

The Association Between Celiac Disease, Dental Enamel Defects, and Aphthous Ulcers in a United States Cohort

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Goals and Background: European studies have demonstrated that dental enamel defects and oral aphthae are observed in celiac disease (CD). We investigated this association in a US population.

Study: Biopsy proven CD patients and controls were recruited from a private dental practice and from CD support meetings. History of aphthae was taken and dental examination was performed by a single dentist. Teeth were photographed and enamel defects graded according to the Aine classification. A second dentist reviewed all photographs.

Results: Among patients ($n = 67$, mean age 34.8 ± 21.6 y) compared with controls ($n = 69$, mean age 28.1 ± 15.7 y), there were significantly more enamel defects [51% vs. 30%, $P = 0.016$, odds ratio (OR) 2.4, 95% confidence interval (CI) 1.2-4.8]. This was confined to children (87% vs. 33%, $P = 0.003$, OR 13.3, 95% CI 3.0-58.6), but not adults (32% vs. 29%, $P = 0.76$, OR 1.2, 95% CI 0.5-2.8). This was reflected in defects being observed in those with mixed dentition compared with those with permanent dentition (68.4% vs. 29.6%, $P < 0.0001$). The degree of agreement between the 2 dentists was good (κ coefficient = 0.53, $P < 0.0001$), aphthous ulcers were more frequent in CD than controls (42.4% vs. 23.2%, $P = 0.02$).

Conclusions: This study supports that CD is highly associated with dental enamel defects in childhood, most likely because of the onset of CD during enamel formation; no such association was found in adults. Our study also supports the association between CD and aphthous ulcer. All physicians should examine the mouth, including the teeth, which may provide an opportunity to diagnose CD. In addition, CD should be added to the differential diagnosis of dental enamel defects and aphthous ulcers.

Key Words: celiac, dental enamel defects, aphthae

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Celiac disease is a genetically determined autoimmune enteropathy characterized by a typical intestinal lesion and a response to a gluten-free diet. It is precipitated by the ingestion of gluten found in wheat, rye, and barley.¹ The disease occurs in about 1% of the US population.² It has a wide spectrum of clinical manifestations from a “classic”

celiac presentation of diarrhea, with or without a malabsorption syndrome to an “atypical” presentation that lacks gastrointestinal symptoms. This great variety of symptoms and presentations make the diagnosis more difficult. There are characteristic, although not specific, pathologic changes in the duodenum that regress on withdrawal of gluten from the diet.³ The disease more closely resembles a multisystem disease because almost any organ system may be involved, including the mouth.

Celiac disease has been reported to influence the mineralization of permanent teeth.⁴ Dental enamel defects are the imperfections in the enamel, they include discoloration and structural changes (Table 1).^{5,6} The results of previous studies are contradictory. Some reported a significant effect of celiac disease on the prevalence of enamel defects in children, adolescents, and adults,⁵⁻¹¹ whereas others did not show such a relationship.^{12,13} Recurrent aphthous ulceration is also associated with celiac disease.¹⁴⁻²⁰

The purpose of this study is to document the prevalence of developmental enamel defects and a history of aphthous ulcers in a group of children and adults with celiac disease. There have been no similar studies in the United States.

MATERIALS AND METHODS

This case-control study included 67 people with celiac disease and 69 controls. Biopsy proven celiac disease patients were recruited from a private dental practice and celiac support group meetings. Controls were selected from the patients in the office of the same dentist and were not relatives of the patients with celiac disease. Celiac disease patients were on a gluten-free diet and controls consumed a regular diet. The study subjects were divided into subgroups: adults (> 18 y) and children (≤ 18 y) as well as according to the type of dentition: mixed dentition (≤ 13 y) and permanent dentition (> 13 y).

Consent forms to participate in the study were signed and a questionnaire was given to all subjects. The questionnaire included demographics, information concerning the biopsy diagnosis of celiac disease, and a history of aphthous ulcers.

A dental examination was performed in a dental operatory in the examiner's office. Patients were examined by drying the teeth but not desiccating the teeth with a light application of air or by wiping them with a 2×2 gauze. Current restorations were noted along with missing teeth and any clinically visible decay. Patients were questioned regarding the frequency and duration of aphthous ulcers. The teeth of all patients were photographed using a Yashika dental eye. All patients were examined by the

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TABLE 1. Classification of Systemic and Chronologic Enamel Defects

Classification	Enamel Defect
Grade 0	No defect
Grade I	Defect in color of enamel consisting of single or multiple cream, yellow or brown opacities (marks), and loss of normal enamel glaze
Grade II	Slight structural defects consisting of a rough surface with horizontal grooves or shallow pits; light opacities and color changes may also be found. A part or the entire surface of enamel is without glaze
Grade III	Obvious structural defects with a part of, or the entire surface of enamel rough and filled with deep horizontal grooves, which vary in width or have large vertical pits; large opacities of different colors or linear discoloration may be present in combination
Grade IV	Severe structural defects. The shape of the tooth changed. The tips of cusps are sharp-pointed and/or the incisal edges are unevenly thinned and rough. The thinning of the enamel material is easily detectable and the lesion may be strongly discolored

Modified from *Proc Finn Dent Soc.* 1986;82:227–229.

same dentist, however, a second dentist also examined the photographs.

Enamel defects were classified using grades 0 to IV according to Aine criteria (Table 1). As only 3 patients had grade II defects and none had grade III or IV, enamel defects were grouped as either present or absent in this study. This study was approved by the Columbia University Institutional Review Board.

Statistical Analysis

Statistical analysis was conducted by 2-sample *t* test and Pearson χ^2 test. Logistic regression models were used to find predictors for enamel defects. Statistical significance were determined at the $\alpha = 0.05$ level with 2-sided tests. Statistical analysis was performed by SAS computer software (SAS Institute, version 9.1, Cary, NC).

RESULTS

In total, 136 subjects were enrolled in this study and their characteristics were shown in Table 1. There were no differences in terms of the proportion of adult, female sex, and permanent dentition between the cases and controls. Celiac disease patients were older than controls (34.8 ± 21.6 y vs. 28.1 ± 15.6 y, $P = 0.04$) and female predominant. The mean age at diagnosis of celiac disease was 29.3 years (SEM 21.9 y). These patients had been on a gluten-free diet a mean of 4.7 years (SEM 5.8 y). The study also had more

subjects in adult age group and subjects with permanent dentition.

Children had significantly higher rate of dental enamel defects (Figs. 1–3) than adults (59.6% vs. 30.3%, $P = 0.001$). There was no significant difference of enamel defects detected in females compared with males.

The dental enamel defects were symmetric and chronologic. They were mostly observed on the maxillary and mandibular incisors and the first molars. The defects were frequently identified in all 4 quadrants of the mouth. The younger the patient with celiac disease the more pronounced the dental enamel defects (Fig. 1).

The comparison of cases and controls among the different subgroups was shown in Table 2. Overall those with celiac disease had significantly higher rate of enamel defects. Among children and those with mixed dentition, celiac disease patients had significantly higher rate of enamel defects than controls, but no differences were detected among adults and those with permanent dentition. Patients with mixed dentition had a significantly higher rate of enamel defects than those with permanent dentition (68.4% vs. 29.6%, $P < 0.0001$) (Table 3); the same association presented in children (68.4% vs. 22.2%, $P = 0.01$), as there is no mixed dentition in adults. Among celiac disease patients, mixed dentition had significantly higher rate of enamel defects than permanent dentition (90% vs. 34.0%, $P < 0.0001$) whereas among controls, there was no significant association between dental defects and dentition ($P = 0.13$). Logistic regression models were fitted and 3 significant predictors for enamel defects were found: age, celiac disease, and mixed dentition (Table 4). Overall celiac



FIGURE 1. Example of grade I dental enamel defects. Mixed dentition with multiple white and cream opacities with clearly defined margins and part of the enamel surface is without a glaze.



FIGURE 2. Grade II dental enamel defects. The enamel surface with slight horizontal and vertical grooves; light symmetric opacities and color changes (yellow) in the surface of enamel.



FIGURE 3. Grade II dental enamel defects. In this case the enamel surface is rough with patchy symmetric opacities and discolorations. In general, the surface of enamel is without glaze.

disease had an odds ratio (OR) of 2.4 [95% confidence interval (CI) 1.2-4.8], but after stratification by adult and children group, celiac disease is a highly significant predictor for dental defect among children but not among adults; for children: OR 13.3, 95% CI 3.0-58.6; for adults: OR 1.2, 95% CI 0.5-2.8.

To increase the reliability of single dental examiner, photographs were taken of the teeth of all participants in the study. A second dental examiner then reviewed the photographs, without the availability of the results of the first examiner, the degree of agreement between the 2 dentists was good (κ coefficient = 0.53, $P < 0.0001$).

There was a significant association of aphthous ulcers with celiac disease (42.4% in those with celiac disease vs. 23.2% in controls, $P = 0.02$). The patients with enamel defects have a significantly higher rate of aphthous ulceration than the patients without enamel defects (41.5% vs. 25.3%, $P = 0.05$).

DISCUSSION

The mouth is examined by both physicians and dentists. However teeth are rarely closely examined by physicians. Abnormalities of the oral cavity (both aphthous ulceration and dental enamel defects) have been reported in celiac disease and increasing awareness of this information could facilitate diagnosis of celiac disease.

This study shows that symmetrically and chronologically distributed dental enamel defects are associated with celiac disease. This association occurs specifically in children with celiac disease (Fig. 2). This result supports

TABLE 2. Characteristics of the Study Sample

	Celiac Disease n (%) N = 67	Controls n (%) N = 69	P
Sex			
Female	53 (79.1%)	54 (78.3%)	0.90
Age distribution			
Adult	44 (65.7%)	45 (65.2%)	0.95
Dentition			
Permanent	47 (70.2%)	51 (73.9%)	0.62
Age mean \pm SD (y)	34.8 \pm 21.6	28.1 \pm 15.7	0.04

TABLE 3. Occurrence Rate of Enamel Defects

	Celiac Disease n (%)	Controls n (%)	P
Among all subjects	34 (51)	21 (30)	0.016
Among adults	14 (32)	13 (29)	0.76
Among children	20 (87)	8 (33)	0.003
Among those with mixed dentition	18 (90)	8 (44)	0.0045
Among those with permanent dentition	16 (34)	13 (25)	0.48

European studies.⁵⁻¹¹ However, adults in our study did not have dental enamel defects in contrast to the work of some European investigators.^{6,9,11} Possible explanations for such age disparity are: firstly, adults might have developed celiac disease after the age of 7 years, thus their adult enamel would not be affected. Alternately, adults might have had severe defects and abnormal teeth extracted or altered.

The exact mechanism of development of dental enamel defects in celiac disease is still unknown. The enamel of permanent teeth develops during first 7 years of life and nutritional, including hypocalcemia, or immunologic disturbances during this time are thought to result in enamel defects. Some studies hypothesized that hypocalcemia results in the formation of enamel defects.^{11,12,21-23}

Dental enamel defects are not specific for celiac disease but the possibility of celiac disease should be considered as one of the causes of dental enamel defects along with the more accepted explanations such as excess fluoride intake or tetracycline. Bulimia is also a cause, we however did not enquire whether this had been a feature of the medical history of the celiac patients or the controls. Many parents reported that the discoloration present on the teeth of their children was attributed by their dentist to high intake of fluoride. The defects identified in our study were not as severe as those identified in the Finnish studies of Aine et al.⁶ For comparison, in the study conducted by Aine, defects were: 38% of celiac adults with grade I and 43% with grade II (Fig. 1). Children with celiac disease in the study were 14% grade I, 53% grade II, 19% grade III, and 11% grade IV. The reason for this discrepancy is not apparent. It may be related to the severity of the clinical presentation of the celiac disease.

In our study patients with celiac disease, both adult and children had a significantly increased rate of aphthous ulcers. In addition, there was a significant association between enamel defects and aphthous ulcers. The literature contains conflicting results in respect to the association of aphthous stomatitis with the majority of studies showing an association,^{14,24-27} with some showing no association.^{18,28} However aphthae usually improve on the gluten-free diet.^{24,28}

TABLE 4. Significant Predictors for Enamel Defects

	OR (95% CI)
Age (≥ 18 y vs. < 18 y)	1.2 (1.1-1.3)
Celiac disease versus controls	2.4 (1.2-4.8)
Mixed dentition versus permanent dentition	5.2 (2.3-11.6)

CI indicates confidence interval; OR, odds ratio.

This is the first study describing an association of enamel defects, oral aphthae, and celiac disease in a population from the United States. We found patients below the age of 18 years in whom celiac disease and mixed dentition were significant predictors for enamel defects. Among those with celiac disease, especially children and those with mixed dentition, there was a significant association with enamel defects. Studies that screen children with dental enamel defects for celiac disease are needed because celiac disease is common and may go undetected into adulthood. As the oral cavity is very easy to examine, oral lesions can provide a valuable clinical clue for early diagnosis of celiac disease, which may lead to a reduction in the complications of the disease. Dentists should be aware of the relationship between celiac disease and disorders in the mouth, however all physicians have the opportunity to examine the teeth and mouth. This study suggests that this may be a worthwhile venture. In addition, celiac disease should be added to the differential diagnosis of dental enamel defects and oral aphthae.

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