Significance of Oral Symptoms in Early Diagnosis and Treatment of Celiac Disease

Çölyak Hastalığının Erken Teşhis ve Tedavisinde Oral Semptomların Önemi

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ABSTRACT Objective: To examine the frequency of oral symptoms in celiac disease and to underline their importance. **Material and Methods:** In the present study, we compared the prevalence of enamel defects, caries, recurrent oral aphthous stomatites, and risk factors of dental caries [levels of salivary mutans streptococci (MS) and Lactobacilli (LB)] between patients diagnosed with celiac disease, and healthy controls. A total of 82 patients with celiac disease and 110 healthy subjects were studied. **Results:** Dental enamel defects were found in 33 (40.2%) of the 82 celiac patients and 8 (7.2%) out of 110 control subjects. Enamel defects were significantly more common in celiac patients (p=0.000). All of the 33 celiac patients with enamel defect had specific dental enamel defects. Statistical analysis showed significantly more specific enamel defects in celiac patients than in control subjects (p=0.000). Regarding recurrent oral aphthous stomatitis (RAS), neither the celiac patients nor the healthy subjects had aphthous ulcers. Healthy individuals had significantly more caries lesions than celiac patients did (p= 0.000). **Conclusion:** Early diagnosis and consequent gluten-free diet may prevent or reduce oral lesions. Dentists play an important role in recognizing patients with celiac disease by means of oral findings.

Key Words: Oral manifestations; diagnosis, celiac disease

ÖZET Amaç: Çölyak hastalığında oral semptomların sıklığını değerlendirmek ve hastalığın tanısında bulguların önemini vurgulamak amaçlanmıştır. **Gereç ve Yöntemler:** Bu çalışmada, çölyak hastalığı tanısı alan hastalar ve sağlıklı kontrol grubu, mine defektleri, çürük, tekrarlayan oral aftöz stomatit ve çürük risk faktörlerinin (tükürükte mutans streptokok ve laktobasil seviyeleri) sıklığı açısından karşılaştırılmıştır. Çölyak hastalığı olan toplam 82 hastada çalışılmış ve 110 sağlıklı birey kontrol grubu olarak değerlendirilmiştir. **Bulgular:** Seksen iki çölyak hastasının 33 (%40.2)'ünde, 110 kontrol bireyinin ise sadece 8 (%7.2)'inde dişte mine defekti saptanmıştır. Mine defekti olan 33 çölyak hastasının hepsinde özel mine defekti defekti saptanmıştır ve çölyak hastalarında özel mine defektlerinin, kontrol bireylerinde görülenden anlamlı ölçüde daha fazla olduğu gösterilmiştir (p= 0.000). Tekrarlayan oral aftöz stomatit açısından değerlendirildiğinde, aftöz ülserlere her iki grupta da rastlanmamıştır. Çürük lezyonları açısından sağlıklı ve çölyaklı hastalar karşılaştırıldığında, sağlıklı bireylerde çürük lezyonlarının, çölyak hastalarına görece önemli ölçüde daha fazla olduğu saptanmıştır (p= 0.000). **Sonuç:** Erken teşhis ve gluten içermeyen gıdalarla beslenme, oral lezyonları önleyebilir ya da azaltabilir. Oral bulguları nedeniyle dişhekimleri, oral bulgular nedeniyle, çölyak hastalığına sahip bireylerin teşhisinde ve hastalığın erken dönemde saptanmasında önemli bir rol üstlenebilirler.

Anahtar Kelimeler: Oral bulgular; teşhis, çölyak hastalığı

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Celiac disease, also known as gluten-sensitive enteropathy, is characterized by inflammation of the small-intestinal mucosa that results from a genetically based immunologic intolerance to ingested gluten.

Gluten is a protein that is found in wheat, rye and barley.[1]

There is clinical and histological improvement on a strict gluten-free diet and relapse when dietary gluten is reintroduced.[2] Inflammation developing in celiac disease classically produces a malabsorption syndrome with diarrhea, steatorrhea, pallor, abdominal distention, vomiting and loss of weight or failure to thrive.[1,3]

Diagnosis is based on the presence of pathological mucous membrane of the small intestine, which is verified by intestinal biopsy. The mucous membrane would normalise on a gluten-free diet.[4,5]

Several authors have described the prevalence of dental problems in patients with celiac disease and have suggested that such problems would constitute a diagnostic clue for the diagnosis of the disease that is difficult to identify.[6,7] These problems usually manifest as dental enamel defects and recurrent oral aphthous stomatitis.[8-13]

The cause of the dental lesions associated with celiac disease is unclear. The low calcium concentrations observed in patients during dental development have been implicated in enamel hypoplasia.[14]

In the present study, the prevalence of enamel defects, caries, recurrent oral aphthous stomatites, and risk factors of dental caries [levels of salivary mutans streptococci (MS) and Lactobacilli (LB)] among patients diagnosed with celiac disease was investigated and the results were compared with those of healthy controls. In addition, the role of pediatric dentists in the early diagnosis and prevention of celiac disease complications were evaluated.

MATERIAL AND METHODS

A total of 82 patients with celiac disease were included; 43 were female and 39 were male. Based on dentition, the patients were divided into two subgroups. One group was composed of 28 patients with deciduous dentition (mean age 5.7 ± 1.2, range 4-7 years) and the other group consisted of 54 patients with mixed or permanent dentition (mean age 10.2 ± 1.8, range 6-16 years). In each case, the diagnosis of celiac disease was based on intestinal biopsy and patient response to gluten-free diet. All patients with celiac disease were diagnosed in the Pediatric Department of Dicle University (Diyarbakır/TURKEY).

The mean age at diagnosis was 3.2± 0.6 (range0.7-6y) in the deciduous dentition group and 7.6± 2.4 (range 3-13 y) in the mixed and permanent dentition group.

A total of 110 healthy subjects (57 female and 53 male) who had no gastrointestinal complaints in the past comprised the control group. The control group was randomly selected with similar characteristics to the study group for geographical area, age and gender. The control group was also divided into two subgroups such as 31 healthy subjects with deciduous dentition (mean age 5.1 ± 0.9 range 3-7 years), and 79 healthy subjects with mixed or permanent dentition (mean age 11.6 ± 2.1 range 6-16 years).

This study was carried out in the University of Dicle, Faculty of Dentistry, Department of Pedodontics, Diyarbakır, Turkey. The oral examination was performed carefully by one dentist (AZ) and was carried out with the help of conventional dental chairs, artificial light, a mirror and probe. A questionnaire was used to detect the symptoms. Toothbrushes and toothpastes were given to all children and they all brushed their teeth before examination. Restorative and/or surgical treatments were applied to all children after examination.

Specific (or systematic) dental enamel defects are defined as occurring symmetrically and chronologically in all four quadrants of dentition, whereas unspecific enamel lesions occur symmetrically and chronologically but involve the superior and inferior hemi-arches on the same side.[9] All specific and unspecific enamel defects were noted were photographed. Specific enamel defects were classified under grades I-IV described by Aine.[6] For all patients, the diagnosis of recurrent aphthous stomatitis was based on clinical examination and medical history.

DMF(T)/df(t) (D: decay, M: missing, F: filling, T: teeth in permanent dentition and d: decay, f: filling, t: teeth in primary dentition) indices were cal-

culated. In both groups a CRT bacteria test, (two in one system, Vivadent Ets., Schaal/Liechtenstein), which is a dip-slide method, was used to determine the salivary levels of MS and LB. In this examination, one surface of a specifically designed test tube was used to spread the saliva for the MS score and the other surface was used for the LB score. Bacteria levels were expressed as colony-forming units (cfu) per milliliter of saliva in accordance with the manufacturer's recommendations. In this procedure, both bacteria were scored from 0 to 3 (0 and 1 $<10^5$, 2 and 3 $>10^5$).

Statistical Analysis

Levene's test was used for equality of variances. Student's t-test or Mann-Whitney U test and Chi-square test were used to determine significant differences between groups ($p< 0.05$). The statistical analyses were performed using a statistical program for PC (SPSS 15.0 for Windows and Med-Calc 10.0.1.0 for Windows) ($\alpha= 0.05$).

RESULT

Overall, 192 children (82 celiac patients, 110 control subjects) were examined. The female/male ratio was 43/39 in the group of celiac patients and 57/53 in the control group. The mean age of the patients with celiac disease and the control group for deciduous dentition was, 5.7 years (range 4-7 years) and 5.1 years (range 3-7 years) respectively. In addition, the ratio for mixed and permanent dentition was 10.2 (range 6-16 years) and 11.6 (range 6-16 years) respectively. There was no statistically significant difference in gender and age between the group of celiac patients and the control group (Table 1).

In 33 (40.2%) of the 82 celiac patients, defects of dental enamel were found. While 30 out of 54 (55.5%) celiac patients with mixed or permanent dentition had enamel defects, enamel defects were detected in 3 of 28 (10.7%) celiac patients with deciduous dentition and in 8 (7.2%) out of 110 control subjects with mixed or permanent dentition. None of the control subjects with deciduous dentition had enamel defect. Enamel defects were significantly more common in celiac patients than in controls ($p= 0.000$) (Table 2).

Table 2 shows that all 33 celiac patients with enamel defects were diagnosed with specific dental enamel defects. In the control group, 5 out 8 subjects with mixed or permanent dentition were diagnosed with nonspecific and the remaining 3 subjects with specific enamel defects. Statistical analysis showed significantly more specific enamel defects in celiac patients than in control subjects ($p= 0.000$). Dental enamel defects of grade I was observed most frequently especially in the incisors. The locations and grades of enamel defects in two groups were shown in Table 2 and 3.

Regarding recurrent oral aphthous stomatitis (RAS), neither celiac patients nor the healthy subjects had aphthous ulcers. The questionnaires filled out by patients or parents and clinical hospital records indicated that all patients with celiac disease had oral aphthous stomatitis in the early stages of disease.

The control group had significantly more caries lesions than patients with celiac disease did. The mean DMF(T) and/or df(t) values of the control group and celiac patients were 6.9 ± 1.7 and 2.4

TABLE 1: Comparison of age, gender, DMF(T)/df(t), salivary MS/LB values between celiac patients and control subjects.

	Patients with celiac disease (n= 82)	Control group (n= 110)	
Age (Deciduous dentition/Mixed or permanent dentition)	5.7 ± 1.2 / 10.2 ± 1.8	5.1 ± 0.9 / 11.6 ± 2.1	NS
Female/Male	43 / 39	57 / 53	
DMF(T)/df(t)	2.4 ± 1.3	6.9 ± 1.7	p= 0.000
Salivary MS	1.6 ± 0.9	2.4 ± 1.0	p= 0.002
Salivary LB	0.5 ± 0.6	2.2 ± 1.2	p= 0.000

DMFT= Decay, missing, filling,teeth MS= Mutans streptococci LB= Lactobacilli.

TABLE 2: Grading of enamel defects in each group of patients according to the classification of Aine.

	Deciduous Denitition		Mixed or Permanent Dentition	
	Celiac (n= 28)	Control (n= 31)	Celiac (n= 54)	Control (n= 79)
Nonspecific defects	-	-	-	5
Specific defects	3	-	30	3
Grade 0	25	31	24	71
Grade 1	3	-	23	3
Grade 2	-	-	6	-
Grade 3	-	-	1	-
Grade 4	-	-	-	-

p= 0.000 Chi-square= 23.490.

TABLE 3: Location of enamel defects in different groups of teeth in patients with celiac disease and the control group.

Locations of enamel defects	Celiac Patients (n= 33)	Control (8)
Incisors	32 (96.9%)	5 (62.5%) p= 0.023 X^2= 5.162
Canines	2 (6.0%)	1 (12.5%) p= 0.901 X^2= 0.015
Premolars	8 (24.2%)	(25%) p= 0.680 X^2= 0.170
Molars	5 (15.1%)	2 (25%) p= 0.885 X^2= 0.023

X^2: Chi-square.

± 1.3 respectively (p= 0.000) (U value= 1183.500) (Table 1).

The rates of mutans streptococci in the control group and patients with celiac disease were 2.4 ± 1.0 and 1.6 ± 0.9 (skor) respectively (p= 0.002) (U value= 2553.000) (Table 1).

The rates of lactobacilli in the two groups were 2.2 ± 1.2 and 0.5 ± 0.6 (skor) respectively (p= 0.000) (U value= 442.500) (Table 1).

DISCUSSION

Studies emphasizing the role of pediatric dentists in the diagnosis of celiac disease in Southeast Turkey are lacking. Retrospective reviews showed that the rate of diagnosis in defined geographic areas varies widely.[15,16] The prevalence of celiac disease in children between 2.5 and 15 years of age in Europe and the USA is approximately 1:300 to 1:80.[17] Recent epidemiological data showed the prevalence of celiac disease had increased up to 1% of the general population.[18-21] In Turkey, celiac disease is highly prevalent among healthy school children. Children with celiac disease should be evaluated more carefully with the understanding of the high prevalence of these disease in Turkey.[22] The rate of diagnosed celiac disease depends on the level of suspicion for the disease. With a better understanding and an increasing suspicion, more patients would be diagnosed in our population. The cumulative frequency of celiac disease increased more in females than males.[23]

A group of Finnish authors described permanent teeth enamel defects in a high percentage of celiac patients, which were systematically, symmetrically and chronologically distributed in all four quadrants of dentition.[6] Similar studies have been performed and almost all have reported a higher prevalence of enamel defects in celiac patients, with varying rates. Our results demonstrated a higher number of enamel defects in patients with celiac disease than in control subjects. Specific enamel defects in the patients with celiac disease were observed in 55.5% with mixed or permanent dentition and in 10.7% with deciduous dentition according to the classification of Aine. These results correspond with the results of other authors.[24-26] The cause enamel defects associated with celiac disease is unclear. Disturbances which may cause enamel defects are thought to be nutritional or immunological. In celiac disease, intestinal damage leads to malabsorption, and a possible explanation for the presence of enamel defects in these patients is that enamel hypoplasia is caused by hypocalcaemia.[6] Reports indicated that the celiac type enamel defects were strongly associated with the HLA allele DR3.[27] An Italian study reported that there were no statistically significant differences in calcium concentrations between celiac patients with and without enamel defects, but reported that 77.2% of the celiac patients with enamel defects were DR3 positive, while 39.1% of patients without enamel defects presented with this antigen.[28]

Therefore, the higher incidence of enamel defects in patients with celiac disease constitutes

a fundamental clue in the clinical identification of the disease, with particular application to the growing number of patients with celiac disease. The incidence of such defects has led dentists to play an important role in screening for celiac disease, which, if not diagnosed and treated with a gluten-free diet may lead to malignancies and death.[29]

A clinical practice guideline for the diagnosis and treatment of celiac disease in children was formulated.[17] Dental enamel defects were mentioned as a symptom of celiac disease. This guideline advises the following procedure when dental enamel defects are noticed. Serological testing is recommended. Children with a positive serologic test are referred to a paediatric gastroenterologist for small intestinal biopsy. Those with histological features of celiac disease on biopsy are treated with a strict gluten-free diet.[17]

The mean age at diagnosis plays an important role in the pathogenesis of dental lesions. An other Italian study reported that the mean age at diagnosis was significantly higher in patients with enamel defects than in a group without enamel defects.[30] In contrast, Bucci et al reported that the mean age at diagnosis did not differ significantly between patients with and without enamel defects.[9] In this study the mean age at diagnosis was higher in patients with enamel defects than in a group without enamel defects.

Some studies have considered recurrent aphthous stomatitis as one of the clinical manifestations of celiac disease.[8-13] A study evaluating the immune-genetic relationships between celiac disease and recurrent aphthous stomatitis reported that 17% of celiac patients also had recurrent aphthous stomatitis.[31] In another study, it was found that the percentage of recurrent aphthous stomatitis in patients with celiac disease was 41%, whereas it was 27% in healthy controls but this difference was not significant.[8] Meini et al observed a marked improvement of oral ulcers in their celiac cases after gluten free diet.[31] In our study, although we did not observe recurrent aphthous stomatitis in any of the groups, some patients with celiac disease had suffered from recurrent aphthous stomatitis before gluten-free diet. Thus, it seems that recurrent aphthous stomatitis requires medical history to be a major part of the diagnostic process and is influenced by the presence of gluten in the diet, supporting the hypothesis of a correlation between celiac disease and recurrent aphthous stomatitis.

In our study, the relationship between DMF(T)/df(t) index of patients with celiac disease and control subjects was evaluated. The mean DMF(T)/df(t) index rate was significantly higher in the control group than in celiac patients. Similar results were observed by Fulstow and Priovolou et al and Akarslan et al.[25,32,33] This may be attributed to a low cariogenic diet and better dental care. We also compared levels of salivary MS and LB between patients with celiac disease and healthy controls. Both the rates of salivary MS and salivary LB were higher in the control group than in celiac patients. But it was surprising that the rates of salivary MS were higher, while the rates of salivary LB were also lower in celiac patients. Although it is not possible to compare our results with other studies, it is known that there is a positive correlation between mutans streptococci, LB and caries prevalence. MS in particular are of major etiologic significance in human dental caries. The capacity of this microorganism to initiate dental caries depends on its ability to release organic acids and to produce adhesive extracellular polysaccharides. LB are related to the development of caries lesions, especially after the initiation of caries. The growth of LB is favored by a frequent intake of fermentable carbohydrates, and salivary LB counts are useful in predicting future caries activity.[34-36] Dietary treatment of celiac patients is assumed to reduce the number of lactobacilli in saliva but to have no effect on mutans streptococci.

In conclusion, it seems that early diagnosis and consequent gluten-free diet may prevent or reduce oral lesions. The mouth-the first part of the gastrointestinal system-is an easily accessible site and an oral examination may contribute considerably to the diagnosis of celiac disease, as it was associated with oral symptoms. Dentists play an important role in recognizing patients with celiac disease.

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