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SYSTEMATIC REVIEW

Relationship Between Celiac Disease and Dental Caries in Children and Adolescents: A Systematic Review and Meta-Analysis

Sylvia Amélia Vasconcelos de Albuquerque[1], Kelly Maria Silva Moreira[1], Djairo Vinícius Alves de Araújo[2], Glória Maria de França[2], Diego Figueiredo Nóbrega[2], Marcelo de Almeida Costa[3], Natanael Barbosa dos Santos[2], José Carlos Pettorossi Imparato[1]

[1]Department of Child Dental Health, Faculty of Dentistry, São Leopoldo Mandic College, Campinas, SP, Brazil.
[2]Professional Master's Degree in Health Research, CESMAC University Center, Maceió, AL, Brazil.
[3]Faculty of Dentistry, Federal University of Alagoas, Maceió, AL, Brazil.

Corresponding author: Glória Maria de França **E-mail:** gloriafracam@gmail.com

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ABSTRACT

Objective: To assess the relationship between celiac disease and the prevalence of dental caries in children and adolescents and also evaluate if dental enamel defects in celiac children predispose to dental caries. **Material and Methods:** Searches were performed in the following databases: PubMed, Scopus, Cochrane Library, Latin American and Caribbean Literature on Health Sciences, and OpenGrey. The risk of bias was assessed using the Newcastle-Ottawa Scale. DMFT/dmft and DMFS/dmfs data of observational studies that compared the prevalence of caries between children and adolescents with celiac disease and healthy individuals. Meta-analysis was performed using a random effects model. Heterogeneity between studies was estimated using Cochran's Q test, and inconsistency was measured using I^2 statistics. **Results:** Of the 121 studies retrieved, 17 were selected, and 12 were included in the meta-analysis. The prevalence of caries in the primary dentition (dmft) did not differ between celiac patients and controls [SMD = -0.35; 95% CI (-0.83; 0.13); p = 0,15; I^2 = 89%]. There was also no difference in the prevalence of caries in permanent teeth (DMFT) between groups [SMD = -0.44; 95% CI (-1.02; 0.14); p = 0.14; I^2 = 95%]. **Conclusion:** Celiac disease is not a determinant factor in the development of dental caries in children and adolescents compared to the control group.

Keywords: Celiac Disease; Dental Caries; Child; Diet, Gluten-Free.

Introduction

Celiac disease is an autoimmune enteropathy that occurs in genetically susceptible individuals and is triggered by the ingestion of foods that contain gluten. It mainly affects the small intestine [1,2]. The disease results from an adaptive immune reaction that depends on the deamidation of gliadin molecules by tissue transglutaminase, which is the primary autoantigen of celiac disease. Deamidation increases the immunogenicity of gliadin, facilitating binding to HLA-DQ2 or HLA-DQ8 molecules on antigen-presenting cells. Antibodies against tissue transglutaminase, gliadin, and actin are produced and may contribute to extra-intestinal manifestations of celiac disease [1].

The estimated global prevalence of celiac disease is 1.4% based on positive test results for anti-tissue transglutaminase or anti-endomysial IgA antibodies and 0.7% in biopsy-confirmed cases. The disease is more prevalent among women (0.6%) than men (0.4%), and children (0.9%) are more affected than adults (0.5%) [3].

Individuals diagnosed with celiac disease exhibit a wide variety of signs and symptoms of the disease. Abdominal discomfort, including abdominal pain, bloating, and distention, were the most common symptoms reported by celiac disease patients in the study [4]. However, other manifestations such as chronic diarrhea, weight loss, iron deficiency with or without anemia, short stature, chronic fatigue, reduced bone mineral density, dermatitis herpetiformis, and gluten ataxia may also be observed, in addition to the asymptomatic form of the disease [5].

The most common oral manifestations of celiac disease reported in the literature are dental enamel defects, recurrent aphthous ulcers, dry mouth (xerostomia), angular cheilitis, and delayed tooth eruption [6-9]. However, comparing the prevalence of dental caries between patients with celiac disease and healthy individuals shows wide variation in the study results. Some studies indicate celiac disease as a factor predisposing to the development of dental caries [10,11], while others reported it to be a protective variable [12-14]. However, some studies did not find statistically significant differences between groups [7,15-17].

This study aimed to perform a systematic review and meta-analysis of observational studies regarding possible associations between celiac disease and dental caries in celiac patients and healthy controls. Following the PECO framework, the null hypothesis was that children and adolescents (patients) diagnosed with celiac disease (exposure) would have the exact prevalence of caries (outcome) as children without the disease (comparison).

Material and Methods

The research question of this systematic review was formulated according to the PECO framework [18]: "Does the prevalence of caries of patients with celiac disease differ from that of healthy individuals?" where P is children and adolescents diagnosed with celiac disease, E is the diagnosis of celiac disease, C are children and adolescent without a diagnosis of celiac disease, and O is the prevalence of caries measured by DMFT, DMFS, dmft, dmfs, and ICDAS.

This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [19]. It was registered in the International Prospective Register of Systematic Reviews (PROSPERO) under registration number CRD42021243084 (supplementary material). Searches were performed in PubMed, Scopus, Cochrane Library, and OpenGrey. The systematic review was carried out in a Latin American country and used the LILACS (Latin American and Caribbean Literature on Health Sciences) database that accepts search terms in English, Portuguese, and Spanish; therefore, this database was included, using the following search terms in titles and abstracts (also in combination with MESH terms): "Child" OR

"Preschool" OR "Adolescent" AND "Celiac Disease" OR "Wheat Hypersensitivity" AND "Dental Caries" OR "DMF Index." In addition, entry terms were added using the Boolean operators "AND" and "OR" to combine search terms, Supplementary Table 1.

The search did not restrict language as long as it did not jeopardize the researchers' understanding after its translation to avoid data collection bias. No publication year restriction was applied, and the search was limited to human studies. The reference list of articles was hand-searched to optimize and broaden the search strategy.

The following inclusion criteria were used for the selection of articles: (i) observational studies (cohort, cross-sectional, case-control) and clinical trials; (ii) children and adolescents with celiac disease (0 to 19 years); and (iii) diagnosis of caries. The exclusion criteria were: (i) literature reviews and case reports, (ii) study design not reported, and (iii) participants outside the age range (adults).

Two authors independently selected the articles. First, duplicate articles were removed. The resulting titles and abstracts were then reassessed to remove unrelated articles according to the established inclusion and exclusion criteria. These steps were conducted using the Mendeley Desktop software. After preliminary screening, the full text of the articles was downloaded, and two authors evaluated their eligibility. The Kappa test was applied to determine the inter-examiner agreement and to define the articles included in the research. During this step, disagreements between the two reviewers were resolved by a third author. Finally, irrelevant articles were removed during the screening step according to the established criteria, and the remaining studies were selected for qualitative synthesis.

The included studies were reviewed, and the following data were extracted: 1) name of first author; 2) year of publication; 3) sample size; 4) age of participants; 5) geographic location of study; 6) study design; 7) DMFT and dmft index (permanent and primary dentition); 8) diagnosis of celiac disease.

The risk of bias in the studies was assessed using the Newcastle-Ottawa Scale NOS [20], which was adapted to cross-sectional studies [21]. The studies were assessed using six items, with a maximum score of 9 stars. This analysis aimed to carefully investigate sample representativeness, group comparability, rater blinding, and appropriate statistical testing. For each item, two reviewers assigned scores corresponding to present or absent. Agreement between the two evaluators was evaluated using Cohen's kappa index. The following results were obtained: selection criteria by representativeness of the sample (k = 0.638, moderate), sample size (k = 1.000, almost perfect), ascertainment of exposure (k = 0.850, excellent), comparability based on design and analysis (k = 1.000, nearly perfect), assessment of outcome (k = 1.000, almost perfect), and statistical test (k = 1.000, almost perfect). A kappa value higher than 0.600 indicates adequate agreement between two evaluators. The analysis was performed using the IBM SPSS Statistics freeware (version 22.0; IBM Corp., Armonk, NY, USA).

For statistical analysis, the null hypothesis was that celiac disease does not interfere with the prevalence of dental caries. The alternative hypothesis was that celiac disease interferes with the prevalence of dental caries. The summary measure (dependent variable) was the prevalence of dental caries in the permanent and primary dentition, measured at the level of the tooth (DMFT/dmft). A diagnosis of celiac disease was the independent variable.

To estimate the effect of celiac disease on the prevalence of dental caries in primary and permanent dentition, the standardized mean difference (SMD) and 95% confidence interval (CI) were calculated. Heterogeneity between studies was estimated using Cochran's Q test [22]. Inconsistency was measured using I^2 statistics [23]. Due to the high heterogeneity observed, a random effects model was used in both analyses

[22]. Sources of heterogeneity were explored based on publication bias (use of a funnel plot) when the variable had been evaluated in more than ten studies. All analyses were performed using the Review Manager® software (RevMan, 2014).

Results

Using the search strategy proposed for this systematic review, 121 articles were retrieved from the databases; 69 remained after duplicate removal. After screening the titles and abstracts, 43 articles were considered potentially eligible, and two evaluators read the full text - Cohen's Kappa K= 0.50 (moderate agreement) for selected articles. Four of the 17 articles included had conflicts and were resolved by a third reviewer. After analysis, 17 articles met all inclusion criteria and were selected for this systematic review. Twelve studies were included in the meta-analysis. Figure 1 illustrates the flow diagram of the article selection process. The articles are listed in the Supplementary Material (Table 2). Excluded articles and justification for exclusion are in Supplementary Material (Table 3).

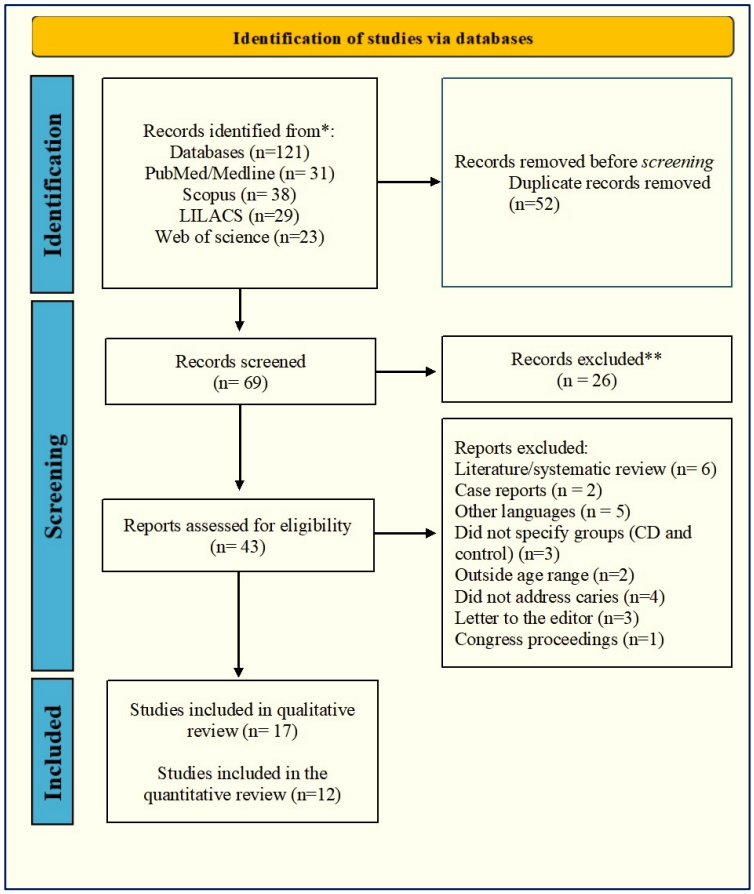

Figure 1. Flow diagram of the article selection process according to the PRISMA statement [19].

All articles were published in English. The studies were conducted in Turkey (n = 6), Brazil (n = 2), Italy (n = 2), Saudi Arabia (n = 1), Argentina (n = 1), Greece (n = 1), Spain (n = 1), England (n = 1), Iran (n = 1), and Israel (n = 1). The year of publication ranged from 2005 to 2021. Most articles (n = 16) were cross-sectional studies; one was longitudinal [17]. The sample size varied widely among studies; the largest sample was 208 participants in the study by Alsadat et al. [24], and the smallest sample was 38 children/adolescents by Farmakis et al. [25] (Supplementary Table 2).

Most participants were boys, and their ages ranged from 2 to 19 years. The primary, mixed, and permanent dentitions were analyzed. Biopsy was the primary method for confirming the histopathological diagnosis of celiac disease in 12 studies; of these, five studies [7,12,14,17,26] performed quantitative serological tests of anti-transglutaminase IgA to rule out possible asymptomatic celiac disease in the group of healthy patients, reducing the risk of bias. The other studies used the self-reported absence of gastrointestinal symptoms obtained from the medical records as an inclusion criterion for healthy individuals in the control group (Supplementary Table 2).

Except for the study that did not specify which index was used to assess dental caries [27], all other studies used the caries index recommended by the World Health Organization [28]: DMFT/dmft and its variation DMFS/dmfs, which corresponds to the total number of decayed, missed and filled teeth or surfaces. Table 1 shows variation among the 16 studied in terms of the evaluated dentition and the presentation of the results. Five articles were not included in the meta-analysis [7,13,15,17,27] because the results were not reported adequately due to their heterogeneity.

Table 1. Synthesis of the main findings on caries in the primary and permanent dentition.

Authors	Caries in the Permanent Dentition			Caries in the Primary Dentition		
	Index	Control Mean±SD	Celiac Mean±SD	Index	Control Mean±SD	Celiac Mean±SD
Zoumpoulakis et al. [7]	DMFT DMFS	NR p=0.788		dmft dmfs	NR	
Cantekin et al. [10]	DMFT	1.83±1.78	3.75±2.62	dmft	4.56±2.87	3.25±3.25
Biçak et al. [12]	DMFT / DMFS	6.77±4.43 / 8.96±8.75	4.48±3.67 / 6.20±6.74	dmft / dmfs	2.33±2.83 / 4.08±5.59	2.88±1.99 / 5.76±5.19
Acar et al. [13]	DMFS	2.60±5.3	2.74±5.70	dmfs	2.60±5.3	2.74± .70
Ortega Páez et al. [14]				dmft / dmfs	0.70±1 / 0.73±1.57	0.17±0.64 / 0.23±0.97
Cruz et al. [15]		n=9 [untreated caries]	n=12 [untreated caries]			
Bramanti et al. [16]**	DMFT	2.41±1.63	2.52±3.22	dmft	1.86±1.98	1.07±1.63
Mina et al. [17]	DMFT	Baseline: 52% DMFT=0 18 months: 57% DMFT=0	Baseline: 76% DMFT=0 18 months: 87% DMFT=0	dmft	Baseline: 39% DMFT=0 18 months: 57% DMFT=0	Baseline: 35% DMFT=0 18 months: 87% DMFT=0
Alsadat et al. [24]	DMFT	1.90±2.18	2.81±3.21	dmft	6.56±4.20	5.01±4.0
Farmakis et al. [25]	DMFT / DMFS	0.71±0.52 / 2.14±1.83	0.13±0.12 / 0.13±0.12	dmft / dmfs	3.43±1.03 / 8.00±3.02	0.50±0.31 / 0.76±0.38
Shahraki et al. [26]	DMFT	0.6±1.2	0.7±1.5	dmft	2.4±2.6	5.1±4.6
Saraceno et al. [27]	NR	n=38 had caries (45%)	n=38 had caries (45%)			
Shteyer et al. [29]	Mean DMFT / dmft	DMFT / dmft (mean 3.4±3.7)	Recently diagnosed celiac: DMFT/dmft (mean 1.5±2.2) Celiac without gluten + 6 months: DMFT/dmft (mean 2.0±2.6)			
Bolgül et al. [30]	DMFT	6.9±1.7	2.4± 1.3			
Avşar and Kalayci [34]	DMFT	6.4±4.32*	6.1±4.28			
de Carvalho et al. [35]	DMFT	3.90±5.2	2.11±3.2			
Dane and Gürbüz [36]	DMFT	4.71±1.9	4.74±3.46	dmft	2.3±2.0	2.63±3

*Mean of the group without gluten restriction; **Potential celiac patients (mean DMFT: 1.57±1.87; mean dmft: 1.60±2.67); NR = Not Reported.

Table 2 shows the quality assessment of the studies using the Newcastle-Ottawa Scale. Only one study obtained the maximum score, i.e., nine stars [12]. Only two studies performed sample size calculations [12,24]. In four studies, clinical examination was performed by one examiner who was blinded to the patient's health condition [12,16,26,29]. Regarding the item comparability, age matching was established to score 1 star, and an additional star would be assigned to studies that used a serological test to rule out celiac disease in the control group. The Farmakis et al. [25] survey received the lowest score (3 stars), demonstrating low quality and a high risk of bias. These results are shown in Table 2.

Table 2. Qualitative analysis of cross-sectional studies (modified Newcastle-Ottawa).

Authors	Study Design	Selection			Comparability	Outcome		Total[#]
		Representativeness of the Sample	Sample Size	Ascertainment of Exposure	Based on Design and Analysis	Assessment of Outcome	Statistical Test	
Zoumpoulakis et al. [7]	Cross-sectional	★	-	★★	★★	-	★	6
Cantekin et al. [10]	Cross-sectional	★	-	★	★	-	★	4
Biçak et al. [12]	Cross-sectional	★	★	★★	★★	★★	★	9
Acar et al. [13]	Cross-sectional	★	-	★★	★	-	★	5
Ortega Páez et al. [14]	Cross-sectional	★	-	★★	★★	-	★	6
Cruz et al. [15]	Cross-sectional	★	-	★★	★	-	★	5
Bramanti et al. [16]	Cross-sectional	★	-	★★	★	★★	★	7
Mina et al. [17]	Longitudinal	★	-	★★	★	-	★	5
Alsadat et al. [24]	Cross-sectional	★	★	★★	★	-	★	6
Farmakis et al. [25]	Cross-sectional	-	-	★	★	-	★	3
Shahraki et al. [26]	Cross-sectional	★	-	★★	★	★★	★	7
Saraceno et al. [27]	Cross-sectional	★	-	★	★	-	★	4
Shteyer et al. [29]	Cross-sectional	★	-	★★		★★	★	6
Bolgül et al. [30]	Cross-sectional	★	-	★★	★	-	★	5
Avşar and Kalayci [34]	Cross-sectional	★	-	★★	★	-	★	5
de Carvalho et al. [35]	Cross-sectional	★	-	★	★	-	★	4
Dane and Gürbüz [36]	Cross-sectional	★	-	★★	★	-	★	5

[#]Maximum = 9 Stars; Selection: (1) (a) truly representative of the mean of the target population or (b) poorly representative of the mean of the target population (1 star), (c) selected group of users, (d) no description; (2) (a) justified and satisfactory (1 star), (b) not justified; (3) (a) biopsy diagnosis (2 stars), (b) no description of the diagnostic method (1 star); Comparability: (1) (a) study controlled for the most critical factor (age matching) (1 star), (b) study controlled for any additional factor (serological test for two groups) (2 stars); Outcome: (1) (a) independent blind assessment of dental caries or (b) record linkage (2 stars), (c) no description; (2) (a) the statistical test used to analyze the data is clearly described and appropriate, and the measurement of the association is present (1 star), (b) the statistical test is not appropriate, not described, or incomplete.

Twelve of the 17 studies evaluated in the qualitative analysis were included in the meta-analysis, totaling 1,164 participants (565 celiac patients and 579 controls). Studies that did not provide information on caries based on the DMFT and dmft index were excluded from the meta-analysis [7,15,17,27].

The prevalence of caries in primary teeth (dmft) was evaluated in nine studies. Meta-analysis showed no differences in the dmft index between celiac patients and healthy controls [SMD = -0.35; 95% CI (-0.83; 0.13); p = 0.15; I^2 = 89%] (Figure 2a). Twelve studies evaluated the prevalence of caries in permanent teeth (DMFT). Similarly, there were no differences in the DMFT index between the celiac and control groups [SMD = -0.44; 95% CI (-1.02; 0.14); p = 0.14; I^2 = 95%] (Figure 2b).

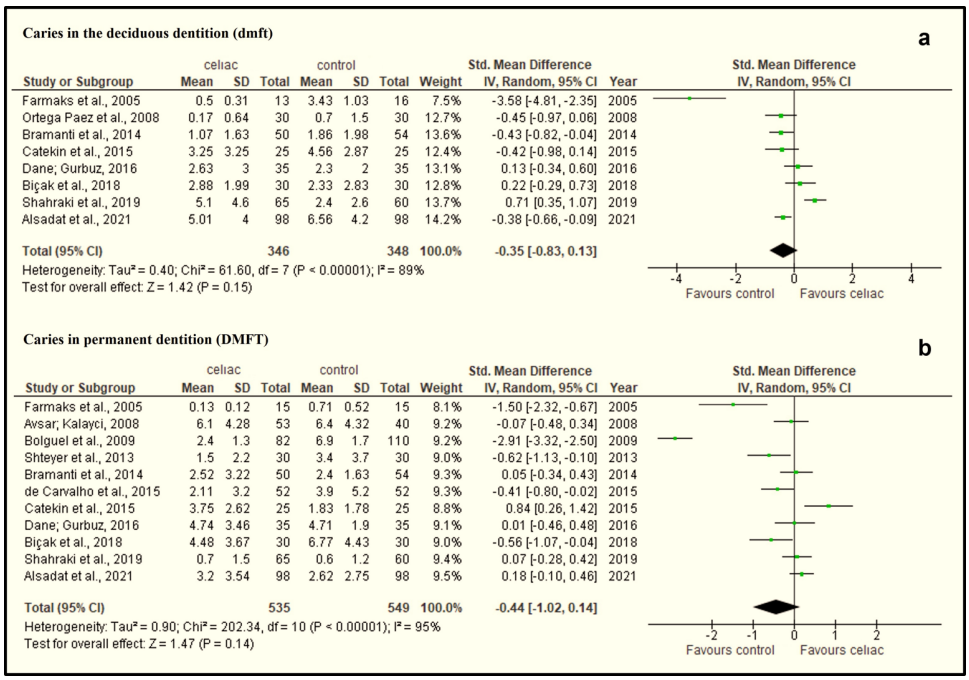

Figure 2. Prevalence of caries in the primary and permanent dentition.

Given the high heterogeneity (95%) and considering that more than ten studies were included in the DMFT meta-analysis, the publication bias risk was assessed. The funnel plot suggested the presence of publication bias (Figure 3).

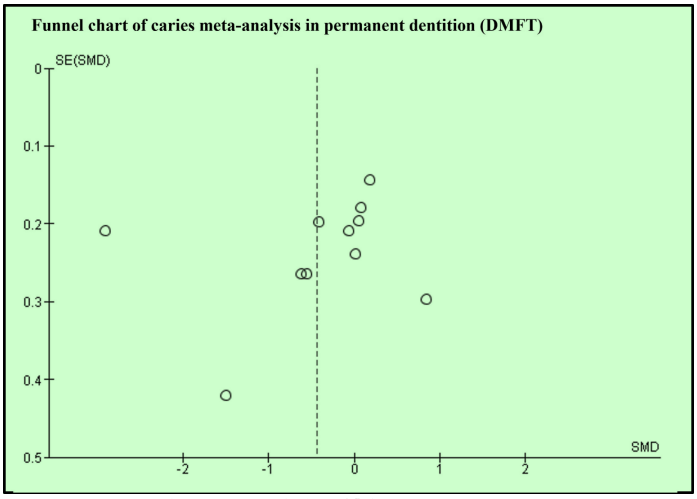

Figure 3. Risk of bias assessment.

Therefore, the study with the most significant effect magnitude [30] was removed from the meta-analysis, and the data were reanalyzed to explore changes in SMD and heterogeneity. The new analysis revealed a reduction in heterogeneity but no change in effect. Thus, the null hypothesis that there is no difference in the prevalence of caries in permanent teeth between celiac patients and healthy controls was maintained [SMD = -0.15; 95% CI (-0.42; 0.13); p = 0.30; I^2 = 75%] (Figure 4).

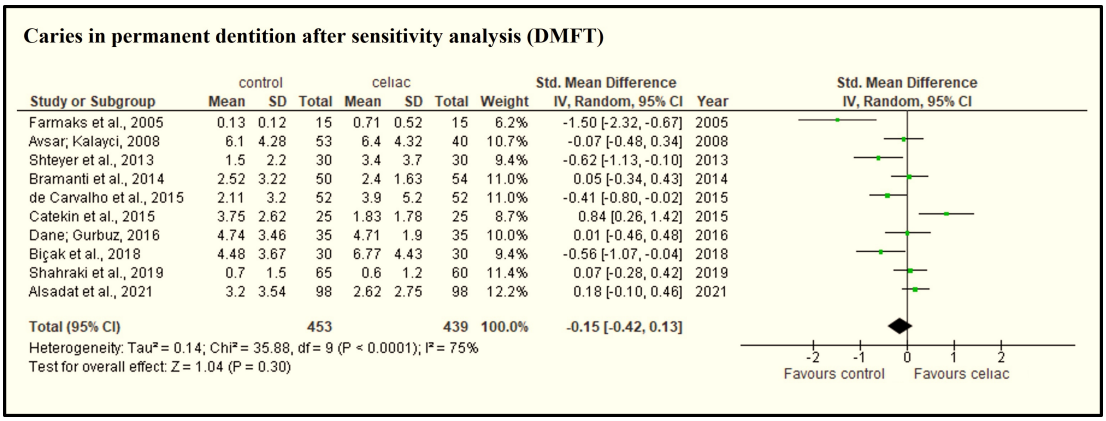

Figure 4. Analysis of sensitivity.

Discussion

Celiac disease is an autoimmune disease that affects the small intestine, triggered by consuming gluten-containing foods. The symptoms are variable and manifest themselves from the classic form of the disease with abdominal pain and diarrhea to extraintestinal manifestations on the skin or asymptomatic presentation [37].

The most common oral findings in celiac patients are dental enamel defects, which range from white spots to the loss of tooth structure [6-9]. These alterations in tooth structure and composition are caused by an increase in enamel porosity as a result of high carbonate concentrations, and they may represent a risk factor for the development and progression of dental caries since hypomineralized dental enamel is less resistant to acids during the demineralization process. In addition, the post-eruption loss of tooth structure, which usually occurs in these teeth, serves as a niche for accumulating dental biofilm [31].

Because of this observation about the alteration in the dental structure of celiac individuals, a deeper investigation is necessary on whether they have a greater predisposition to the development of dental caries since the findings in the literature are divergent.

Dental caries is a multifactorial disease, dependent on sugar consumption, the presence of dental biofilm, and a niche for its accumulation, as well as the length of time this biofilm remains in contact with the tooth surface [33]. Patients with celiac disease have a medical recommendation to control symptoms: a gluten-free diet. The gluten is present in highly cariogenic foods, such as cakes and cookies. So, in the face of this dietary restriction, the following question arises: Would a gluten-free diet and, consequently, low access to cariogenic foods be a protective factor against dental caries in celiac disease patients?

This systematic review included 1,706 participants; 844 were diagnosed with celiac disease and were residents of three continents (America, Asia, and Europe) in 10 different countries.

Although this review includes studies of patients with dental enamel defects who have dental caries, no significant differences were observed in the health-disease process compared to healthy individuals, corroborating literature findings that caries is a multifactorial disease that also depends on the patient's educational and socioeconomic level as well as on food quality [32], in addition to being a biofilm-mediated, diet-

modulated, multifactorial, non-transmissible and dynamic disease that results in the net loss of minerals from hard tissues [33].

Some of the selected studies in this review [12,25,30] found a lower DMFT/dmft index in patients with celiac disease. This finding might be explained by the gluten restriction for managing celiac disease, eliminating the frequent consumption of highly cariogenic foods commonly made with added sugar. To reduce this diet heterogeneity in sugar intake, two studies [12,16] excluded patients with celiac disease who had consumed a gluten-free diet for more than one year. In the study by Bramanti et al. [16], there was no statistical difference between the groups, and in the study by Biçak et al. [12], the group of people with celiac disease had a DMFT/S statistically lower than the control group.

The mechanical control of biofilm through brushing is an effective way to prevent and control caries. When Acar et al. [13] and Avşar and Kalayci [34] observed the frequency of toothbrushing in both groups and observed similarities. In the first study, there was no significant difference in the presence of dental caries between groups. At the same time, Avşar and Kalayci [34] found a significantly smaller number of caries-free individuals in the celiac disease group. However, in the study by Alsadat et al. [24], the number of children/adolescents who brushed their teeth was significantly higher in the group with celiac disease. This finding possibly contributed to a considerably lower caries experience in the group of celiac patients.

The European Society of Gastropediatrics [38] recommends that in children with suspected CD, the diagnosis can be made without the need for an intestinal biopsy through the serological test IgA and total IgA for transglutaminase 2 with a result ten times greater than the limit considered normal and subsequent testing for positive endomysial antibodies (EMA-IgA). To avoid false positive results, an intestinal biopsy is recommended for children with positive IgA antibodies but less than ten times the average value. Of the studies selected for qualitative analysis, four did not report which test was used to diagnose celiac patients [10,25,27,35]. The others used intestinal biopsy as one of the diagnostic tests.

The meta-analysis did not refute the null hypothesis, and the factor of celiac disease did not influence the development of dental caries. This result was observed for both primary and permanent dentition. The present meta-analysis revealed the absence of a significant difference in the prevalence of caries between children and adolescents with celiac disease and healthy controls. However, this finding must be interpreted with caution since, in some of the selected studies [10,13,16,25,26,29,34,35], the control group was recruited among children and adolescents who sought dental clinics either for restorative treatment or prevention/maintenance and may, therefore, have a large number of caries lesions. This fact would contribute to a high DMFT/dmft index that is not consistent with the reality of the general population and would alter the comparison between groups, which is a limitation of the present study.

In some studies, the DMFT grouped primary and permanent teeth in the mixed dentition according to the more significant number of teeth of the adolescent by World Health Organization criteria [15,27,30,34,35]. Another limitation of our study was the heterogeneity in sample size, participant age, ethnicity, and quality of the studies; hence, the results must be interpreted cautiously. Therefore, it is necessary to conduct new studies involving non-institutionalized groups of the local community as a control to reduce possible sample selection bias.

Conclusion

The present meta-analysis revealed no significant differences in the prevalence of dental caries in the primary or permanent dentition between children and adolescents with celiac disease and healthy individuals.

This finding suggests that caries is much more related to diet and oral hygiene habits as determinants of the health-disease process than to the susceptibility of celiac patients to enamel defects.

Authors' Contributions

SAVA	https://orcid.org/0000-0002-6449-1625	Conceptualization, Formal Analysis, Data Curation and Supervision.
KMSM	https://orcid.org/0000-0002-1137-3908	Software, Formal Analysis and Resources.
DVAA	https://orcid.org/0009-0004-0199-5406	Methodology, Validation Investigation and Project Administration.
GMF	https://orcid.org/0000-0002-0483-6601	Conceptualization, Methodology and Investigation.
DFN	https://orcid.org/0000-0003-2288-4102	Validation, Writing - Review and Editing, Visualization, and Project Administration.
MAC	https://orcid.org/0009-0008-1130-3564	Validation and Funding Acquisition.
NBS	https://orcid.org/0000-0003-1811-2927	Software, Investigation, Writing - Original Draft and Supervision.
JCPI	https://orcid.org/0000-0002-1990-2851	Validation, Writing - Review and Editing, Visualization and Supervision.

All authors declare that they contributed to a critical review of intellectual content and approval of the final version to be published.

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None.

Conflict of Interest

The authors declare no conflicts of interest.

Data Availability

The data used to support the findings of this study can be made available upon request to the corresponding author.

References

[1] Lebwohl B, Sanders DS, Green PH. Coeliac disease. Lancet 2018; 391(10115):70-81. https://doi.org/10.1016/S0140-6736(17)31796-8

[2] Husby S, Koletzko S, Korponay-Szabó IR, Mearin ML, Phillips A, Shamir R, et al. European Society for Pediatric Gastroenterology, Hepatology, and Nutrition guidelines for the diagnosis of coeliac disease. J Pediatr Gastroenterol Nutr 2012; 54(1):136-160. https://doi.org/10.1097/MPG.0b013e31821a23d0

[3] Singh P, Arora A, Strand TA, Leffler DA, Catassi C, Green PH, et al. Global prevalence of celiac disease: Systematic review and meta-analysis. Clin Gastroenterol Hepatol 2018; 16(6):823-836.e2. https://doi.org/10.1016/j.cgh.2017.06.037

[4] Niknam R, Salehi A, Molavi-Vardanjani H, Fattahi MR, Dehghani SM, Honar N, et al. Different clinical features of celiac disease in children, adolescents, and adults; a cross-sectional study. Middle East J Dig Dis 2021; 13(2):121-130. https://doi.org/10.34172/mejdd.2021.215

[5] Fassano A, Catassi C. Celiac disease. N Engl J Med 2012; 367(25):2419-2426. https://doi.org/10.1056/NEJMcp1113994

[6] Ahmed A, Singh A, Kajal S, Chauhan A, Rajput MS, Banyal V, et al. Dental enamel defects and oral cavity manifestations in Asian patients with celiac disease. Indian J Gastroenterol 2021; 40(4):402-409. https://doi.org/10.1007/s12664-021-01175-7

[7] Zoumpoulakis M, Fotoulaki M, Topitsoglou V, Lazidou P, Zouloumis L, Kotsanos N. Prevalence of dental enamel defects, aphthous-like ulcers and other oral manifestations in celiac children and adolescents: A comparative study. J Clin Pediatr Dent 2019; 43(4):274-280. https://doi.org/10.17796/1053-4625-43.4.9

[8] Souto-Souza D, Soares MEC, Rezende VS, Dantas PCL, Galvão EL, Falci SGM. Association between developmental defects of enamel and celiac disease: A meta-analysis. Arch Oral Biol 2018; 87:180–190. https://doi.org/10.1016/j.archoralbio.2017.12.025

[9] Pastore L, Carroccio A, Compilato D, Panzarella V, Serpico R, Lo Muzio L. Oral manifestations of celiac disease. J Clin Gastroenterol 2008; 42(3):224-232. https://doi.org/10.1097/MCG.0b013e318074dd98

[10] Cantekin K, Arslan D, Delikan E. Presence and distribution of dental enamel defects, recurrent aphthous lesions and dental caries in children with celiac disease. Pak J Med Sci 2015; 31(3):606-609. https://doi.org/10.12669/pjms.313.6960

[11] Costacurta M, Maturo P, Bartolino M, Docimo R. Oral manifestations of coeliac disease: A clinical-statistic study. Oral Implantol 2010; 3(1):12-19.

[12] Bıçak DA, Urgancı N, Akyüz S, Usta M, Kızılkan NU, Alev B, et al. Clinical evaluation of dental enamel defects and oral findings in coeliac children. Eur Oral Res 2018; 52(3):150-156. https://doi.org/10.26650/eor.2018.525

[13] Acar S, Yetkıner AA, Ersın N, Oncag O, Aydogdu S, Arıkan C. Oral findings and salivary parameters in children with celiac disease: A preliminary study. Med Princ Pract 2012; 21:129-133. https://doi.org/10.1159/000331794

[14] Ortega-Páez E, Lafuente PJ, García PB, Lozano JM, Calvo JCL. Prevalence of dental enamel defects in celiac patients with deciduous dentition: A pilot study. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2008; 106(1):74-78. https://doi.org/10.1016/j.tripleo.2008.01.022

[15] Cruz ITSA, Fraiz FC, Celli A, Amenabar JM, Assunção LRS. Dental and oral manifestations of celiac disease. Med Oral Patol Oral Cir Bucal 2018; 23(6):e639-645. https://doi.org/10.4317/medoral.22506

[16] Bramanti E, Cicciù M, Matacena G, Costa S, Magazzù G. Clinical evaluation of specific oral manifestations in pediatric patients with ascertained versus potential coeliac disease: A cross-sectional study. Gastroenterol Res Pract 2014; 2014:934159. https://doi.org/10.1155/2014/934159

[17] Mina S, Riga C, Azcurra AI, Brunotto M. Oral ecosystem alterations in celiac children: A follow-up study. Arch Oral Biol 2012; 57(2):154-160. https://doi.org/10.1016/j.archoralbio.2011.08.017

[18] Needleman IG. A guide to systematic reviews. J Clin Periodontol 2002; 29(Suppl 3):6-9; discussion 37-38. https://doi.org/10.1034/j.1600-051x.29.s3.15.x

[19] Page MJ, Moher D, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. PRISMA 2020 explanation and elaboration: Updated guidance and exemplars for reporting systematic reviews. BMJ 2021; 372:n160. https://doi.org/10.1136/bmj.n160

[20] Wells G, Wells G, Shea B, Shea B, O'Connell D, Peterson J, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. 2014.. Available from: https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp [Accessed on April 07, 2023].

[21] Herzog R, Álvarez-Pasquin MJ, Díaz C, Del Barrio JL, Estrada JM, Gil Á. Are healthcare workers' intentions to vaccinate related to their knowledge, beliefs and attitudes? A systematic review. BMC Public Health 2013; 13:154. https://doi.org/10.1186/1471-2458-13-154

[22] Dersimonian R, Laird N. Meta-analysis in clinical trials. Control Clin Trials 1986; 7(3):177-188. https://doi.org/10.1016/0197-2456(86)90046-2

[23] Higgins JPT, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011; 343:d5928. https://doi.org/10.1136/bmj.d5928

[24] Alsadat FA, Alamoudi NM, El-Housseiny AA, Felemban OM, Dardeer FM, Saadah OI. Oral and dental manifestations of celiac disease in children: A case-control study. BMC Oral Health 2021; 21(1):669. https://doi.org/10.1186/s12903-021-01976-4

[25] Farmakis E, Puntis JWL, Toumba KJ. Enamel defects in children with coeliac disease. Eur J Paediatr Dent 2005; 6(3):129-132.

[26] Shahraki T, Mehr SO, Hill ID, Shahraki M. A comparison of the prevalence of dental enamel defects and other oral findings in children with and without celiac disease. Iran J Pediatr 2019; 29(1):e64353. https://doi.org/10.5812/ijp.64353

[27] Saraceno R, Perugia C, Ventura A, Lore B, Chimenti S, Docimo R. Aphthous, coeliac disease and other dental disorders in childhood. G Ital Dermatol Venereol 2016; 151(3):239-243.

[28] World Health Organization. Oral health surveys: basic methods. 5th ed. Geneva: World Health Organization; 2013.

[29] Shteyer E, Berson T, Lachmanovitz O, Hidas A, Wilschanski M, Menachem M, et al. Oral health status and salivary properties in relation to gluten-free diet in children with celiac disease. J Pediatr Gastroenterol Nutr 2013; 57(1):49-52. https://doi.org/10.1097/MPG.0b013e31828b3705

[30] Bolgül BS, Arslanoğlu Z, Tumen EC, Yavuz I, Çelenk S, Atakul F. Significance of oral symptoms in early diagnosis and treatment of celiac disease. Turkiye Klinikleri J Med Sci 2009; 29(3):599-604.

[31] Elhennawy K, Manton DJ, Crombie F, Zaslansky P, Radlanski RJ, Jost-Brinkmann PG, et al. Structural, mechanical and chemical evaluation of molar-incisor hypomineralization-affected enamel: A systematic review. Arch Oral Biol 2017; 83:272-281. https://doi.org/10.1016/j.archoralbio.2017.08.008

[32] Bukmir RP, Paljević E, Pezelj-Ribarić S, Pršo IB. Association of the self-reported socioeconomic and health status with untreated dental caries and the oral hygiene level in adult patients. Dent Med Probl 2022; 59(4):539-545. https://doi.org/10.17219/dmp/138908

[33] Machiulskiene V, Campus G, Carvalho JC, Dige I, Ekstrand KR, Jablonski-Momeni A, et al. Terminology of dental caries and dental caries management: Consensus report of a workshop organized by ORCA and cariology research group of IADR. Caries Res 2020; 54(1):7-14. https://doi.org/10.1159/000503309

[34] Avşar A, Kalayci AG. The presence and distribution of dental enamel defects and caries in children with celiac disease. Turk J Pediatr 2008; 50(1):45-50.

[35] de Carvalho FK, Queiroz AM, Silva RAB, Sawamura R, Bachmann L, Silva LAB, et al. Oral aspects in celiac disease children: Clinical and dental enamel chemical evaluation. Oral Surg Oral Med Oral Pathol Oral Radiol 2015; 119(6):636-643. https://doi.org/10.1016/j.oooo.2015.02.483

[36] Dane A, Gürbüz T. Clinical evaluation of specific oral and salivary findings of coeliac disease in eastern Turkish paediatric patients. Eur J Paediatr Dent 2016; 17(1):53-56.

[37] Catassi C, Verdu EF, Bai JC, Lionetti E. Coeliac disease. Lancet 2022; 399(10344):2413-2426. https://doi.org/10.1016/S0140-6736(22)00794-2

[38] Husby S, Koletzko S, Korponay-Szabó I, Kurppa K, Mearin ML, Ribes-Koninckx C, et al. European Society Paediatric Gastroenterology, Hepatology and Nutrition guidelines for diagnosing coeliac disease 2020. J Pediatr Gastroenterol Nutr 2020; 70(1):141-156. https://doi.org/10.1097/MPG.0000000000002497