Clinical evaluation of dental enamel defects and oral findings in coeliac children

Purpose
To examine dental hard and soft tissue changes of coeliac children in order to increase the awareness of the pediatric dentists in prediagnosis of especially undiagnosed coeliac disease.

Materials and methods
Sixty children, 28 (46.7%) boys and 32 (53.3%) girls whose ages were between 6 to 16 years were included in the present study. Thirty children who had undergone endoscopy and diagnosed with the coeliac disease in the Şişli Hamidiye Etfal Hospital, İstanbul, Turkey, formed the study group. Also, thirty children clinically suspected of having the coeliac disease with the same gastrointestinal complaints had undergone endoscopy and proven not coeliac were chosen as the control group. Oral examination involved assessment of dentition and specific and unspecific dental enamel defects. Also, soft tissue lesions, clinical delay of the dental eruption, salivary flow rate, pH, and buffering capacity were examined.

Results
Twenty coeliac patients had enamel defects, however none in the control subjects. In the coeliac group, all enamel defects were diagnosed in permanent teeth and as specific in all children. Grade I dental enamel defects found mainly in the incisors. The clinical delayed eruption was observed in 10 (33.3%) of 30 coeliac children and none of the children in the control group. While the level of DMFT/S numbers and stimulated salivary flow rate were found significantly lower in the coeliac group, pH was found significantly higher.

Conclusion
Oral cavity may be involved in coeliac disease and pediatric dentists can play an important role in the early diagnosis of the coeliac disease.

Keywords: Caries; coeliac disease; dental enamel defects; dental eruption; recurrent aphthous stomatitis

Introduction

Coeliac disease is a systemic immune-mediated primary small bowel disease characterized by inflammation in the small intestine mucosa and submucosa, often accompanied by malabsorption, which results in hypersensitivity to gluten found in cereal and cereal products. Coeliac disease is sometimes called gluten-sensitive enteropathy or celiac sprue. Clinical findings have improved with the removal of gluten from the diet (1, 2). Gluten is an insoluble protein found especially in wheat, barley, oats, and rye and reacts with alcohol, resulting in a molecule called gliadin. Although the mechanism of gliadin damage to the small intestinal mucosa is not fully understood, environmental and immunological factors in genetically susceptible individuals initiate disease (1, 3). Typical clinical features of the coeliac disease include malabsorption, chronic diarrhea, abdominal pain, and

weight loss. However, many cases are asymptomatic and do not show gastroenterological symptoms (4, 5). The oral cavity which is the entrance of the gastrointestinal tract is also affected in individuals with the coeliac disease, it can be easily examined and has a great prospect for early detection of coeliac disease. Dental enamel defects, recurrent aphthous stomatitis (RAS), dermatitis herpetiformis, Sjörgen’s syndrome and oral lichen planus have been reported in patients with coeliac disease (4-6). Dental enamel defects were first reported by Aine (7). Enamel defects are due to genetic factors that cause hypocalcemia-induced or glutamine-dependent specific immunological response. In addition, enamel hypoplasia may also occur due to malnutrition and vitamin D and A deficiency (8-10). The association of oral lesions with coeliac disease is controversial but it is thought to be the indirect effect of malabsorption (11). Based on this previous information, the null hypothesis of this study is that the dental enamel defects, oral diseases, and mouth dryness are not common in children with coeliac disease when compared to children having similar gastrointestinal complaints but not having coeliac disease.

Materials and methods

Study groups

All parents of the patients gave informed written consent for the participation of their children in the study, all study protocols were also approved by the Marmara University, Institute of Health Sciences Non-invasive Clinical Research Studies Ethics Committee (26.11.2013-1). Sixty children, 28 (46.7%) boys and 32 (53.3%) girls with ages between 6-16 years (mean age=12.76 ±3.08 years) from January 1, 2014 to December 31, 2014, living in Istanbul, Turkey during that entire time period were included in this study. Thirty children had undergone endoscopy diagnosed with the coeliac disease who attended to the gastroenterology unit of the Şişli Hamidiye Etfal Hospital, Istanbul, Turkey, formed the study group. Also, thirty children clinically suspected of having the coeliac disease with the same gastrointestinal complaints had undergone endoscopy and proven not coeliac were chosen as the control group.

Inclusion criteria

The study group consisted of children whose ages were between 6 to 16, whose caregivers consented and endoscopically proven to have coeliac disease. The control group consisted of children having the same complaints with the coeliac group, willing to give consent, and endoscopically proven not to have coeliac disease (12, 13).

Exclusion criteria

Exclusion criteria for the study and control groups were not having a definite diagnosis about the presence or absence of coeliac disease. Children whose first permanent incisors and molars were not yet totally erupted and children with fixed orthodontic treatment were also removed from the study. Furthermore, coeliac children, who previously followed a gluten-free diet for a period of one year or more, were excluded from the study (14).

Gastric examination

Endoscopy was performed with a gastro-duodenoscope (Olympus’ GIF-XP 150N, Tokyo, Japan) to children attending the gastroenterology unit of the Şişli Hamidiye Etfal Hospital. Biopsy forceps were sterilized and endoscopes were fully disinfected before and after each examination. Diagnosis of coeliac disease was based on European Society for Paediatric Gastroenterology, Hepatology, and Nutrition criteria (15).

Demographic questionnaire

A detailed medical history was taken from all children. Questions about use of medication, comorbidities for dental enamel defects (fluoride exposure, premature birth, fall on the front teeth, diabetes mellitus, long period of high fever, icterus, antibiotic use), history of coeliac disease among family members, frequency of daily toothbrushing (none or irregular, 1 or more per day), sugar intake (none or several times per week, at least once a day), education status of mothers and fathers (primary school, high school) and socioeconomic status of the family (low income<3000₺, high income>3000₺) were asked to parents of children participating in this study. The questionnaire was validated statistically and created according to previous studies (14, 16-18).

Oral examination

All children were clinically examined in order to assess their dental status. They have all brushed their teeth before the examination. The clinical measurements were recorded by one examiner. Oral examinations were done before endoscopy procedure without knowing whether the children were coeliac or not. The teeth were air dried using the portable dental equipment and examined with the help of a disposable mirror for the presence of dental defects (19). Both specific and unspecific defects were screened on the buccal surfaces of primary and permanent teeth. Enamel defects were classified as unspecific if only one tooth was affected on one side of the dentition. Specific defects had to be symmetrical, involving the same teeth in both hemiarches. Classification of specific enamel defects were evaluated according to Aine was shown in Table 1 (20). Also, oral examination involved assessment of dentition involving the number of teeth and carious teeth. Dental caries were diagnosed at the tooth surface level according to the WHO criteria (21). To determine the DMFT/dmft indices, the total numbers of decayed, missing, and filled teeth were calculated. Soft tissue lesions (presence of RAS, geographical tongue, angular cheilitis, atrophic glossitis) and clinical delay of the dental eruption were also examined (14, 22, 23). Oral mucosal surfaces including tongue, lips and their mucosa were observed (24). RAS was detected as recurrent, round, small ulcers with circumscribed margins, erythematous halos and yellow or gray floors (25). Minor RAS lesions are round ulcers less than 10 mm in diameter, major lesions are clinically similar to the minor but are larger than 10 mm in diameter and more persistent (26).
After chewing paraffin wax gums, the children were requested to spit for 5 minutes in order to detect stimulated salivary flow rates. Salivary pH was measured with the pH meter (Thermo Scientific™ Orion™ 3-Star Benchtop pH Meter, Thermo Fisher Scientific Inc. Waltham, MA, USA) and the buffering capacity was measured using Ericsson method from all subjects participated in this study (27, 28). All the tests in the study were carried out by a specialist.

### Statistical analysis

IBM Statistical Package for the Social Sciences Statistics 22 program (IBM Corp.; Released 2013. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY, USA) was used for statistical analysis. The normal distribution of the variables was evaluated by the Shapiro-Wilk test. Student t test was used for the comparison of two groups with normal distribution, and Mann-Whitney-U test was used for the comparison of two groups with non-normal distribution. Chi-square test, Fisher’s Exact Chi-square test, and Pearson Chi-square tests were used for the comparison of categorical data. Significance was assessed at p<0.05 level. Sample size was calculated with power analysis prior to the study. With 80% targeted power and 0.05 confidence level, using the previous literature, 28 individuals had to be enrolled in each group. To ensure the statistical power, 30 children were included in each group.

### Results

In total, 60 subjects were enrolled in this study were between 6 to 16 years of age. Twenty-five (41.6%) children were in mixed dentition and 35 (58.3%) children were in permanent dentition. Fifty percent of coeliac children (15/30) were typical, 46.7% of them were atypical and the rest of them (3.3%) were asymptomatic and the mean diagnosis age of the disease was 7.23±4.32 years. Four (13.3%) children had a
family member suffering from the same disease. There were no differences between coeliac and control groups in mean age, gender distribution, height, body mass and the presence of comorbidities. Twenty coeliac children had enamel defects while the control subjects had none. In the coeliac group, all enamel defects were diagnosed as specific and located on the permanent teeth. The most frequently seen dental enamel defects among coeliac children were in Grade I. Grade I was found in 14 (46.6%) and Grade II was found in 6 (20%) of coeliac patients (Table 2), (Figure 1, 2).

Grade III and IV were not observed in the current study. Enamel defects were found mainly in the incisors. The location and frequency of the specific enamel defects are given in Table 3.

The clinical delayed eruption was observed in 10 (33.3%) coeliac children. Delay of the eruption was found none of the children without the coeliac disease. The difference was statistically significant (p<0.05). The overall prevalence of RAS was 5 (16.6%) in control group and none in the coeliac group. The difference was not significant between groups (p>0.05). While the level of DMFT/S numbers and stimulated salivary flow rate was found significantly lower in the study group, pH was found significantly higher. The consumption of sugar in the control group was more than the coeliac group (p<0.05). The level of dmft/s numbers and the mean buffering capacity scores did not differ significantly between study and control groups. Oral findings among coeliac and control groups are shown in Table 4.

The frequency of daily tooth brushing did not differ significantly between coeliac and control groups. The sugar consumption frequency of 16 (53.3%) children in the control group were at least once a day, however, it was found in 5 (16.7%) children in the coeliac group. The influence of family income did not significantly contribute to the study and control groups. Mother’s and father’s education levels of the coeliac group were found higher than the control group.

**Discussion**

Coeliac disease is a common disorder affecting both children and adults. As many people with the disease do not present gastrointestinal symptoms, delays in diagnosis are very common and cause malignancies (29). In our report, we evaluated the prevalence of dental enamel defects, RAS, some oral and demographic parameters in patients with diagnosed coeliac diseases, and compared the results with subjects without coeliac disease. Mean age of diagnosis was 7.23±4.32 years in this study. Aguirre et al. (30) diagnosed the coeliac disease in the first 2 years of life in 64% of all the cases which was earlier than our study. Mina et al. (25) did not observe dental defects in coeliac children who had been diagnosed as coeliac at around 1 year old. Early introduction of gluten-free diet might have prevented the disturbances of dental enamel mineralization. Even though coeliac children had gluten-free diet immediately after diagnosis, late diagnosis might have led to disturbances in the permanent dentition. Acar et al. (31) detected the mean diagnosis age as 9.5 years in coeliac patients with enamel defects and 7.8 years in coeliac patients without enamel defects.

Although our study did not show any enamel defects in the control group and unspecific defects in the coeliac group, the greater number of systematic enamel defects in coeliac children demonstrated that enamel hypoplasia was more frequent in coeliac children than the control group. The enamel defects in the present study were generally symmetrical and mostly seen in anterior teeth. Similar observations were reported in previous studies (5, 7, 12, 17, 19, 24, 32–36) and only some studies (6, 37) contradicted the present findings. Similarly, Acar et al. (31) demonstrated enamel defects in 14 (40%) of 35 coeliac patients, while 21 of the coeliac patients did not have any defect. Also, none of the subjects in the control group had enamel defects. This finding showed that the dental enamel defects occurred significantly more often in coeliac patients.

**Table 3. Location of systematic enamel defects in coeliac group**

<table>
<thead>
<tr>
<th>Location of enamel defects</th>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incisors</td>
<td>17</td>
<td>53.4%</td>
</tr>
<tr>
<td>Incisors &amp; canines</td>
<td>2</td>
<td>6.7%</td>
</tr>
<tr>
<td>Molars</td>
<td>1</td>
<td>3.3%</td>
</tr>
<tr>
<td>Incisors &amp; molars</td>
<td>1</td>
<td>3.3%</td>
</tr>
<tr>
<td>No defects</td>
<td>10</td>
<td>33.3%</td>
</tr>
<tr>
<td>Total</td>
<td>30</td>
<td>100%</td>
</tr>
</tbody>
</table>

**Table 4. Oral findings in coeliac and control groups**

<table>
<thead>
<tr>
<th></th>
<th>Study group (n=30)</th>
<th>Control group (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>DMFT</td>
<td>4.48</td>
<td>3.67</td>
</tr>
<tr>
<td>DMFS</td>
<td>6.20</td>
<td>6.74</td>
</tr>
<tr>
<td>dmft</td>
<td>2.84</td>
<td>1.99</td>
</tr>
<tr>
<td>dmfs</td>
<td>5.76</td>
<td>5.19</td>
</tr>
<tr>
<td>Salivary flow fate</td>
<td>3.65</td>
<td>2.08</td>
</tr>
<tr>
<td>Buffering capacity</td>
<td>5.99</td>
<td>0.55</td>
</tr>
<tr>
<td>Saliva pH</td>
<td>7.99</td>
<td>0.46</td>
</tr>
</tbody>
</table>

p<0.05 significant difference between groups
SD: standard deviation; DMFT/S: decayed, missing and filled permanent teeth/surfaces; dmft/s: decayed, missing, and filled primary teeth/surfaces
According to Aine’s classification; Grade I was found in 14 (46.6%) and Grade II was found in 6 (20%) of 30 coeliac children. Grade III and IV were not observed in the current study. The findings of our study was found to be in accordance with those of Aguirre et al. (30) and Avşar et al. (17). In the study of Costacurta et al. (16) 80% of enamel defects were classified as Grade I, 15% Grade II, 3% Grade III, and 2% Grade IV. Cheng et al. (38) reported that dental enamel defects of children distributed as 14% Grade I, 53% Grade II, 19% Grade III and 11% Grade IV. Campisi et al. (5) reported dental enamel defects as 87% Grade I, 11% Grade II and 4% Grade IV. In the study of Aine et al. (7) 30% of coeliac children had grade III-IV defects. Differences in the severity and diagnosis age of coeliac disease, time to start and compliance to gluten-free diet, type of population studied might be responsible for the different results in the studies. Enamel defects were found mainly in the incisors (53.4%) also they were symmetric and chronologic in the current study. According to Aine (20); the central incisors are always affected in children with coeliac disease. Aguirre et al. (30), Costacurta et al. (16), Wierink et al. (12) and Cantekin et al. (34) also determined enamel defects mainly in the anterior teeth. The exact mechanism of development of dental enamel defects in coeliac disease is still not clear. The central incisors are the first dental elements where the mineralization process begin and affected through an influence on dental mineralization during odontogenesis. In coeliac children malabsorption due to enteropathy determines an alteration of phospho-calcium metabolism and cause hypocalcemia (37, 39).

The clinical delayed eruption was observed in 10 (33.3%) out of 30 coeliac children in the present study. Delay of the eruption was found none of the children in the control group. This findings was consistent with those Costacurta et al. (16) Campisi et al. (5) but not in accordance with Mina et al. (25).

In the previous studies (6, 16, 24, 26, 31, 34, 38) RAS was found to be more frequent in coeliac patients. On the contrary in the present study; RAS frequency was found to be higher in the control group rather than coeliac children but the difference was not statistically significant. Sedghizadeh et al. (40) reported that there were no significant differences between coeliac patients and healthy controls in the prevalence of RAS and they referred coeliac disease as a ‘risk indicator’ and not a ‘risk factor’ for RAS. Yaşar et al. (41) concluded that there is no apparent etiological link between RAS and coeliac disease and that screening RAS for coeliac disease has little clinical value. Conflicting data have been published on the real frequency of RAS in coeliac patients and there were few data on the effect of a gluten-free diet on RAS in coeliac patients. It must be remembered that RAS can also be associated with other inflammatory bowel diseases and consequently the association cannot be considered specific (26). Also, patients in this study might not present RAS at the time of oral examination, this did not mean that they did not suffer from RAS at any other times before. Families or children might not notice or remember whether they had RAS before clinical examination.

The relationship of caries and coeliac disease was the other aspect of this research. Amongst the coeliac group, the level of DMFT/S numbers was found to be lower than the control group. This was in agreement with the studies of Aguirre et al. (30), Farmakis et al. (32), Priovolou et al. (33) and Cantekin et al. (34), on the other hand; not in agreement with Costacurta et al. (16), Avşar et al. (17), Acar et al. (31), and Bramanti et al. (14). In the study of Shteyer et al. (36) no significant difference was reported among coeliac group and control group in mean DMFT/dmft scores although there was a tendency toward a higher DMFT/dmft scores in the control group which was consistent with the present study. Mina et al. (25) reported no statistical differences in the mean DMFT or dmft scores of coeliac children and control children. Páez et al. (19) investigated children with complete deciduous dentition and found higher numbers of caries in the control subjects. In contrast, dmft/s numbers did not differ between coeliac and control groups in the present study in which 25 (41.6%) children were in mixed dentition and 35 (58.3%) children were in permanent dentition. Our results were similar to the studies of Cantekin et al. (34) and Acar et al. (31).

Patients with the coeliac disease more frequently suffer from Sjögren’s syndrome than do healthy controls (43). In the present study, stimulated salivary flow rate of coeliac children was found lower than the control group as previous studies (13, 24, 34, 42). However, in another pilot study including 30 coeliac patients and 30 healthy age and sex matched controls, no differences in saliva secretion rate was found (43). Moreover, pH was found to be higher amongst the coeliac group and the level of buffering capacity did not differ between groups in the current study. In the study of Shteyer et al. (36) pH and buffering capacity were not different between coeliac and control groups. Acar et al. (31) demonstrated that the salivary pH, salivary flow rate, and buffering capacity were also similar in coeliac and control groups. In another study (25) buffering capacity and flow rate revealed no statistically significant differences.

The differences in toothbrushing habits such as frequency of daily tooth brushing between the coeliac group and control group were not statistically significant in our study as in the study of Avşar et al. (17). Also, daily sugar intake of the coeliac group was found lower than those of without coeliac. Sugar contains gliadin that coeliac patients do not want to consume (19). This result strongly supported the assumption that lower DMFT/S numbers might be related to low cariogenic dietary habits of the coeliac group. The reason for no significant difference in the mean number of DMFS/dmfs values between groups in the study of Acar et al. (31) might be related to similar daily sugar exposures of coeliac and healthy groups. The influence of family income did not significantly contribute to the coeliac and control groups. Mother’s and father’s education levels of the coeliac group were found higher than the control group. In the study of Avşar et al. (17) socio-economic status and education levels of the parents between the coeliac group and control group were not statistically significant.

Control group of our study consisted of children who had gastrointestinal complaints and proved not coeliac endoscopically. Besides clinical examination biopsy procedures had also been performed to these children in order to examine the type of the gastrointestinal problem had increased the reliability of our study. Because previous studies had
shown that the incidence of undetected celiac disease was very high and the ratio between diagnosed and undiagnosed patients even 1:7 (44). The limitation of our study is the lack of investigation of specific antigens which increases the risk for enamel defects (45). Further studies must be done in order to elucidate the genetic relationship between the celiac disease and enamel defects. Also, more extensive population-based studies are needed in order to demonstrate the oral effects of the celiac disease.

Conclusion

The changes in the oral cavity can be involved in celiac disease and pediatric dentists therefore play an important role in the early diagnosis of the disease. As celiac children may have various developmental disabilities in the dentition, they must be examined by pediatric dentists at least 2 to 3 times per year.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Marmara University, Institute of Health Sciences (26.11.2013-1).

Informed Consent: Written informed consent was obtained from patients’ parents who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: All authors designed the study and generated the data. All authors participated in gathering the data for the study. DAB and AY analyzed the data. DAB and AY wrote the majority of the original draft. All authors participated in writing the paper. All authors had access to all of the raw data of the study. All authors approved the final version of the paper.

Conflict of Interest: The authors have no conflicts of interest to declare.

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