1.18±1.57 and 0.46±1.17, 0.74±1.31 and 0.12±0.70, 0.34±0.94 and 0.05±0.32 in liver transplantation and healthy groups, respectively. There was a statistically significant difference between two groups in all the dmft components (Table 2).

Periodontal health data elaboration showed that 23.7% of the liver transplantation subjects and 48.7% of the controls had healthy periodontal status. 39.5% of the liver transplantation children and 25.6% of the controls had plaque and calculus; 44.7% of the liver transplantation patients and 28.2% of the control subjects showed bleeding on probing (Fig. 1).

Logistic regression analysis showed no statistical differences between liver transplantation subjects and healthy subjects for presence of bleeding on probing and plaque and calculus.

Dental enamel defects data elaboration showed that 65.8% of the liver transplantation children had enamel defects compared to 21.8% of the control group. In

![FIG. 1 Periodontal health in liver transplant children and healthy children.](image)

<table>
<thead>
<tr>
<th></th>
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<th>Mean</th>
<th>Std. Deviation</th>
<th>Std. Error</th>
<th>Lower Bound</th>
<th>Upper Bound</th>
<th>F</th>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
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<tr>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>1.57</td>
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<td>0.66</td>
<td>1.71</td>
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<td>0.13</td>
<td>0.45</td>
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</tr>
<tr>
<td>healthy group</td>
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<td>0.12</td>
<td>0.70</td>
<td>0.08</td>
<td>0.04</td>
<td>0.27</td>
<td>11.10</td>
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<td>0.31</td>
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<td>0.09</td>
<td>0.14</td>
<td>0.50</td>
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<tr>
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<td>0.32</td>
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<td>0.12</td>
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<td>0.94</td>
<td>0.15</td>
<td>0.03</td>
<td>0.65</td>
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<tr>
<td>total</td>
<td>116</td>
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<td>0.61</td>
<td>0.06</td>
<td>0.03</td>
<td>0.26</td>
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</table>

**TABLE 2** Dmft index and distribution of its components for healthy and liver transplantation group.
liver transplantation group, the most prevalent defect was greenish discoloration presented in 36.8% of the subjects. This defect was recorded in none of the control subjects. Marked opacity white/cream was presented in 5.3% of the liver transplantation group in comparison to 8.9% of the control group, while the irregular diffused opacity was recorded in 13.2% of liver transplantation subjects and in 7.7% of healthy subjects (Fig. 2).

Furthermore, hypoplasia with enamel loss was present in 21% of liver transplantation patients, while in none of the control subjects. Besides, the opacity yellow/brown was recorded in 2.6% of liver transplantation subjects and in 5.1% of healthy subjects, respectively (Fig. 2).

Logistic regression analysis showed a statistically significant difference between the two groups for the presence of dental enamel defects (OR: 6.9; CI = 2.9-16.2) (Table 3).

**Questionnaire data**

There was no statistical difference between the two groups for oral health behaviour. Before this study, only 21.05% of healthy children and 24.36% of liver transplant children had received a dental examination.

In both groups, the mean caries experience of the children with a history of recent dental visit was significantly higher compared to children who had never been to the dentists (Table 4). No difference in gingival health was observed across dental visit habits.

Eighty-nine percent of the subjects of the control group and 92% of those in the liver transplantation group reported the use of fluoridated toothpaste, but differences in caries level could not be observed between users of fluoridated and non-fluoridated toothpaste. Only in 18.42% of liver transplantation subjects and 19.23% of healthy subjects, parents personally brushed their children's teeth at least once a day.

There were no statistical differences between both groups with regards to consumption of sugar. No differences in caries levels and gingival health were observed in relation to eating habits.

Finally, the family socioeconomic level was similar for the two groups; 31.6%, 44.7% and 23.7% of liver transplantation group had high, medium and low family income, respectively. In the healthy group, the family income was high for 23.1%, medium for 46.2% and low for 30.7%.

**TABLE 3** Difference between the two groups for the presence of dental enamel defects.

<table>
<thead>
<tr>
<th></th>
<th>Sig.</th>
<th>OR</th>
<th>95% C.I. for EXP(B)</th>
<th>Lower</th>
<th>Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>DDE</td>
<td>.000</td>
<td>6.900</td>
<td>2.923</td>
<td>16.292</td>
<td></td>
</tr>
<tr>
<td></td>
<td>.056</td>
<td>.520</td>
<td></td>
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</tbody>
</table>

**TABLE 4** Dmft values in relation to dental visit before the study.

<table>
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<th>Mean</th>
<th>Std. Deviation</th>
<th>Lower Bound</th>
<th>Upper Bound</th>
<th>F</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>dmft</td>
<td>no dental visit before the study</td>
<td>0.75</td>
<td>1.49</td>
<td>0.49</td>
<td>1.99</td>
<td>5.088</td>
</tr>
<tr>
<td></td>
<td>dental visit before the study</td>
<td>2.67</td>
<td>2.26</td>
<td>1.82</td>
<td>3.51</td>
<td></td>
</tr>
<tr>
<td></td>
<td>total</td>
<td>2.26</td>
<td>2.25</td>
<td>1.52</td>
<td>3.00</td>
<td></td>
</tr>
</tbody>
</table>
Discussion

The results of this investigation show that children submitted to liver transplantation have higher caries prevalence, gingivitis and dental enamel defects with respect to the healthy control group.

These data were in line with previous studies, which showed a correlation between liver disease and dental caries, sustaining the hypothesis that the presence of systemic diseases in early childhood may interfere with the correct development of hard tissues such as teeth, and represent a risk factor for dental diseases [Crombie et al., 2009].

In this study, the liver transplantation group showed not only the higher caries prevalence, but also a greater severity of this disease with respect to the healthy group; in fact in the liver transplantation group, 46.4% of dental caries needed endodontic treatment, compared to 23% recorded in the control group. It is possible that these subjects, in addition of having a green-stained tooth structure, also show hypomaturation of dental tissues. In fact, the presence of liver disease during amelogenesis may cause alterations in the enamel ultrastructure, given that ameloblasts are extremely sensitive to environmental alterations [Kellerhoff and Lussi, 2004]. Such alterations may, in turn, be associated with modifications in the physical and chemical behaviour of the enamel, making it more susceptible to faster progression of demineralisation [Takahashi et al., 2009].

Periodontal health data elaboration showed that only 23.7% of the liver transplantation subjects had a healthy periodontal status compared to 48.7% registered in the controls.

Periodontal diseases could be due both to the immunosuppressive therapy that these patients undergo and to the poor oral hygiene. In fact, although it has been observed that replacing cyclosporine (associated with gingival hyperplasia) with some other immunosuppressor such as tacrolimus leads to reduction in gingival overgrowth [Thorpe et al., 2000], a recent study demonstrated that renal transplant recipients receiving everolimus (a more advanced form of calcineurin inhibitor) presented lower visible plaque index and lower values for bleeding on probing when compared to renal transplant recipients receiving tacrolimus. In addition, in the same study, patients receiving everolimus presented a gingival index varying from normal to moderate inflammation, whereas renal transplant recipients receiving tacrolimus presented a gingival index varying from mild to severe inflammation [Pereira-Lopes et al., 2012]. Furthermore, it is plausible that due to long hospitalisations and serious systemic discomforts, parents are disinterested in their children’s oral hygiene, since only 18.42% of the parents of liver transplantation subjects personally brushed their children's teeth at least once a day.

In addition, dental enamel defects data elaboration showed a significant difference in enamel defects between the two groups. In this study, 65.8% of the liver transplantation children had enamel defects compared to 21.8% of the control group.

It is likely that the higher prevalence of green-stained teeth appears to be associated with foetal or neonatal hyperbilirubinemia as a result of chronic liver failure. One of the manifestations of these disorders is the elevated serum levels of bilirubin (hyperbilirubinemia), a product of hemoglobin degradation, which is deposited in different tissues, including mineralised and soft tissues.

When hyperbilirubinemia occurs during dental development, teeth can develop a green coloration, which remains permanently, because after maturation dental tissues lose their metabolic activity.

An extracted tooth of a stained case showed that the deeply stained portion of the root formed prior to liver transplantation was clearly demarcated from that normally formed after transplantation [Lin et al., 2003].

Of the liver transplantation children, 89.5% had biliary atresia; this could explain the higher presence of greenish discoloration recorded. In addition, stained cases showed various degrees of green staining in the primary dentition, suggesting a correlation between the degree of tooth staining and severity of disease [Lin et al., 2003].

Finally, the irregular diffused opacity recorded in 13.2% of liver transplantation children could be due to the immunosuppressive therapy. In fact, as reported by Olczak-Kowalczyk [2012], tacrolimus administration predisposes patients to enamel opacity.

Conclusion

It is, therefore, important that the dentists, as members of a team for liver transplantation, monitor the dental health of patients. Routine dental care and caries prevention programmes need to be planned for these children during pre-liver or post-liver transplantation in order to reduce the risk of systemic infection arising from the oral cavity. Oral hygiene instructions to parents should begin as early as possible before liver transplantation.

References