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ORIGINAL RESEARCH

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Diet compliance, serology and dental caries in children with celiac disease

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Abstract

Background: Celiac disease (CD) is an immune-mediated enteropathy. The first recognizable symptom in children may also be dental manifestation rather than the typical gastrointestinal symptoms. **Methods**: The study included 82 children with CD at the age of 6–16 years. Decay-missing-filled in teeth (dmft/DMFT) indexes of the patients were recorded. The serology level, calcium, Phosphorus and vitamin D status of the patients at the time of diagnosis were obtained. Data were analyzed using descriptive statistics and bivariate and multivariate analysis. **Results**: The mean age for CD participants was 8.1 $\pm$ 3.2 years at the time of diagnosis. Decay and dmft/DMFT values of patients who did not comply with the diet were statistically higher than those who complied (7.36 $\pm$ 3.21 *vs.* 4.89 $\pm$ 2.34, $p < 0.001$ and 8.06 $\pm$ 2.83 *vs.* 5.78 $\pm$ 2.39, $p < 0.001$). dmft/DMFT values were statistically higher in patients with low calcium and Phosphorus levels ($p = 0.005$ and $p < 0.001$). Decay was higher in patients with low vitamin D levels compared to patients with high levels ($p = 0.046$). The dmft/DMFT value with a tissue transglutaminase antibody (tTGA) level of >200 U/mL (>10 $\times$ Upper Limits of Normal (ULN)) is statistically higher than the patients with a tTGA value of 100–139 U/mL (5–7 $\times$ ULN) ($p = 0.003$). **Conclusions**: Dental findings are more common in patients with CD who have low serum calcium, Phosphorus and vitamin D. Dentists and pediatricians should be aware of higher risks of dental caries among patients with CD with higher tTGA levels and in pediatric patients with CD who have diet incompatibility.

Keywords

Celiac disease; Serology; DMFT; Caries

1. Introduction

Celiac disease (CD) is an immune-mediated inflammatory disease of the small intestine triggered by gluten consumption in genetically susceptible individuals [1, 2]. The "gold standard" CD diagnosis is small bowel biopsy. Diagnosis still relies on endomysial and tissue transglutaminase antibodies. Those with confirmed CD are advised to eat gluten-free their entire lives. Approximately 1% of the general population suffers from CD, and 1.58% of school-aged children do [3]. CD has a wide clinical spectrum. It usually presents as typical CD with symptoms of intestinal malabsorption early in life such as chronic diarrhea, weight loss, growth retardation or atypical CD with findings such as iron deficiency anemia, short stature, cryptogenic hepatitis, osteoporosis, osteopenia and ataxia, as well as silent form of CD with mild and nonspecific gastrointestinal symptoms [4]. Up to our knowledge CD has gastrointestinal manifestations, such as diarrhea, abdominal distention and weight loss, but increasingly extraintestinal manifestations (EIM) are being reported as well [5]. EIM's exact prevalence has not yet been demonstrated [6]. Dental manifestations such as dental enamel defects (DED) and delayed dental eruption are well-known EIMs of CD [7].

Other orodental manifestations include dental caries, atrophic glossitis and recurrent aphthous stomatitis [8]. DEDs previously been suggested to be associated with hypocalcemia or a specific genetic condition that elicits a specific immune response to gluten [7]. Hypocalcemia, malnutrition, vitamin D and vitamin A deficiencies have been demonstrated in enamel hypoplasia [9], but a similar comparison with the dmft/DMFT index (D = decay-caries, M = missing, F = filled-filling) has not been conducted. A direct manifestation of CD or an indirect result of malabsorption remains unclear [9]. This retrospective observational study aimed to investigate the association between dmft/DMFT and dietary compliance, serum Calcium, Phosphorus and vitamin D levels and serological levels in CD patients.

2. Materials and methods

2.1 Study design

This study analyzed the patient characteristics and outcomes from Erciyes university faculty of medicine, department of

pediatric gastroenterology and Erciyes university faculty of dentistry department of pedodontics databases to screen for dental caries related factors in CD patients. From April 2022 to October 2022, medical data was obtained on the patients. Patients provided informed consent.

Data included the follow-up period of CD, the time between dental examination and CD, family history of CD and anti-tissue transglutaminase and serum vitamin levels over a 10-year period. Each participant's caries experience was assessed using the dmft/DMFT indices by a pediatric dentist. This study will examine dmft/DMFT, rather than the often studied DEDs.

2.2 dmft/DMFT index

The dmft/DMFT index is a quantitative expression of an individual's lifetime caries experience in the dentition [10]. It was developed to determine coronal caries prevalence. Dental hard tissues cannot heal themselves, therefore this index is universally accepted. When a tooth is decayed, it is either pulled or filled [10]. dmft/DMFT were measured by clinical examination. The examination was based on the standardized international criteria proposed by World Health Organization (WHO) for oral health surveys using WHO probe, disposable mouth mirrors and gauze pads [11].

2.3 Definition of CD

The European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) recommends diagnostic criteria for CD [12]. It is stated in the guidelines that CD diagnosis depends on gluten-related CD symptoms, and CD-specific antibody levels (high serum tTGA Immunoglobulin A (IgA) levels $\geq 10 \times$ ULN) in cases without a histopathological diagnosis. In addition, a second positive EMA-IgA test is recommended if a biopsy has not been performed [12].

This study was ethically approved by the local ethics committee (2022/554) and complied with the Declaration of Helsinki [13].

2.4 Selection participants

Hospital records were consulted for data collection. This study included celiac patients aged 6–16 years previously examined by a pediatric dentist with at least five years' experience in clinic. 92 cases were selected and recorded from 120 examined in both departments. 82 patients' records, excluding 10 with missing data, were analyzed.

2.5 Statistical analysis

Power analysis was performed with G*Power 3.1.9.4 (University of Düsseldorf, Düsseldorf, NRW, Germany). An effect size of 0.50, a power of 0.80 and an alpha of 0.05 require a minimum of 42 observations. Data analysis was performed using SPSS 22.0 (IBM, Armonk, NY, USA) software. Descriptive statistics were given as number of units (n), percent (%), mean $\pm$ standard deviation, median, minimum, maximum and interquartile range. The kurtosis and skewness measures were used to evaluate the normality of the numerical variables. Homogeneity of variances was evaluated with Levene's test. Pearson and Spearman correlation coefficients were applied to evaluate the relationship of D, M, F and DMFT with numerical variables according to the data distribution. Using the Kruskal-Wallis test, we compared the age of celiac diagnosis based on dentition types, the time between celiac diagnosis and the first dental examination, and the celiac follow-up period. As a multiple comparison test, the Dunn-Bonferroni test was used in Kruskal-Wallis analysis. For D, M, F and DMFT two-group comparisons, a *t*-test for independent samples and one-way analysis of variance from more than two-group comparisons were used. A one-way analysis of variance used the Duncan test as a multiple comparison test. $p < 0.05$ indicates statistically significant differences.

3. Results

The descriptive statistics of patients are presented in Table 1.

There was no statistically significant relationship between the time between the diagnose of CD and the first dental examination and D, M, F and DMFT ($p = 0.286$, $p = 0.739$, $p = 0.734$ and $p = 0.308$, respectively).

There was no statistically significant relationship between CD follow-up period and D, M, F and dmft/ DMFT ($p = 0.191$, $p = 0.161$, $p = 0.446$ and $p = 0.239$, respectively). D, M, F and DMFT values were not statistically different according to the family history of CD ($p = 0.891$, $p = 0.471$, $p = 0.600$ and $p = 0.816$, respectively).

According to Table 2, there was no statistically significant relationship between weight Standard Deviation Score (SDS) and height SDS and D, M, F and DMFT.

According to Table 3, the decay and dmft/DMFT values of patients who did not comply with the diet were statistically higher than those who complied with the diet.

According to Table 4, dmft/DMFT values of patients with a Calcium (Ca) of $\leq$9 are statistically higher than patients with a Ca of >9 and a Phosphorus (P) in the range of 2–4.5 are statistically higher than those with a P of >4.5. Decay values of patients with a vitamin D of $\leq$10 are statistically higher than patients with a vitamin D of >20. The DMFT value of the patients with a tTGA >200 is statistically higher than the patients with a tTGA of 100–139.

4. Discussion

This study aimed to elucidate the role of serum biochemical levels, serological test levels and dietary compliance in the pathogenesis of CD dental manifestations. To the best of our knowledge, this is the first study to examine the relationship between dmft/DMFT and serum serological levels, calcium, Phosphorus, vitamin D and dietary compliance CD patients. CD atypical manifestations include DED and aphthous ulcers [14]. Evidence suggests that CD may increase the risk of dental decay. The underlying mechanisms are unclear, but several possible factors have been suggested. Our CD patients had mean DMFTs similar to those reported in the literature [14, 15]. In this study, D, M, F and dmft/DMFT scores did not show a statistically significant relationship with age at CD diagnosis, time between CD diagnosis and first dental examination, or D, M, F and dmft/DMFT scores. This result suggests that a lagged dental examination in patients with CD will not delay

TABLE 1. Descriptive statistics (n = 82).

	Statistics
Age at the time of diagnosis (yr)	8.1 ± 3.2† (2–16)&
Sex, n (%)	
Female	52 (63.4)
Dentition type, n (%)	
Primary	7 (8.5)
Permanent	18 (22.0)
Mixed	57 (69.5)
Dental anomalies, n (%)	
No	74 (90.2)
Yes	8 (9.8)
Decay	6.22 ± 3.08†
Missing	0.07 ± 0.38†
Filled	0.72 ± 1.56†
dmft/DMFT score	7.01 ± 2.86†
Symptom of CD, n (%)	
Insufficient weight gain	19 (23.2)
Abdominal swelling and diarrhea	29 (35.4)
Short stature	11 (13.4)
Anemia	6 (7.3)
Family screening for CD	8 (9.8)
Screening for autoimmune disease	9 (11.0)
Time Between CD Diagnosis and Dental Examination (mon)	7.5 (7.0)‡
Follow-up Period of CD (yr)	3.7 (4.0)‡
Weight SDS	−0.548 ± 1.231†
Height SDS	−0.338 ± 1.429†
Hb	12.68 ± 1.65†
WBC	7.47 ± 2.76†
Platelet	338.6 ± 114.6†
Vitamin B12	331.9 ± 171.8†
Ferritin	12.60 ± 9.43†
Folate	11.33 ± 7.37†
Calcium	9.52 ± 0.77†
Phosphorus	4.50 ± 0.74†
Vitamin D	20.48 ± 10.38†
Diet compliance, n (%)	
Yes	38 (46.3)
No	44 (53.7)
Family History of CD, n (%)	
Yes	12 (14.6)
No	70 (85.4)
Other Diseases, n (%)	
No	65 (79.3)
Endocrine disorders (Type 1 DM, Hypothyroidism, GH deficiency or precocious puberty)	14 (17.1)
JIA	1 (1.2)
Down Syndrome	2 (2.4)

†: *mean ± standard deviation*, &: *minimum-maximum*, ‡: *median (interquartile range).*
dmft/DMFT: Decayed, Missed, Filled Teeth; CD: Celiac Disease; SDS: Standard Deviation Score; Hb: Hemoglobin; WBC: White Blood Cells; DM: Diabetes Mellitus; GH: Growth Hormone; JIA: Juvenile Idiopathic Arthritis; mon: month; yr: year.

TABLE 2. Relationship between weight SDS and height SDS with D, M, F and DMFT.

	Weight SDS		Height SDS	
	rho	*p*	*rho*	*p*
Decay	−0.085	0.448	−0.123	0.271
Missing	−0.030	0.788	−0.038	0.732
Filled	0.094	0.401	0.068	0.546
dmft/DMFT	−0.053	0.654	−0.103	0.355

rho: Spearman correlation coefficient. SDS: Standard Deviation Score; dmft/DMFT: Decayed, Missed, Filled Teeth.

TABLE 3. Comparisons of D, M, F and DMFT by diet compliance.

	Diet compliance		Test statistics	
	Yes	No	*t*	*p*
Decay	4.89 ± 2.34	7.36 ± 3.21	3.294	<0.001
Missing	0.05 ± 0.32	0.09 ± 0.42	0.455	0.650
Filled	0.84 ± 1.48	0.61 ± 1.63	0.660	0.511
dmft/DMFT	5.78 ± 2.39	8.06 ± 2.83	3.899	<0.001

Data are given as mean ± standard deviation, t: independent samples t test.
dmft/DMFT: Decayed, Missed, Filled Teeth.

the diagnosis of dental caries.

There is some controversy surrounding dental caries. As compared to healthy individuals, individuals with CD have a low prevalence rate of dental caries [16]. The results could be explained by the study population's strict gluten-free diet. Some CD patients may have successfully abstained from gluten, a protein found in many cariogenic foods like oatmeal, flours and breads. This restriction may contribute to lower dental caries prevalence rates. However, caries prevalence is higher in CD patients for various reasons, including hypoplastic enamel, low salivary flow rate and changes in salivary composition [8]. Active CD individuals have lower salivary flow rates, despite adhering to a gluten-free diet, which may lead to oral cavity dryness, increasing the risk of oro-dental infections, including dental caries. There is a similar relationship between salivary flow rate and caries was also demonstrated in another chronic autoinflammatory disease, Multiple Sclerosis [17]. Furthermore, some authors have reported that CD patients on a gluten-free diet have smaller saliva volumes, a lower buffering capacity and a lower salivary calcium/Phosphorus ratio, which may contribute to an increased dental caries prevalence [18].

The number of caries patients was higher in the CD group than healthy ones [19]. In contrast, a study reported dental caries rates of 30.6% and 63.4%, respectively, among treatment-naive and gluten-free diet-treated patients [7]. Compared with long-term gluten-free diet patients, recently diagnosed CD patients had similar plaque presence and decay [15]. Our study showed that dental caries were more common in non-compliant CD groups. Confirmation of these findings requires further research. With a strict gluten-free diet, improvement in serological tests and regression in disease-related signs and symptoms can be observed within one year. When the diet is not strictly adhered to, malabsorption of nutrients, including calcium and vitamin D, due to damage to the small intestine lining, may lead to weakened tooth enamel and an increased risk of dental decay. Furthermore, gluten exposure can directly affect oral health by increasing the risk of dental decay through the formation of dental plaque. Our cohort showed high DMFT scores among non-diet compliant participants. Researchers found that strict diet adherents maintained better oral hygiene [20]. Therefore, greater compliance with the diet may also reduce dental caries.

None of the patients in our study had hypocalcemia or hypercalcemia. We divided the patients into two groups with serum levels ≤9 mg/dL and above 9 mg/dL. A definite correlation could be found between the DMFT score and total serum calcium content in our patients.

dmft/DMFT was higher in patients with low calcium levels. School children with decayed teeth have lower salivary calcium levels than those without dental caries [20]. Our study confirmed the existing literature in finding a greater prevalence of decay in the group with calcium levels ≤9 mg/dL compared to the group with calcium levels >9 mg/dL, although this difference did not reach statistically significance. Calcium and Phosphorus malabsorption may contribute to dental caries in gluten enteropathy. Both decay and DMFT were associated with lower Phosphorus levels in our study. The literature, however, suggests salivary phosphorus levels in healthy children and CD patient groups do not differ [19]. However, there was no literature relating calcium and Phosphorus levels to DMFT in CD. Serum 25 hydroxy vitamin D (25(OH)D) levels are used to assess Vitamin D presence. A concentration of less than 75 nmol/L (or 30 ng/mL) is indicative of Vitamin D deficiency, while concentrations below 25 nmol/L (10 ng/mL) represent severe Vitamin D deficiency [21]. A significant portion of the patients in our study exhibited Vitamin D deficiency, with some patients having serum Vitamin D levels below the optimal level [22].

We found that patients with severe vitamin D deficiency

TABLE 4. Comparison of D, M, F and DMFT values by Ca, P, Hb, vitamin B12, vitamin D, ferritin, folate and tTGA.

	Decay	Missing	Filled	dmft/DMFT
Ca (mg/dL)				
≤9	7.06 ± 3.24	0.06 ± 0.36	1.03 ± 2.15	8.16 ± 2.67
>9	5.73 ± 2.91	0.07 ± 0.39	0.53 ± 1.05	6.34 ± 2.77
t; *p*	1.92; 0.058	0.118; 0.907	1.178; 0.246	2.900; 0.005
P (mg/dL)				
2–4.5	7.46 ± 2.82	0.10 ± 0.44	0.64 ± 1.42	8.21 ± 2.67
>4.5	5.09 ± 2.89	0.05 ± 0.31	0.79 ± 1.68	5.93 ± 2.60
t; *p*	3.742; <0.001	0.669; 0.506	0.432; 0.667	3.898; <0.001
Hb (g/dL)				
≤12	6.30 ± 3.38	0.00 ± 0.00	0.60 ± 1.16	6.90 ± 3.03
>12	6.17 ± 2.92	0.12 ± 0.47	0.78 ± 1.75	7.07 ± 2.78
t; *p*	0.178; 0.859	1.767; 0.083	0.525; 0.601	0.268; 0.789
Vitamin B12 (pg/mL)				
≤300	6.45 ± 3.21	0.09 ± 0.43	0.78 ± 1.66	7.33 ± 2.71
>300	5.97 ± 2.95	0.05 ± 0.31	0.65 ± 1.45	6.67 ± 3.01
t; *p*	0.699; 0.487	0.540; 0.591	0.392; 0.696	1.042; 0.300
Vitamin D (ng/mL)				
≤10	7.28 ± 2.65^{a}	0.11 ± 0.47	0.27 ± 0.82	7.67 ± 2.61
11–20	6.83 ± 2.29^{ab}	0.18 ± 0.56	0.66 ± 1.12	7.67 ± 2.12
>20	5.37 ± 3.47^{b}	0.00 ± 0.00	0.95 ± 1.96	6.32 ± 3.22
F; *p*	3.201; 0.046	1.599; 0.209	1.181; 0.312	2.327; 0.104
Ferritin (mg/L)				
≤10	6.58 ± 3.11	0.05 ± 0.31	0.79 ± 1.68	7.41 ± 2.53
>10	5.82 ± 3.04	0.103 ± 0.45	0.64 ± 1.42	6.56 ± 3.15
t; *p*	1.118; 0.267	0.669; 0.506	0.432; 0.667	1.358; 0.178
Folate (ng/mL)				
≤5	7.13 ± 2.50	0.27 ± 0.70	0.53 ± 0.99	7.93 ± 2.60
5–15	6.12 ± 3.32	0.04 ± 0.28	0.77 ± 1.73	6.92 ± 3.09
>15	5.67 ± 2.69	0.00 ± 0.00	0.73 ± 1.43	6.40 ± 2.09
F; *p*	0.928; 0.400	2.563; 0.083	0.131; 0.877	1.150; 0.322
tTGA (U/mL)				
100–139	4.50 ± 3.32	0.0 ± 0.0	0.0 ± 0.0	4.50 ± 3.31^{a}
140–200	5.21 ± 2.97	0.0 ± 0.0	0.58 ± 1.05	5.79 ± 2.76^{ab}
>200	6.79 ± 3.01	0.11 ± 0.46	0.83 ± 1.77	7.74 ± 2.62^{b}
F; *p*	2.999; 0.056	0.793; 0.456	0.657; 0.521	6.177; 0.003
Other diseases				
No	5.74 ± 2.84^{a}	0.09 ± 0.42	0.68 ± 1.33	6.51 ± 2.76^{a}
Type 1 DM or down syndrome	7.11 ± 3.51^{ab}	0.0 ± 0.0	1.44 ± 3.00	8.55 ± 1.87^{ab}
Other endocrine disorders	9.28 ± 3.19^{b}	0.0 ± 0.0	0.28 ± 0.76	9.57 ± 3.15^{b}
F; *p*	5.054; 0.009	0.373; 0.690	1.265; 0.288	5.654; 0.005

Data are given as mean ± standard deviation, t: independent samples t test, F: One-way analysis of variance, ^{a} and ^{b} superscripts indicate differences between categories at each column. There was no statistically differences between categories with the same superscripts.

dmft/DMFT: Decayed, Missed, Filled Teeth; Ca: Calcium; P: Phosphorus; Hb: Hemoglobin; tTGA: tissue transglutaminase; DM: Diabetes Mellitus.

had statistically higher than patients with vitamin D deficiency or a suboptimal vitamin D status. dmft/DMFT and vitamin D status have been associated with conflicting data in the literature. Several studies have found no significant correlation between vitamin D deficiency and caries in children [23, 24], while others found serum vitamin D levels below 20 or 30 ng/mL were associated with dmft/ DMFT scores [25, 26]. In general, the aforementioned investigations incorporated a broad range of adjustments for covariates, but differed in terms of the covariate types examined, the definition of caries experience, the methodology employed for caries diagnosis, and the classification of vitamin D status. Also, meta-analyses have shown that low serum vitamin D levels are associated with dental caries, and that dental caries incidences decreases with increasing serum vitamin D levels [27, 28]. In school children, certain studies have found correlations between vitamin D status and caries experience, whereas others have not. However, more comprehensive studies or meta-analyses would provide more information.

Detection of CD-specific antibodies (tTGA) in the serum becomes important for the initial screening of patients with suspected CD [29]. Histopathological staging and serum serological test levels show a parallel correlation in CD diagnosis [30]. Positive biopsy results are more likely to occur when the titer is higher [30]. An analysis of 120 children with dental caries found no correlation between CD serology and dental caries [31]. A notable association was found between DMFT variables and CD serology. A significant increase in DMFT scores was observed in those with tTGA levels exceeding 200 U/mL.

Additionally, the severity of inflammation is positively correlated with an increase in dmft/DMFT scores. The dmft/DMFT value of patients with tTGA IgA levels $\geq 10\times$ ULN is statistically higher than patients with tTGA IgA levels 5–7 $\times$ ULN. We are unaware of any other scientific publications that investigate the relationship between CD serologic levels, dental manifestations and DMFT. This study is the first to investigate this potential correlation. In CD, the impaired absorption of vitamins and minerals from the intestines is well-documented. In our study, possible mechanisms explaining increased dental caries and higher DMFT scores are illustrated (Fig. 1): (I) Malabsorption due to dietary non-adherence in CD leads to reduced calcium and Phosphorus absorption from the intestines. (II) Vitamin D plays a critical role in transporting calcium and Phosphorus from the intestines into the bloodstream and subsequently to the teeth; malabsorption may lower Vitamin D levels. (III) Increased gluten exposure may contribute to a higher dental plaque accumulation. (IV) Poor oral hygiene may also result from diet non-compliance. (V) Systemic inflammation could further increase DMFT scores and dental caries incidence.

5. Limitations

This study had certain limitations. This cross-sectional study would have been strengthened by a larger sample size. A lack of previous studies on dental and biochemical parameters also prevented us from obtaining reference ranges.

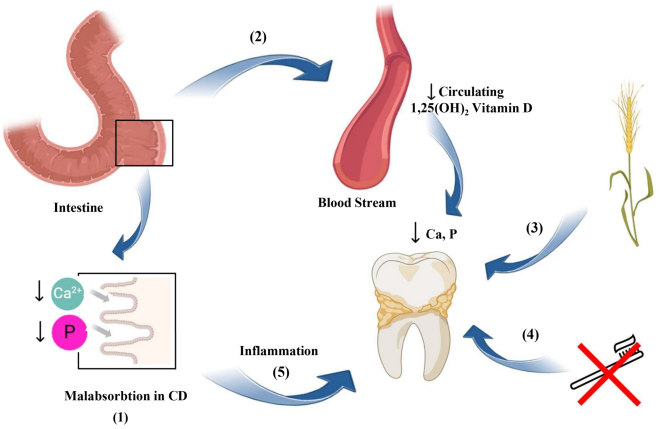

FIGURE 1. Possible mechanisms explaining increased dental caries and higher. OH: hydroxy; Ca: Calcium; P: Phosphorus; CD: Celiac Disease.

6. Conclusions

Children with CD have higher dental caries chances. Therefore, their oral health should be monitored attentively. Pediatric gastroenterologists, pediatricians and pediatric dentists can help prevent the progression and long-term complications of dental disease that has developed or will develop CD by early identification. Therefore, children with dental problems, particularly caries, should be screened for CD regardless of whether they display symptoms of gastrointestinal illness, and children with CD should also be evaluated for dental problems.

AVAILABILITY OF DATA AND MATERIALS

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

AUTHOR CONTRIBUTIONS

BDS and KK—contributed to the conceptualization, supervision, writing, editing first drafted and critical review of the article. DeA and DuA—contributed to the literature search, writing and editing. All authors approved the final version of this article.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

The Clinical Research Committee of Erciyes University (No: 2022/554). Written consent was obtained from all the parents confirming that they would provide serology, diet and dental anamnesis knowledge of their children with celiac for the research, and they would allow it to be published.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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