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Oral findings in children with celiac disease

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Aim: To investigate whether Turkish children with celiac disease (CD) show dental enamel defects (DEDs), recurrent aphthous stomatitis (RAS), teeth missing, and xerostomia, and to compare the results with age- and sex-matched healthy children.

Materials and methods: The oral cavity was explored in 81 patients with CD (mean age 8.7 ± 3.7 years; age range 2.5 to 17 years) and in 20 healthy controls. Enamel defects, teeth missing, RAS, and xerostomia were established.

Results: Forty-three (53.1%) celiac patients and 5 (25%) control subjects had enamel defects. Enamel defects occurred more frequently in patients (P = 0.025) compared to controls. Regarding RAS, 39 (48.1%) patients and 1 (5%) control had aphthous ulcers (P = 0.0001). Teeth missing and xerostomia were detected in 11 (13.6%) and 47 (58%) patients, respectively. Patients with xerostomia were significantly greater in number compared to healthy children (P = 0.008). In the present study, the prevalence of DEDs, RAS, and xerostomia was greater in celiac patients than in healthy controls.

Conclusion: Early recognition of children with specific DEDs, RAS, and xerostomia and thus their referral to pediatricians might help in early diagnosis of CD.

Key words: Celiac disease, child, enamel defects, recurrent aphthous stomatitis

Çölyak hastalığı olan çocuklarda oral bulgular

Amaç: Çölyak hastalığı (ÇH) olan Türk çocuklarında dental enamel defekt (DED)'ler, tekrarlayan aftöz stomatit (TAS), diş kaybı ve ağız kuruluğu olup olmadığını araştırmak ve bunu yaş ve cinsiyete göre karşılaştırmak.

Yöntem ve gereç: 81 çölyak hastası (ortalama yaş 8,7 ± 3,7 yıl, yaş aralığı 2,5-17 yıl) ve 20 sağlıklı kontrol grubunun ağız boşluğu incelendi. Enamel defektler, diş kaybı, aftöz stomatit ve ağız kuruluğu tespit edildi.

Bulgular: 43 (% 53,1) çölyak hastasına karşılık 5 (% 25) kontrol grubunda enamel defekt vardı. Çölyak hastalarında enamel defekt daha fazla gözlendi (P = 0,025). TAS ile ilgili 39 (% 48,1) hastada ve 1 (% 5) kontrol grubunda aftöz ülserler vardı (P = 0,0001). 11 (% 13,6) hastada diş kaybı ve 47 (% 58) hastada ağız kuruluğu tespit edildi. ÇH'larında ağız kuruluğu kontrol grubuna göre anlamlı derecede daha yüksekti (P = 0,008). Bu çalışmada DED, TAS ve ağız kuruluğu kontrol grubuna göre çölyak hastalarında daha yüksek bulundu.

Sonuç: Spesifik DED, TAS ve ağız kuruluğu olan çocukların erkenden tanınıp pediatristlere yönlendirilmesi daha erken ÇH tanısının konulmasına yardım edebilir.

Anahtar sözcükler: Çölyak hastalığı, çocuk, enamel defekt, tekrarlayan aftöz stomatit

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Introduction

Celiac disease (CD) is a lifelong immune-mediated enteropathy found in genetically susceptible subjects and related to permanent intolerance to the polypeptide fragments of gluten, a protein contained in some cereals, such as wheat, rye, and barley (1-4). It is associated with severe atrophy of the mucosa of the upper small intestine, resulting in poor absorption of the majority of nutrients and vitamins (2,3). The reported prevalence of CD appears to have increased in recent years since the introduction of serologic tests for screening the general population (3). Its estimated prevalence in the general population of North America and Western Europe appears to be close to 1% (1). This prevalence in children between 2.5 and 15 years of age is approximately 1:300 to 1:80 (5,6). In the first CD prevalence study in our country, the prevalence of CD was found to be 1:115 (7).

It is apparent that the 'typical' clinical presentation of CD (characterized by malabsorption syndrome, i.e. chronic diarrhea, abdominal pain and distention, and weight loss) is currently less frequent and many CD patients show 'atypical'(nongastroenterologic al) symptoms, such as short stature, iron-deficient anemia, abnormalities in liver function test, or are asymptomatic (1,4).

When the disease is not treated, there is the possibility of several complications, such as sterility, osteoporosis, endocrinopathies, neurological and psychiatric disturbances, hepatic diseases, and association with autoimmune diseases (herpetiform dermatitis, diabetes mellitus, selective IgA deficiency, and thyroid diseases) (2). The importance of early diagnosis is that it allows for immediate treatment with a gluten-free diet, restores health, and prevents the development of the salient features or complications associated with CD, one of which is an increased risk for the development of non-Hodgkin's lymphoma of the gut (8).

The oral cavity, a part of the gastrointestinal system, can also be affected by several abnormalities in patients with CD. As the mouth is very easy to examine, oral lesions can provide a valuable clinical clue for early diagnosis of CD (6). Dental enamel defects (DEDs) and recurrent aphthous stomatitis (RAS) have been reported to be associated with CD (1,4,6). The association of oral lesions, such as RAS and DEDs, with CD is well known and other oral findings accompanying CD have been reported (for example, atrophic glossitis, oral manifestations of dermatitis herpetiformis, Sjögren's syndrome, and oral lichen planus) (6).

The primary aim of the present study was to assess whether Turkish children with CD show DEDs, RAS, teeth missing, and xerostomia, and to compare the results with age- and sex-matched healthy children.

Materials and methods

Twelve CD patients at the deciduous dentition stage, 34 CD patients at the mixed dentition stage, and 35 CD patients at the permanent dentition stage at the Pediatric Gastroenterology Unit were selected randomly to be included in the study group. A total of 81 CD patients, aged between 2.5 and 17 years old (mean age 8.7 ± 3.7 years), were enrolled in the study. The diagnosis of CD was based on serological tests (IgA and IgG endomysial antibodies, IgA and IgG gliadin antibodies, IgA and IgG human tissue transglutaminase antibodies), small-bowel biopsy during upper endoscopies, and histological evidence of villous atrophy with crypt hyperplasia and increase in intraepithelial lymphocytes. The control group was made up of 20 healthy children matched for dental stage, age, and sex. The children in the celiac and control groups were examined clinically by an experienced dentist who has expertise in oral diagnosis and radiology (M.A.S.).

RAS and DEDs were determined via oral clinical examination. The DEDs affecting deciduous and/or permanent teeth were graded 0 to IV according to Aine's classification (9). Overall oral mucosal surfaces were observed (including tongue, lips, palate, and their mucosa) and RAS was determined via oral examination. Only minor aphthous lesions were determined; therefore classification for RAS was not needed.

Unstimulated salivary flow rates were determined at the dental clinic. Unstimulated whole saliva flow rates less than 1 mL in 5 min (0.2 mL/min) were considered to indicate xerostomia (10).

The cases of the congenitally missing teeth germ were defined as missing teeth. The number of patients with congenitally missing teeth was determined

based on patient history as well as via clinical and radiological examinations. Patients with premature tooth loss or extracted teeth were not included in the group of patients with missing teeth.

Data were analyzed by means of SPSS 12.00 for Windows (SPSS Inc., Chicago, IL, USA). Mean ± standard deviation (SD), Mann-Whitney U test, and chi-square test were used for statistical analysis. P value less than 0.05 was regarded as statistically significant.

Results

There was no significant difference between celiac and control groups in terms of mean age, sex distribution, or serum calcium level. Of the 81 patients with CD, 56 (69.1%) and 25 (30.9%) patients had 'typical' and 'atypical' form, respectively. None of the patients or controls used fluoride pills.

Dental enamel defects were present in 53.1% (43 patients) of the celiac patients versus 25% (5 controls) of the controls (P = 0.025). The DEDs occurred more frequently in celiac patients, profoundly in first permanent molar teeth. With respect to the severity score of DEDs, 39/43 CD patients showed lesions of grade 1 and 2/43 grade 2, and 2/43 grade 3; in controls all were grade 1.

Oral examinations revealed that the subjects in both study and control groups had only minor RAS. Regarding RAS, 48.1% (39 patients) of the celiac patients and 5% (1 control) of control group had aphthous ulcers (P = 0.0001). Teeth missing and xerostomia were detected in 11 (13.6%) and 47 (58%) patients, respectively. Patients with xerostomia were significantly greater in number compared to the control group (P = 0.008). Comparison of oral manifestations between celiac and control groups is presented in Table 1.

In the present study, the prevalence of DEDs, RAS, and xerostomia was greater in celiac patients than in the control group. Although it is not statistically significant, patients with typical CD had DEDs more frequently. DEDs were present in 11/25 patients with the atypical forms (44%) and in 32/56 patients with the typical forms (57.1%) of CD (P > 0.05). RAS was present in 11/25 atypical celiac patients (44%) and 28/56 typical celiac patients (50%) (P > 0.05). Teeth missing was recorded in 3/25 (12%) patients with the atypical forms and 8/56 (14.3%) patients with typical forms of CD (P > 0.05), and xerostomia was observed in 10/25 (40%) atypical celiac patients and 37/56 (66.1%) typical celiac patients (P < 0.05). A comparison of oral manifestations according to clinical presentation of CD is shown in Table 2.

Table 1. Comparison of celiac and control groups in terms of oral manifestations.

Parameters	CD Patients (n = 81)	Controls (n = 20)	P value
DEDs	43 (53.1%)	5 (25%)	P = 0.025
RAS	39 (48.1%)	1 (5%)	P = 0.0001
Teeth missing	11 (13.6%)	4 (20%)	P > 0.05
Xerostomia	47 (58%)	5 (25%)	P = 0.008

Table 2. Comparison of oral manifestations according to clinical presentation of CD.

Parameters	Typical CD patients n = 56 (69.1%)	Atypical CD patients n = 25 (30.9%)	P Value
DEDs	32 (57.1%)	11 (44%)	P > 0.05
RAS	28 (50%)	11(44%)	P > 0.05
Teeth missing	8 (14.3%)	3 (12%)	P > 0.05
Xerostomia	37 (66.1%)	10 (40%)	P < 0.05

Discussion

Recent epidemiologic data indicated a prevalence of CD approaching from 1:300 to 1:80 in children between 2.5 and 15 years of age (5). Diagnosis of CD is relatively easy in cases with typical signs and symptoms (i.e. chronic diarrhea, abdominal pain and distention, and weight loss) (1). However, there has been a noticeable change in the clinical presentation of CD, as almost 50% of the patients with newly diagnosed CD do not present with gastrointestinal symptoms, thus making the diagnosis difficult. To identify the greatest number of 'atypical' or 'silent' CD patients and prevent long-term complications, clinicians must investigate 'at-risk subjects', e.g., those with chronic anemia, hypertransaminasemia or hyperamylasemia of an unknown origin, osteoporosis, or autoimmune thyroid disorders (4,6).

Among the atypical clinical presentations of CD, several oral manifestations have been described (e.g., DEDs and recurrent mouth ulcers) and these signs could help to identify CD patients (11). Aine reported that the prevalence of DEDs of permanent teeth in 74 children with CD were 95.94%, thereafter the author provided the strongest evidence that DEDs may be an extraintestinal manifestations of CD. In this study, the celiac-type DEDs were defined as 'systematic', as they were symmetrically and chronologically distributed in all 4 sections, reflecting the period in which disruptions interfered with amelogenesis (12).

In the study conducted by Cheng et al. (13), children had a significantly higher rate of dental enamel defects than adults (59.6% vs. 30.3%, P = 0.001). The authors interpreted these results as follows: first adults might have developed celiac disease after the age of 7; thus their adult enamel was not affected. Alternately, adults might have had severe defects and abnormal teeth extracted or altered.

The reason for the presence of DEDs in celiac patients remains unclear (1,4,5,13). Hypocalcemia caused by malabsorption during enamel formation is a specific determinate of enamel hypoplasia (1,2,4,5). In addition to hypocalcemia, other systemic factors are associated with enamel hypoplasia, such as malnutrition and vitamin D and A deficiency (2). Aine et al. (12) and Mäki et al. (14) explained the damage of the enamel organ by an autoimmune response. A gluten-induced immune-mediated process may occur between 6 months and 7 years in the enamel producing organ, resulting in defective enamel formation (1,2,4). Finally, these dental anomalies have been found to be significantly related to HLA antigen DR3, suggesting a genetic cause (1,3-6,15).

The overall prevalence of systematic CD-related DEDs in patients with permanent dentition ranges from 9.52% to 95.94% (with a mean value of 51.12%) (1). In our study, the prevalence of DEDs in Turkish children was 53.1%, which appears to be in line with the literature. We found a significant difference between celiac patients and healthy controls (P = 0.025) in terms of the prevalence of DEDs.

Recurrent aphthous stomatitis (RAS) is one of the most common mucosal diseases. The cause of RAS is unknown, although local and systemic factors, such as stress, allergies, nutritional deficiencies, trauma, hormones, and infectious agents, have all been implicated in certain subgroups of patients (8). RAS is characterized by painful, recurrent, single or multiple ulcers of the oral mucosa, which are round or ovoid and have an erythematous halos and a yellow or gray floor. The prevalence of RAS in the general population is estimated to vary from 5% to 66%, with a mean of 20% (1,8). In several studies, the prevalence of RAS in CD patients ranged between 9.66% and 40.98%. Furthermore, all the controlled studies failed to demonstrate any statistically significant difference between CD and control groups, even though it is worth noting that prevalence values of RAS were constantly higher in celiac patients than in controls (1). According to Sedghizadeh et al. (8), CD is a 'risk indicator', not a 'risk factor' for RAS. Contrary to the literature, we established that there were statistically significant differences between the celiac and control groups. We found that the prevalence of RAS was 48.1% in CD patients versus 5% in controls (P = 0.0001). In our previous study, investigating mucocutaneous manifestations associated with CD, we found that the prevalence of RAS was 1.8%. Dermatologists examined all patients in that study (16). In our current study, all oral examinations were performed by an experienced dentist who has expertise in oral diagnosis and radiology, which may explain why the prevalence of RAS was different between these 2 studies.

CD contributes to the occurrence of oral alterations, such as delayed tooth eruption, diminished size of the teeth, problems in enamel formation, and salivary gland dysfunction (14). Regarding salivary gland dysfunctions, the alterations caused by gluten do not affect the total stimulated salivary flow, but the composition of saliva may be affected, causing alterations in the total protein, albumin, IgA, IgM, amylase, and myeloperoxidase concentrations (17). Lähteenoja et al. (18) observed that celiac patients frequently complained of dry mouth symptoms. The xerostomia could have been the consequence of the diminished salivary flow. However, subjective sensation of dry mouth may occur even in the presence of normal salivary flow (2). Our study is the first prevalence study regarding xerostomia in CD patients. Xerostomia was detected in 58% of CD patients. Occurrence of xerostomia in CD patients was significantly higher compared to healthy controls (P = 0.008). Teeth missing was detected in 13.6% of CD patients. There was no significant difference between the 2 groups. In the present study, the prevalence of DEDs, RAS, and xerostomia was found to be greater in celiac patients compared to healthy controls.

Studies that screen children with DEDs for CD are needed because CD is common and may go undetected into adulthood (13).

Finally, we think that both dentists and pediatricians should be aware of various oral manifestations of CD. Oral examination of patients with CD should be performed by dentists. Early recognition of children with specific DEDs, RAS, and xerostomia and their referral to pediatricians might help in early diagnosis of CD.

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