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Enamel development defects and oral symptoms: A hierarchical approach.

Diego P A Carneiro, Luziane M F Reis, Giovana R Gouvêa, Vivian F Furletti-Góis, Mario Vedovello-Filho and Silvia A S Vedovello

Orthodontics, University Center of Hermínio Ometto Foundation, Brazil

Objective: This study aimed to determine the relationship between enamel developmental defects (DDEs) and children's oral symptoms in the early and late mixed dentition in a hierarchical approach. ***Methods***: Population-based cross-sectional study of 772 children. Calibrated dental examiners examined for DDEs, malocclusion, and dental caries. Parents answered questions related to the socioeconomic condition of the family. The Child Perception Questionnaire (CPQ_{8-10}) was used to identify oral symptoms as the outcome variable. Analysis was adjusted in a backward stepwise hierarchical multiple logistic regression model. ***Results***: Symptoms were predicted by being female, having a father with low education and having DDEs in the upper first molars (ORs = 1.42; 95% CI: 1.06-1.89; 1.46: 1.10-1.96 and 2.02: 0.99-4.05 respectively). ***Conclusion***: DDEs are associated with oral symptoms in Brazilian children.

Keywords*: children, enamel developmental defects, oral symptoms.*

Introduction

Enamel developmental defects (DDEs) affect enamel formation (FDI, 1992; Jalevik *et al*., 2018) in a quantitative or qualitative manner (FDI, 1992; Ghanim *et al*., 2015). Quantitative defects involve enamel thickness, resulting in hypoplasia (Ghanim *et al*., 2015; Ravindran and Saji, 2016) qualitative defects involve changes in translucency, resulting in opacities or hypomineralisation (Salas *et al*., 2016; Folayan *et al*., 2018; Ghanim *et al*., 2015). Prenatal and neonatal problems have been related to the presence of DDEs in the primary dentition (Salas *et al*., 2016), while in permanent dentition, the presence of DDEs is associated with dental trauma, experience of caries and systemic diseases in childhood (Salas *et al*., 2016).

DDEs may have negative aesthetic, functional and clinical effects, and cause discoloration, tooth sensitivity, susceptibility to caries and malocclusion, and may influence oral health-related quality of life (OHRQoL) (Ravindran and Saji, 2016; Seow, 2014; Dantas-Neta *et al*., 2016; Wagner, 2017). Post-eruptive damage may also potentiate the pre-eruptive effects of the condition (Dantas-Neta *et al*., 2016; Lima *et al*., 2019).

The clinical assessment of oral conditions must be complemented by assessing their effects on the lives of those affected (Dantas-Neta *et al*., 2016; Corrêa-Faria *et al*., 2016). Such assessment of OHRQoL can help to understand the population's needs (Salas *et al*., 2016; Dantas-Neta *et al*., 2016; Corrêa-Faria *et al*., 2016).

In general, studies that have investigated the impact of DDEs have focused mainly on the primary or the permanent dentition (Salas *et al*., 2016; Corrêa-Faria *et al*., 2016). The literature reports one study in the mixed dentition (Portella *et al*., 2019), but only molar incisor hypomineralisation (MIH) was evaluated; other types of defects and the extent of DDEs have not been studied. There is still a need to understand the impact of the more severe defects at this stage of occlusion development on children's everyday life, also considering children's socioeconomic and demographic conditions, as well as the hierarchy of possible associations (Victora *et al*., 1997).

Thus, this study was based on the hypothesis that DDEs have a negative impact on children's oral symptoms in the mixed dentition. Oral symptoms can capture the negative impact of enamel defects on children's daily lives, because they include discomfort, toothache, bad breath, or food impaction from the child's perception (Dantas-Neta *et al*., 2016; Portella *et al*., 2019; Barbosa *et al*., 2011). In the mixed dentition, the teeth may have experienced more post-eruptive effects, modulated by contextual, social, and demographic factors. The aim of the study was to determine the relationship between DDEs and children's oral symptoms in the early and late mixed dentition.

Methods

This study was approved by the Ethics Committee (#72059517.5.0000.5385) and performed according to the STROBE statement. Children and their legal guardians were informed that participation in the study was entirely voluntary. Once they agreed to participate, the children's legal guardians signed a free statement of informed consent. The children also signed an assent form. They were informed about the objectives of the study and assured of the confidentiality of the data collected.

Correspondence to: Prof. Silvia Amélia Scudeler Vedovello Email: silviavedovello@gmail.com

A population-based cross-sectional study was conducted involving children enrolled in public schools throughout every neighborhood of the city of Araras, Southeast Brazil. The city had an estimated population of 188,843 inhabitants at the time of data collection, and a human development index of 0.78 (Atlas of Human Development in Brazil).

The sample size was calculated considering a confidence interval of 95% and a test power of 80%. The finite population was used by considering a prevalence of 50% of symptoms, with an accuracy of 5% and drawing effect of 1.5 (Vedovello *et al*., 2016). In addition, the sample size was enlarged by 20% (to 722 children) to account for non-response.

A representative sample of 8-10-years-old children enrolled in all public schools of the city was selected. In the first stage, 11 of the 15 schools were selected through stratified random sampling according to the population of schoolchildren across the neighborhoods. In the second stage, all children at the target age of the study were invited to participate. Only children in the mixed dentition stage were selected. Mixed dentition status was determined based on the child's dental age (Van der Linden, 1983). This transition stage involves the early (first transitional period) and late (second transitional period) mixed dentition. The early mixed dentition stage includes the presence of the first permanent molars and incisors. The transition of the posterior teeth (canines and premolars) and the emergence of the second permanent molars characterizes the late mixed dentition. Children with apparent mental and/or physical disability that made the interview or oral examination impossible were excluded.

Data collection took place between August and November 2018. A questionnaire was sent to parents together with the informed consent form. Interviews and dental examinations were carried out with the children at school.

Socioeconomic information was collected with a structured questionnaire, containing questions on gender, family income and the educational level of the parents. The education of the father and mother were dichotomized by the median of the answers (Gomes *et al*., 2018).

The Brazilian version of the Child Perceptions Questionnaire for children from 8 to 10 years old (CPQ_{8-10}) was used to record oral symptoms (Barbosa *et al*., 2011). The CPQ_{8-10} is composed of 25 questions distributed across four subscales: Oral Symptoms (questions 1 to 5), Functional Limitations (questions 6 to 10), Emotional Well-Being (questions 11 to 15), and Social Well-Being (questions 16 to 25). Each question addresses the frequency of events in the previous three months. A scale of responses with the following options is used: "Never" = 0; "Once/twice" = 1; "Sometimes" = 2; "Often" = 3; and "Every day/almost every day" = 4. The CPQ_{8-10} was self-applied and questionnaires in which answers for more than two items (questions) were missing were excluded. The questions of the oral symptoms domain referred to the frequency that pain, discomfort, food impaction, or bad breath was present in the child's daily life. This domain was the outcome variable, and higher scores (> 5.33) were taken to indicate greater negative impacts on oral symptoms (Vedovello *et al*., 2016; Sun *et al*., 2018).

The DDE diagnosis was performed according to the Modified Enamel Development Defects Index (mDDE index) (FDI, 1992) criteria. The first permanent incisors and first molars were dried with gauze before the examination. The final score for each child was based on the worst score for these teeth. Individuals who were classified as having DDE had at least one of the conditions shown in Figure 1. The extent of the defect was further classified according to the amount of tooth surface affected: i.e. +/- one third of the surface (Jalevik *et al*., 2018; Ravindran and Saji, 2016). Teeth with dental caries or in the process of the eruption were excluded.

Intermaxillary relationships were diagnosed in the anterior and posterior regions in the sagittal, transverse, and vertical planes, according to Grabowski et al. (2007).

Code	Condition[a] / Combination[b]
0	Normal
1	Demarcated opacity
2	Diffuse opacity
3	Hypoplasia
4	Other defects
5	Demarcated and diffuse
6	Demarcated and hypoplasia
7	Diffuse and hypoplasia
8	All three defects

[a]Codes 0 to 3 correspond to the listed conditions.
[b]Codes 5 to 8 correspond to the listed combinations.

Figure 1. *Modified Index of Enamel Development Defects (mDDE-index) (FDI).*

This method is specifically indicated to examine the prevalence of malocclusions in the mixed dentition. The measurement (in millimeters) was performed with the teeth in centric occlusion with the probe parallel to the occlusal plane. The sagittal occlusal relationship in the anterior region was evaluated by the overjet. The overjet was measured in mm as the distance between the labial surfaces of the lower incisors and the palatal surfaces of the upper incisors. Normal overjet was defined as 0 - 2mm between the maxillary and mandibular incisors. Increased overjet was > 2 mm and anterior crossbite was < 0 mm. Anterior crossbite was recorded when the mandibular incisors were in front of the maxillary incisors. The sagittal occlusal relationship in the posterior region was determined by canine intercuspidation. Class I relationship was considered when the maxillary deciduous canine was in the same plane as the distal surface of the mandibular canine; Class II, when the maxillary deciduous canine was anterior to the distal surface of the mandibular deciduous canine); and Class III, when the maxillary deciduous canine was posterior. Asymmetrical relationships between the deciduous canines were also recorded. Transverse occlusal relationships in the posterior region were recorded when the maxillary deciduous molars occluded lingually to the mandibular deciduous molars in centric occlusion. The vertical occlusal relationship in the anterior region was described by the overbite. Normal overbite was designated when the maxillary incisors overlapped the mandibular incisors by up to 2 mm. Overbite greater than 2 mm was designated as deep bite. Anterior open bite was recorded in children with no contact between the anterior teeth when the posterior teeth were in occlusion. Malocclusion was classified in children with at least one of the aforementioned conditions (Vedovello *et al*., 2016; Sun *et al*., 2018; Gomes *et al*., 2018).

Dental caries was diagnosed using World Health Organization (WHO) criteria (1997). The dmft and DMFT indexes described the number of decayed, missing, and filled teeth. Dental caries data was dichotomized as dmft/DMFT = 0 (no caries experience) or dmft/DMFT > 1 (with caries experience).

The clinical examinations were performed by one calibrated dentist, who participated in theoretical training exercises and clinical calibration based on the examination protocol. The theoretical training for the Grabowski criteria was performed using plaster models, with the objective of discussing the main clinical characteristics of each condition. Photographs were used for dental caries and DDEs. For the clinical calibration, 50 children who did not take part in the main study sample were examined by the researcher separately to determine intra-examiner agreement (Kappa coefficients exceeded 0.90, 0.92, and 0.98 for the assessment of DDEs, malocclusion and dental caries, respectively.

Statistical analysis

The variables were allocated to levels according to their proximity to the outcome (Figure 2). Level 1 (distal) consisted of socioeconomic factors. These variables were categorized according to their median: parents'/caregivers' schooling (> 8 years of study/≤ 8 years of study) and child's gender (male/female). Level 2 (proximal) was composed of the following clinical conditions: dental caries (no caries experience/with caries experience), malocclusion (with malocclusion/without malocclusion) and the presence/absence and extent (+/- 1/3) of DDEs on the first permanent incisors and first molars.

Backward stepwise selection was used in the multiple regression models to test the associations between oral symptoms and their distal and proximal determinants according to the theoretical hierarchical framework (Figure 2). All variables in the individual analyses with $p \leq 0.20$ were tested with multiple logistic regression at the same time, but only those with $p \leq 0.05$ remained in the final model. Adjusted odds ratios (ORs) were estimated with the respective 95% confidence intervals. The analyses were performed in the R Program (R Foundation for Statistical Computing, Vienna, Austria) at a 5% significance level.

Results

Key characteristics of the participants are described in Table 1. The final sample comprised 772 children aged 8 to 10 years, 51.2% of whom were female. Most children had parents/caregivers with more than 8 years of schooling. The prevalence of dental caries experience was 37.7% and malocclusion was 69.8%. DDEs were more prevalent in the upper central incisors (9.1%) than the upper first molars (4.5%). Regarding the extent of the defect, the first permanent molar (1.4%) presented more enamel defects than the upper central incisor (1.0%).

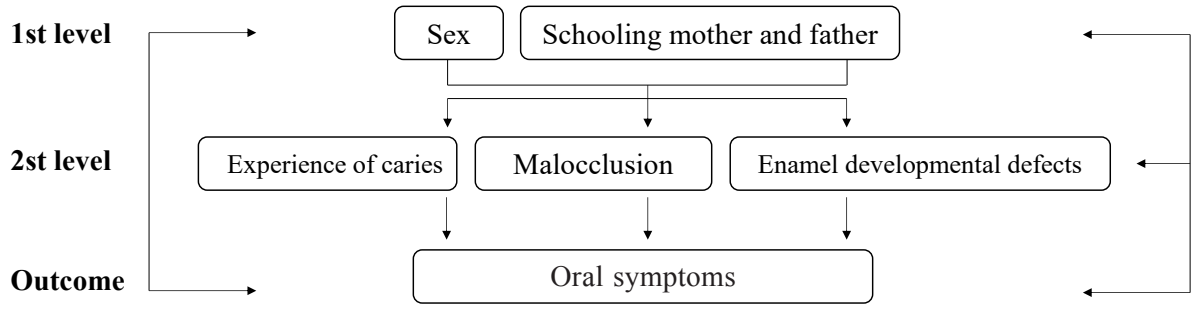

Figure 2. *Conceptual hierarchical framework of associations between DDE factors, clinical conditions, and the impact on oral symptoms of* $CPQ_{8\text{-}10}$.

The mean total CPQ8-10 score was 13.22 and the scores for the four domains were: 5.33 (oral symptoms); 2.27 (functional limitation); 3.35 (emotional well-being) and 2.26 (well-being).

Table 1. Characteristics of 772 children in the mixed dentition.

Variable	*Category*	*%*
Level 1 – Sociodemographic		
Sex	Male	48.8
	Female	51.2
Schooling Mother	Up to 8th grade complete	42.2
	Greater than 8th grade	57.8
Schooling Father	Up to 8th grade complete	53.8
	Greater than 8th grade	46.2
Level 2 – Clinical		
Experience of caries	No caries experience	62.3
	With caries experience	37.7
Malocclusion	Absent	30.2
	Present	69.8
Incisors DDE	Absent	90.9
	Present	9.1
Incisors DDE extent	Up to 1/3	99.0
	More than 1/3	1.0
First molars DDE	Absent	95.5
	Present	4.5
First molars DDE extent	Up to 1/3	98.6
	More than 1/3	1.4

The associations between the presence of oral symptoms and sociodemographic and clinical variables are presented in Table 2. In the adjusted analysis (adjusted OR), being female, having a father of low education and having first molars affected by DDE were associated with 1.42 (95% CI: 1.06-1.89), 1.46 (95% CI: 1.10-1.96), and 2.02 (95% CI: 0.99-4.05) times higher likelihood of reporting oral symptoms.

Discussion

This study assessed the association between DDEs and oral symptoms in a representative sample in the mixed dentition stage. The oral symptoms domain of the CPQ_{8-10} was used to record negative impacts on children's daily lives (Dantas-Neta *et al*., 2016; Portella *et al*., 2019). Oral symptoms include discomfort, toothache, bad breath or food impaction from the child's perception in the last 30 days (Dantas-Neta *et al*., 2016; Portella *et al*., 2019; Barbosa *et al*., 2011). DDEs may involve porous enamel, severe occlusal wear, cracks, or post-eruptive fractures (Dantas-Neta *et al*., 2016; Lima *et al*., 2019), conditions that favor the formation of bacterial biofilm and consequently increase the chance of developing dental caries and dentin hypersensitivity (Seow, 2014; Wagner, 2017; Lima *et al*., 2019; Corrêa-Faria *et al*., 2019). This study highlights possible new negative impacts of DDEs.

The impact of DDEs on children's lives in the transition stage between primary and permanent dentition is still poorly understood. The few studies with children in the early mixed dentition stage (Portella *et al*., 2019; Gutiérrez *et al*., 2019) evaluated DDEs based on the European Association of Pediatric Dentistry (EAPD) criteria, defining defects only when the permanent first molar had molar incisor hypomineralisation (MIH). Our study recorded DDEs according to FDI recommendations. In addition, the sample included children in the early and late mixed dentition with any type of defect observed in the molars and permanent incisors.

DDEs in the upper first molars were associated with oral symptoms in the children. Other forms and sites of DDEs were not associated with oral symptoms. Affected first molars had more extensive lesions and, consequently, greater severity, which may explain our finding.

More girls had oral symptoms. This a finding was similar to that of a previous study that evaluated only MIH (Portella *et al*., 2019), suggesting that girls have more aesthetic concerns (Dantas-Neta *et al*., 2016). This concern seems to accompany the development of girls more significantly than boys, suggesting that, in addition to aesthetic self-perception, girls also feel the impact of discomfort.

Low paternal education was also associated with susceptibility to symptoms (Dantas-Neta *et al*., 2016; Vedovello *et al*., 2016; Singh *et al*., 2019). It may be that parental education influences oral health habits due to the difficulty of access to information and health services, which is directly influenced by the householder's knowledge level (Perazzo *et al*., 2016; Neves *et al*., 2017).

Malocclusion was not related to children's oral symptoms. Previous studies have shown similar results in the same age range (Dantas-Neta *et al*., 2016; Sun *et al*., 2018). Malocclusion has a direct influence on the individual's self-image, interfering with their social well-being (Dantas-Neta *et al*., 2016). Some reports also show that it negatively affects oral symptoms (Sun *et al*., 2018) related to OHRQoL. Our study did not find an association between dental caries and the presence of oral symptoms. We note that some studies corroborate (Portella *et al*., 2019) our results, and others differ (Mota-Veloso *et al*., 2016; Americano *et al*., 2017). According to the literature, children with DDEs tend to avoid their molars and incisors while brushing, leading to biofilm accumulation and food stagnation. However, our sample had a lower dental caries prevalence than in previous studies (Gutiérrez *et al*., 2019; Mota-Veloso *et al*., 2016), and only severe cases may cause symptoms. In addition, the dichotomization of malocclusion and dental caries may have masked any association with oral symptoms.

Because the prevalence of DDEs varies, future studies should assess the defects separately, as prevalence changes according to the type of defect, and severity is directly related to the negative effect (Portella *et al*., 2019). The limitations of the present study are related to the cross-sectional design. The study assessed oral symptoms only

Table 2. Socio-demographic and clinical predictors of the presence of oral symptoms.

Variable	*Category*	*Oral symptoms n = 429 (%)*	*No symptoms n = 343 (%)*	*[$]OR crude ([#]CI 95%)*	*[$]OR adjusted ([#]CI 95%)*
Sex	Male	60.2	39.8	1	1
	Female	51.1	48.9	1.45 (1.09-1.92)	1.42 (1.06-1.89)
Schooling	Up to 8th grade complete	52.4	47.6	1.24 (0.93-1.66)	
Mother	Greater than 8th grade	57.8	42.2	1	
Schooling	Up to 8th grade complete	51.1	48.9	1.48 (1.11-1.98)	1.46 (1.10-1.96)
Father	Greater than 8th grade	60.8	39.2	1	1
Experience of caries	No caries experience	53.3	43.7	1	
	With caries experience	54.3	45.7	1.09 (0.81-1.46)	
Malocclusion	Absent	51.1	48.9	1	
	Present	57.5	42.5	1.30 (0.95-1.76)	
Incisors DDE	Absent	55.7	44.3	1	
	Present	54.3	45.7	1.06 (0.65 -1.73)	
Incisors DDE extent	Up to 1/3	55.4	44.6	1	
	More than 1/3	75.0	25.0	0.41 (0.08-2.06)	
First molars DDE	Absent	56.3	43.7	1	1
	Present	40.0	60.0	1.93 (0.97-3.86)	*2.02 (0.99-4.05)
First molars DDE extent	Up to 1/3	55.6	44.4	1	
	More than 1/3	54.6	45.4	1.04 (0.32-3.45)	

*Reference category for outcome variable.
[$]Odds ratio.
[#]Confidence interval.

over a specific period of time. A longitudinal design would also allow attribution of cause/effect relationships during the development of the dentition. The study would further also be strengthened if specifics characteristics of malocclusion and dental caries were incorporated in the analysis.

Considering their aesthetic, functional and social impacts, DDEs are still poorly studied (Salas *et al*., 2016). In addition, there is no specific protocol for each observed enamel defect. Educational strategies in health are necessary to provide information to parents and professionals. Efforts should be made to diagnose DDE early, drawing attention to the need for correct treatment.

Conclusion

This is the first study to assess the association between DDEs and children's oral symptoms in early and late mixed dentition in a hierarchical approach, considering the presence and extent of the defect in molars and permanent incisors. DDEs were associated with the presence of oral symptoms in Brazilian children.

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