

## Prevalence of developmental defects of enamel in children and adolescents with asthma<sup>\*, \*\*</sup>

Prevalência de defeitos do desenvolvimento do esmalte dentário em crianças e adolescentes com asma

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### Abstract

**Objective:** This study aimed to evaluate the prevalence of developmental defects of enamel (DDEs) in relation to asthma severity, symptom onset and pharmacological treatment in pediatric asthma patients. **Methods:** Children and adolescents (68 asthma patients and 68 controls), 5-15 years of age and residents of the city of Londrina, Brazil, were enrolled in the study. Medical and dental histories were collected through the use of a structured questionnaire. Each participant underwent a dental examination in which the examiner employed the DDE index. **Results:** Of the 68 asthma group subjects, 61 (89.7%) presented dental enamel defects, compared with only 26 (38.2%) of those in the control group. Using multivariate logistic regression analysis, we estimated the risk of DDEs in permanent dentition to be 11 times higher in pediatric subjects with asthma than in those without (OR = 11.88,  $p = 0.0001$ ). The occurrence of dental enamel defects correlated with greater asthma severity ( $p = 0.0001$ ) and earlier symptom onset ( $p = 0.0001$ ). However, dental enamel defects did not correlate with the initiation of treatment ( $p = 0.08$ ) or the frequency of medication use ( $p = 0.93$ ). **Conclusions:** Pediatric patients with severe, early-onset asthma are at increased risk of dental enamel defects and therefore require priority dental care.

**Keywords:** Asthma/prevention & control; Bronchodilator agents; Adrenal cortex hormones/therapeutic use; Dental enamel; Amelogenesis.

### Resumo

**Objetivo:** Avaliou-se a prevalência de *developmental defects of enamel* (DDEs, defeitos de desenvolvimento do esmalte dentário) em pacientes pediátricos com asma e sua relação com a severidade da asma, o início dos sintomas e o tratamento medicamentoso. **Métodos:** Os participantes do estudo eram residentes do município de Londrina (PR), com 5 a 15 anos, sendo 68 asmáticos e 68 controles. Foram levantados dados retrospectivos da história médica e de saúde bucal da população do estudo através de um questionário estruturado. Todos os participantes foram submetidos a um exame dental. Para a avaliação dos defeitos de desenvolvimento do esmalte dentário, utilizou-se o Índice DDE. **Resultados:** Neste estudo, foi observado que 61 (89,7%) dos 68 pacientes asmáticos apresentavam defeitos de desenvolvimento do esmalte dentário quando comparado à ocorrência em 26 (38,2%) dos no grupo controle. Através da análise multivariada por regressão logística, foi observado que um paciente pediátrico com asma apresenta risco aumentado em 11 vezes para o aparecimento de defeitos de desenvolvimento do esmalte em dentes permanentes (OR = 11,88,  $p = 0,0001$ ). Além disso, foi observado uma associação entre defeitos do esmalte dentário e maior severidade da asma ( $p = 0,0001$ ) e início dos sintomas mais precoce ( $p = 0,0001$ ). Não se observou associação entre o início do tratamento ( $p = 0,08$ ) ou frequência de uso da medicação ( $p = 0,93$ ) com o aparecimento de defeitos de desenvolvimento do esmalte dentário. **Conclusões:** Pacientes pediátricos com asma apresentam risco aumentado para a ocorrência de defeitos de desenvolvimento do esmalte dentário relacionado à severidade da asma e início dos sintomas e, portanto, necessitam de atenção odontológica prioritária.

**Descritores:** Asma/prevenção & controle; Broncodilatadores; Corticosteroides/uso terapêutico; Esmalte dentário; Amelogênese.

\* Study carried out at Londrina State University – UEL – and the University of Northern Paraná – UNOPAR – Londrina, Brazil.

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## Introduction

Asthma is a major public health problem,<sup>(1)</sup> and the prevalence of asthma has recently presented a marked increase in many countries.<sup>(2)</sup>

Some studies have reported that the prevalence of dental caries is higher and that salivary flow levels are lower in children with asthma than in those without asthma.<sup>(3-5)</sup> There have also been reports suggesting that respiratory disorders are associated with dental enamel defects.<sup>(6)</sup> However, such reports have presented no epidemiological data regarding its prevalence in children with asthma—nor have there been any studies investigating the potential role that pharmacological treatment plays in this association.

Dental enamel defects are a frequent finding in primary and permanent dentition. These defects are generally classified as enamel hypoplasia or enamel hypomineralization. Enamel hypoplasia is a quantitative defect, whereas enamel hypomineralization is a qualitative defect characterized by abnormal enamel translucency and is therefore also known as enamel opacity.<sup>(7)</sup>

Enamel formation occurs in three stages: matrix formation, during which proteins involved in amelogenesis are produced; calcification, during which mineral content is acquired and the proteins are removed; maturation, during which the enamel is calcified and the remaining proteins are removed. Disorders in the early stages of enamel development evoke enamel hypoplasia, clinically detectable as fissures or enamel loss.<sup>(8)</sup> In contrast, disorders occurring in the calcification or maturation stage can cause hypomineralization.<sup>(9)</sup>

Dental enamel defects have been associated with a broad spectrum of etiologies, including systemic, genetic, local and environmental factors.<sup>(10)</sup> Some authors have stated that systemic conditions, such as prenatal or perinatal illness, low birth weight, regular antibiotic consump-

tion, celiac disease and respiratory disorders, are associated with dental enamel defects.<sup>(11-14)</sup> However, due to a lack of medical and dental records providing data related to young children, it can be difficult to establish the relationship between systemic factors and developmental defects of enamel (DDEs).<sup>(15)</sup> Therefore, epidemiological studies of enamel defects in children with systemic disease are quite important for public health, since they can identify possible etiological factors responsible for the occurrence of the enamel defects,<sup>(10)</sup> as well as identifying populations that merit priority preventive interventions.<sup>(16)</sup> Therefore, this study aimed to evaluate the prevalence of DDEs in children with asthma, drawing correlations with specific characteristics of the disease (symptom onset and asthma severity) and its treatment (timing of treatment initiation and frequency of medication use).

## Methods

This was a cross-sectional study involving children and adolescents (5-15 years of age) in two groups: asthma (n = 68) and control (n = 68).

The asthma group consisted of children and adolescents randomly selected from among patients treated via the *Programa Respira Londrina* (Breathe Londrina Program) or at the Londrina State University Hospital, located in the city of Londrina, Brazil. All asthma group subjects were either under continuous treatment with corticosteroids or were using bronchodilators for acute attacks. The control group subjects, who were selected from Londrina public schools, were using no chronic medication and had no systemic diseases. The control group subjects were matched for age and gender with the asthma group subjects. However, any child or adolescent selected from a public school and later found to have asthma was then included at the asthma group.

**Table 1** - Distribution of developmental defects of enamel index in the study sample.

Group	DDE index				Total
	Normal	Demarcated opacities	Diffuse opacities	Demarcated and diffuse opacities	
Asthma	7 (10.3%)	2 (2.9%)	4 (5.9%)	55 (80.9%)	68 (100%)
Control	39 (57.4%)	2 (2.9%)	4 (5.9%)	23 (33.8%)	68 (100%)
Total	46 (33.8%)	4 (2.9%)	8 (5.9%)	78 (57.4%)	136 (100%)

DDE: developmental defects of enamel.

The exclusion criteria were as follows: presenting any other systemic disease; using a fixed orthodontic appliance; and presenting extensive carious lesions that might mask dental enamel defects.

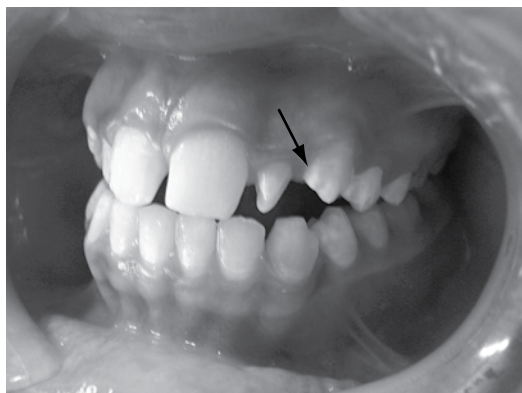
This study was approved by the Ethics Committee of the University of Northern Paraná, as well as by the administrations of the Breathe Londrina Program and the Londrina State University *Hospital das Clínicas*. The parents or legal guardians of the participants received information regarding the purpose of the study, and all gave written informed consent prior to the clinical examinations. All participants received instructions related to oral health maintenance, and each was given a new toothbrush at the end of the clinical examination.

Two examiners were involved in the study, the first being responsible for data collection (patient medical and dental history), and the second being responsible for the evaluation of dental enamel defects.

A questionnaire related to personal medical and dental history, formulated by the authors of the study, was completed by all of the participating children and adolescents, with the assistance of their parents or legal guardians. After the questionnaire had been completed, participants were identified only by assigned numbers and as belonging to the asthma or control group. The examiner performing the clinical diagnosis of dental enamel defects was blinded to the group to which any given child belonged.

Clinical examinations were carried out at the Dental Clinic of the University of Northern Paraná. All examinations were conducted by the same examiner, who had been previously trained and certified as a reference examiner using the modified DDE index,<sup>(17)</sup> as recommended by World Health Organization for the evaluation of enamel defects. In this index, all enamel defects, regardless of location or size, are recorded, being classified as follows: absent (normal condition); demarcated opacities (white or yellow—single or multiple); diffuse opacities (parallel lines or with a patchy distribution); and hypoplasia (pits, grooves, or larger areas of missing enamel—single or multiple).

The kappa value obtained to estimate the consistency of the fieldwork examiner was  $k = 0.84$  for the DDE diagnosis. During clinical



**Figure 1** – Representative photograph of a child with asthma presenting demarcated opacities in the left maxillary canine tooth (arrow).

examinations, the children were placed in a conventional dental chair. The teeth were dried for 30 s, after which they were examined with the aid of artificial light and a small mirror.

In order to perform a clinical assessment of possible mouth breathing, the examiner used the test described by Menezes et al. (2006)<sup>(18)</sup> in which patients are asked to hold water in their mouth, lips closed and without swallowing, for 3 min. Patients who swallow the water or open their lips during this period are presumed to have reduced nasal breathing capacity.

### Statistical analysis

Statistical analysis was performed using the program Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA). For all statistical tests, a confidence interval of 95% and significance level of 5% ( $p < 0.05$ ) were adopted. In order to compare the means of the two groups, we used the Student's t-test for independent samples and for variables with normal distribution.

The chi-square test, followed by Yates' correction, was used in order to compare the prevalence of DDEs in the asthma group with that observed in the control group.

**Table 2** – Occurrence, adjusted for gender and age, of dental enamel defects in the permanent teeth of children and adolescents presenting asthma, allergic rhinitis or mouth breathing.

Variable	OR	95% CI	p
Asthma	11.88	4.38-32.19	0.0001
Allergic rhinitis	3.16	0.60-16.59	0.1730
Mouth breathing	1.08	0.41-2.85	0.8650

**Table 3** - Prevalence of dental enamel defects according to asthma severity.

Asthma severity	Dental enamel defects		Total
	Absent	Present	
Mild	8 (34.8%)	15 (65.2%)	23 (100%)
Moderate or severe	00 (0%)	45 (100%)*	45 (100%)

\*p = 0.0001 vs. mild.

Logistic regression was used in order to assess the risk of dental enamel defects in a multivariate analysis. The model included the variables asthma, allergic rhinitis and mouth breathing, all adjusted for age and gender.

The phi coefficient was used in order to determine whether the prevalence of dental enamel defects correlated with asthma severity, symptom onset, timing of the initiation of treatment and frequency of medication use. In order to perform this analysis, those variables were considered dichotomous: asthma severity (mild or moderate/severe); symptoms onset (before or after 3 years of age); initiation of treatment (before or after 3 years of age); and frequency of medication use (continuous and for acute attacks only).

## Results

Of the 68 children and adolescents in the asthma group, 35 (51.5%) were girls and 33 (48.5%) were boys, compared with 42 (61.8%) and 26 (38.2%), respectively, of those in the control group. There were no gender-related differences between the asthma and control groups. The mean age in the asthma group was  $9.61 \pm 0.31$  years, compared with  $9.79 \pm 0.18$  years in the control group ( $p > 0.05$ ).

Permanent-tooth DDEs were observed in 61 (89.7%) of the asthma group subjects and 26 (38.2%) control group subjects. The teeth were free of dental enamel defects in only 7 (10.3%) of the asthma group subjects and 42 (61.8%) of the control group subjects. Therefore, the prevalence of dental enamel defects in permanent

**Table 4** - Prevalence of dental enamel defects according to symptom onset.

Symptom onset	Dental enamel defects	
	Absent	Present
Before 3 years of age	01 (1.8%)	55 (98.2%)*
After 3 years of age	07 (58.3%)	05 (41.7%)

\*p = 0.0001 vs. after 3 years of age.

dentition was higher in the asthma group than in the control group ( $p = 0.0001$ ).

Demarcated diffuse opacities, which were observed in 34 asthma group subjects (54%) and 16 control group subjects (20.8%), constituted the most prevalent enamel defect observed in this population (Table 1).

A representative photograph of the DDEs observed in one child with asthma is shown in Figure 1.

Logistic regression revealed that the risk of dental enamel defects is approximately 11 times higher for children with asthma (Table 2).

The occurrence of dental enamel defects correlated with asthma severity ( $r\phi$ : 0.51,  $p = 0.0001$ ), as well as with symptom onset ( $r\phi$ : 0.67,  $p = 0.0001$ ), as shown in Tables 3 and 4, respectively.

The occurrence of dental enamel defects was not found to correlate with the initiation of treatment ( $r\phi$ : 0.27,  $p = 0.08$ ) or with the frequency of medication use ( $r\phi$ : 0.05,  $p = 0.93$ ).

## Discussion

In the present study, the prevalence of DDEs was found to be high among Brazilian pediatric patients with asthma, which was estimated to increase the risk of dental enamel defects in permanent dentition by 11 times.

Our findings are in agreement with those of another group of authors,<sup>(11)</sup> who observed a positive correlation between respiratory disorders, such as asthma, and the presence of demarcated opacities in first permanent molars. Other authors have also suggested that asthma is associated with the occurrence of DDEs in permanent teeth.<sup>(19,20)</sup>

Despite the fact that some studies have identified asthma as a potential etiological factor in the occurrence of dental enamel defects,<sup>(11)</sup> there have been no studies investigating the possible interactions between such occurrence and the onset of asthma symptoms or the timing of treatment.

In our study, we found that the occurrence of dental enamel defects presented a statistically significant correlation with asthma severity, as well as with symptom onset, the risk being greater in pediatric patients with moderate/severe asthma, especially in those presenting symptoms before 3 years of age. One group of authors reported that the risk of dental enamel

defects is higher in children with poor health during the first three years of life (the critical period for crown formation of first permanent molars, permanent incisors and canines).<sup>(21)</sup> In addition, it has been suggested that any health problem prior to 5 years of age can modulate ameloblast activity and therefore impair amelogenesis.<sup>(6)</sup> One study showed that 67% of Dutch children who present DDEs suffer from respiratory disease.<sup>(19)</sup> Since ameloblasts are highly sensitive to oxygen supply,<sup>(6,7)</sup> we can hypothesize that pediatric asthma patients with dental enamel defects have probably experienced previous episodes of oxygen deprivation. Therefore, these defects might be related to the disease itself rather than to its treatment.

Further studies of the prevalence of dental enamel defects in patients with asthma are needed. It has been recommended that administrators of asthma programs be alerted to any such epidemiological data.<sup>(22)</sup> Longitudinal studies could establish the mechanisms by which respiratory disorders affect enamel formation.

Dental enamel is an atypical tissue. Unlike other hard tissues, dental enamel, once formed, cannot remodel. Since changes during its formation are permanent and are recorded in the tooth surface, dental enamel defects can constitute a biological marker of adverse events during development, and this marker could have clinical and epidemiological applications.<sup>(7)</sup>

The prevalence of dental caries is high among children with DDEs. Therefore, we suggest that priority dental programs be provided for this population in order to reduce aesthetic and dento-facial abnormalities, as well as to lower the prevalence of dental caries. In addition, we recommend that dentists be included in multidisciplinary teams affiliated with asthma programs.

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