Molar incisor hypomineralization and celiac disease

Helen Helene Kuklik, Izabela Taiatella Siqueira Alves Cruz, Adriane Celli, Fabian Calixto Fraiz and Luciana Reichert da Silva Assunção

INTRODUCTION

The molar incisor hypomineralization (MIH) is a type of qualitative enamel defect that affects the first permanent molars and may also be present in the incisors of the same dentition. Clinically it is characterized by demarcated opacities of white, yellow or brown coloration and, in more severe cases, by the post-eruptive collapse of the enamel which may facilitate the development of dental caries and the increase of dental sensitivity.

The cause of MIH is still uncertain, and the studies suggest a multifactorial etiology associated with the defect, which may be of environmental or genetic origin. Thus, because dental enamel cells are highly sensitive to external injuries, disturbances during the enamel maturation stage can lead to permanent defects in dental structures. Systematic reviews have shown that complications during prenatal, perinatal and postnatal periods may be associated with MIH, including complications during pregnancy, low birth weight, respiratory diseases, recurrent fevers and the use of antibiotics in the first years of life. Metabolic diseases and those that produce deficiencies in calcium and phosphate absorption are also associated with the onset of MIH.

Studies have shown that poor enamel formation may also be the result of hypocalcemia present in some diseases, such as celiac disease. Celiac disease (CD) is an immune-mediated enteropathy induced by the ingestion of certain proteins (called gluten) in individuals of any age genetically predisposed. Gluten is the main protein component of wheat, barley, and rye, cereals that are individualized by any age genetically predisposed. Gluten is the main protein component of wheat, barley, and rye, cereals that are associated with its clinical manifestations can assist in the diagnosis of CD.

ABSTRACT – Background – Molar incisor hypomineralization (MIH) is a developmental enamel defect with multifactorial etiology. Although the relationship between celiac disease (CD) and developmental enamel defect was demonstrated, the association between CD and MIH is uncertain. Objective – The objective of this study was to analyze the occurrence of MIH in CD patients. Methods – Forty CD patients and a control group with 40 healthy individuals were selected. A calibrated examiner (k=0.889) according to the European Academy of Pediatric Dentistry criteria performed the diagnosis of MIH. Data were analyzed by descriptive statistics and Fischer’s exact test (α=0.05). Results – Of the 80 participants, ten presented MIH with eight individuals with CD. Celiac patients presented 4.75 times the chance of occurrence of MIH than the control group (95% CI: 2.22–10.18; P=0.044). In all the evaluated teeth (n=978), 22 had MIH: 20 teeth in individuals with CD and two in those without the disease. All CD participants with MIH presented the classic form of the disease. CD participants showed 17 teeth (85.0%) with demarcated opacities, two (10.0%) post-eruptive collapses and one (5.0%) atypical restoration. The control group presented only demarcated opacities. Conclusion – CD increased the chance of MIH and associated with its clinical manifestations can assist in the diagnosis of CD.

HEADING – Celiac disease. Tooth demineralization, etiology. Molar. Incisor. Permanent dentition.

METHODS

Ethical aspects

This research followed the parameters of the Declaration of Helsinki and was approved by the Human Ethics Committee of the Federal University of Paraná (process n. 41861015.0.0000.0102). The free and informed consent form was signed by all participants or their legal representatives.

Declared conflict of interest of all authors: none

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Corresponding author: Luciana Reichert da Silva Assunção. E-mail: lurassuncao@yahoo.com.br
Study population

Forty patients with a celiac disease diagnosis were selected at the gastroenterology outpatient clinic of the Hospital de Clínicas of the Federal University of Paraná, Curitiba, Brazil. Another 40 participants without the disease, matched by age, and who attended the dental service of the Federal University of Paraná, Curitiba, Brazil, were also selected for this study.

For the group of patients with celiac disease, participants previously diagnosed through a positive anti-endomysial-antibody test (IgA) and a definitive confirmation of the disease through a small-bowel biopsy associated with positive serology for celiac disease were included. For the group of participants without celiac disease, patients who had no confirmed diagnosis for CD and who did not have gastrointestinal signs and symptoms were selected.

Participants who exhibited fluorosis, enamel development defects associated with other systemic diseases such as congenital porphyria, hemolytic anemias, and chronic renal failure, and those who used drugs that may have caused dentin pigmentation, such as tetracyclines, were excluded. Also excluded were patients who were using orthodontic braces at the time of examination.

Types of celiac disease

Celiac disease was classified according to the clinical signs and symptoms of the disease in the classic, nonclassical and asymptomatic. The classic form develops from the introduction of gluten protein in the diet, between 6 and 24 months of age and has gastrointestinal symptoms such as chronic diarrhea, anorexia, abdominal distension, abdominal pain, weight loss, and vomiting. Some patients with the classical form of the disease can still present severe malnutrition, leading to hypocalcemia. The non-classical form has extra intestinal symptoms, such as dermatitis herpetiformis, enamel hypoplasia in permanent teeth, osteoporosis, short stature, delayed puberty and iron deficiency anemia not responsive to oral treatments. The asymptomatic or silent form is characterized by histological changes in the intestinal mucosa and absence of clinical manifestations. It usually occurs among first-degree relatives of celiac patients.

Calibration

One of the study researchers (ITSAC) was previously calibrated for clinical identification of hypomineralization of molars and incisors, according to the criteria of the European Academy of Pediatric Dentistry (EAPD), which includes demarcated opacity, atypical restoration, post-eruptive fracture and extraction due to MIH.

The training and the calibration were performed in two stages, and in both, 30 photographs with different clinical situations of the MIH were used. The examiner’s results were compared with a standard examiner (LRSA) with experience in this type of research. The data were statistically analyzed according to the calculation of the kappa coefficient for the evaluation of inter-examiner agreement (kappa =0.926). After one week, the same photographs were again evaluated by the examiner in training (duplicate examination) and statistically analyzed by the kappa coefficient for the evaluation of the intra-examiner agreement (kappa =0.889).

Clinical examination

The clinical examination was performed in a conventional chair and under natural light, using a flat mirror and a blunt tip, after cleaning the dental surfaces with sterile gauze. The criteria for a diagnosis of MIH followed the proposal of the European Academy of Pediatric Dentistry (EAPD), in which at least one first molar must have demarcated opacity (FIGURE 1.A), post-eruptive fracture (FIGURE 1.B), the presence of atypical restoration (FIGURE 1.C) or exodontia due to the condition. The opacities were classified according to their coloration in white (FIGURE 2.A), yellow (FIGURE 2.B) or brown (FIGURE 2.C). The demarcated opacities were considered mild injuries, while post-eruptive fractures, atypical restorations, and MIH exodontia were considered severe. Only defects greater than 1.0 mm in diameter were evaluated and the differential diagnosis for white caries lesions was based on the criteria of Seow, 1997.

Statistical analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS – IBM Corp. Released 2017. IBM SPSS Statistics for Windows, version 25.0, Armonk, NY: IBM Corp.). The variables were analyzed in a descriptive way, through the absolute and relative frequencies. Fischer’s exact test was used to verify the association between the presence of MIH and celiac disease. Odds ratio (OR) and its respective confidence intervals were also evaluated. The level of significance adopted for the analyzes was 5%.
RESULTS

Of the 40 participants with CD, 29 (72.5%) were female, while of the 40 participants without CD, 28 (70.0%) were female. The groups showed a homogeneous distribution regarding sex (P=0.805). The median age of the participants was 16.50 and the minimum age was 5 years and a maximum of 34 years for both groups.

From the total of the participants, ten individuals presented the MIH (12.5%), being in eight individuals with CD (TABLE 1). There was a statistically significant association between MIH and DC, and individuals with the disease presented 4.75 times the chance of MIH occurrence when compared to participants without the disease (95% CI: 2.22–10.18; P=0.044).

Of the 40 participants with CD, 30 (75%) presented the classic form of the disease, seven (17.5%) the nonclassical form and three (7.5%) the asymptomatic. All participants with MIH were related to the manifestation of the classic form of the disease (TABLE 2).

In all teeth evaluated (n=978), 22 presented MIH, with 20 teeth present in individuals with CD and two among those without the disease. Of the 22 teeth with MIH, 19 (86.4%) were demarcated opacities, 2 (9.1%) post-eruptive collapse and 1 (4.5%) atypical restoration (FIGURE 3.A). Of the 20 teeth affected by MIH among participants with CD, 17 (85.0%) were demarcated opacities, 2 (10.0%) post-eruptive collapses and 1 (5.0%) atypical restoration (FIGURE 3.B). On the other hand, all (two teeth) affected by MIH among the participants without CD were demarcated opacities (FIGURE 3.C).

TABLE 1. Occurrence of MIH according to the presence or absence of celiac disease (n=80).

| Celiac disease | Total n (100%) | P*  |
|---------------|----------------|-----|
| MIH           | Yes            | No  |     |
|               | n (%)          | n (%)|  |
| Yes           | 8 (80.0)       | 2 (20.0) | 10  |  |
| No            | 32 (45.7)      | 38 (54.3) | 70  | **0.044** |
| Total         | 40             | 40 | 80  |  |

* Fisher's Exact Test. Significant value highlighted in bold.

TABLE 2. Distribution of MIH in relation to the type of celiac disease (n=40).

| Type of celiac disease | MIH |       |       |
|------------------------|-----|-------|-------|
|                        | Yes | No    | Total |
| Classic                | 8 (73.3) | 22 (26.7) | 30 |
| Nonclassical           | 0 (0) | 7 (100) | 7 |
| Asymptomatic           | 0 (0) | 3 (100) | 3 |
| Total                  | 8    | 32    | 40 |

MIH: molar incisor hypomineralization.
This study showed that the chance of occurrence of MIH is greater in individuals with celiac disease when compared to those without the disease. To our knowledge, no study evaluated the association of this specific type of DED with CD. A recent systematic review and meta-analysis observed a strong association considering both types DED and CD. In the selected studies, of the total of 2840 individuals with celiac disease approximately half had some type of DED. A recent study in Brazil found a 138% greater chance of DED in patients with celiac disease, when compared to those without the disease. In this sense, the North American Society of Pediatric Gastroenterology, Hepatology and Nutrition included DED as an important signal for the diagnosis of celiac disease, which shows that this oral condition can be an important tool for tracking the disease.

The classification used in most of the studies evaluating the presence of DED in participants with CD was the one proposed by AINE (1986), which it includes degrees of severity of the clinical aspect of the defect ranging from 0 to 4 (0 = no defect, 1 = defects in enamel coloring, 2 = slight structural defects, 3 = obvious structural defects, 4 = severe structural defects). In this classification, opacities without loss of structure, such as MIH, are included in category 1. Several studies have shown a higher prevalence of grade I defects in celiac patients.

The most observed form of celiac disease in the study was the classic one, in which the individuals presented mainly gastrointestinal symptoms, such as abdominal pain, diarrhea, vomiting, and abdominal distension. This subgroup of the disease has its manifestation from the introduction of gluten in the diet, at around six months to one year of age. Among individuals with celiac disease, only those with the classic form of the disease had MIH. This is likely to occur because of the lower absorption of nutrients in the gastrointestinal tract in individuals with the classical form of the disease, which may result in hypocalcemia, which may render patients with low calcium levels more susceptible to defects of enamel.

The demarcated opacities were the types of MIH most frequent in the teeth evaluated in both the CD group and the disease. The most severe MIH lesions, i.e., post-eruptive collapse and atypical restoration, were present in only two participants (8 and 11 years old), both with CD. Although this number can be considered without significance, this result can be justified due to a lower rate of calcium and phosphorus in the teeth of individuals with the disease when compared to those without the disease, making these teeth more brittle and less resistant to masticatory forces. Further studies should be conducted to verify this association. To avoid the evolution of more serious consequences of MIH, such as the onset of caries lesions, topical applications of fluoride in opacities have been suggested, enabling the remineralization of impacted teeth.

The limitation of this study refers to its methodological design and sample size. Prevalence studies are limited in concluding a temporal relationship between exposure and outcome. Thus, longitudinal studies are indispensable to verify this association. In addition, larger sample searches are needed to increase the generalization of results.

The data from this study allow us to conclude that celiac disease increased the chance of molar incisor hypomineralization. The occurrence of MIH associated with other clinical manifestations may be an important tool in the diagnosis of the disease. In addition, the results show the importance of dental follow-up of individuals with CD, allowing preventive and/or therapeutic clinical actions to be performed in cases of MIH detection, avoiding more serious consequences such as post-eruptive fractures and even loss of the dental element.
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