Association Between Molar-Incisor Hypomineralization and Enamel Hypoplasia

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Objective: *To investigate the association between molar-incisor hypomineralization (MIH) and enamel hypoplasia.* ***Study design:*** *The sample consisted of 311 orthodontic files of patients aged between 12 and 18 years, divided into two groups: patients with MIH (109) and without MIH (202). MIH and enamel hypoplasia were diagnosed via panoramic radiographs and intraoral photographs, followed by clinical examination of the MIH-affected patients as per the modified EAPD scoring criteria. Chi-square test and t test were used to assess intergroup comparisons regarding sex, age and race. Fisher's Exact test was used to compare the groups regarding the presence of enamel hypoplasia and the Adjusted Odds Ratios (OR) were calculated.* ***Results:*** *There was an association between MIH and enamel hypoplasia. The prevalence of enamel hypoplasia (5.5%) was significantly higher in patients with MIH compared to the control group (0.49%). MIH lesions increase 12.45-fold the risk of having enamel hypoplasia.* ***Conclusion****: Patients with MIH have a higher prevalence of enamel hypoplasia and these defects seem to share the same etiological factor.*

Keywords: *Enamel hypoplasia, Molar incisor hypomineralization, comparison, Paediatric dentistry.*

INTRODUCTION

Developmental defects of enamel (DDE) are alterations in the quality and/or quantity of enamel that may affect the shape, hardness and color of teeth, as a result of disturbances during amelogenesis[1]. Different kinds of enamel defects may occur depending on the stage of enamel formation in which the ameloblast has been affected. Quantitative enamel defects result from changes occurring during the stage of matrix formation, whereas qualitative defects result from changes that affect the major part of the mineralization process[2].

Enamel defects may be expressed as hypomineralizations or hypoplasia lesions. Hypomineralized enamel can be seen due to differences in translucency that may be diffuse or demarcated. This enamel looks soft and porous, and for this reason, teeth may undergo irregularly shaped post-eruptive breakdown (PBE)[3]. Enamel hypoplasia is a reduced quantity of enamel thickness that produces smooth, even edges[3].

DDE may affect both primary and permanent teeth, although the etiology is still unclear. The appearance of these lesions seems to be influenced by some conditions, such as dental trauma[3], maternal diseases[4], use of medication[5] and infections in early childhood[5]. However, DDE may be caused not only by environmental and systemic factors, but also by genetic disorders[6].

Based on the hypothesis that the enamel formation process is influenced by genetics, it is fair to assume that genetic variations could be related to alterations in the amelogenesis. Studies suggest there is an association between hypomineralised enamel and genetic variation in enamel formation genes[6]. A similar pattern has been observed for other dental development defects[2]. There is a pattern of

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association between several types of dental anomalies with genetic origin, such as agenesis, microdontia and tooth transposition[7]. However, the true association between MIH and enamel hypoplasia is still unknown. Thus, given this scenario and considering the scarcity of scientific information on the subject, the aim of this study was to evaluate the association between MH and enamel hypoplasia.

MATERIALS AND METHOD

Ethical aspects

This cross-sectional study was approved by the Human Research Ethics Committee (Opinion No. 4,184,167).

Study design and sample selection

The sample size for each group was performed based on an alpha of 0.05 and a beta of 0.2 to achieve 80% power using prevalence rates of enamel hypoplasia previously reported[8]. The sample size calculation showed that 53 patients were needed for each group.

The sample was selected from the Departments of Orthodontics and Paediatrics Dentistry files, of State University of Rio Grande do Norte, which consisted of more than 3,500 patients. Records of all patients aged between 12 and 18 years who had all permanent teeth erupted (excepting third molars) were selected and divided into two groups.

Group 1 consisted of 109 patients with MIH (56 girls and 53 boys) with a mean age of 14.5 years. Group 2 consisted of 202 patients without MIH (102 girls and 100 boys) with a mean age of 14.73 years.

Patients with amelogenesis imperfecta, tetracycline staining or those who were undergoing orthodontic treatment at the time of evaluation were excluded.

Calibration

The two researchers have undergone training and calibration exercises for the diagnosis of enamel defects under the supervision of an experienced dentist ('gold standard'). An interval of 14 days between assessments was established. The intra-examiner agreement (Kappa coefficient) was 0.79 and the inter-examiner agreement between the main investigator and the experienced dentist was 0.9.

Data collection

The diagnosis of MIH and enamel hypoplasia was made evaluating panoramic radiographs and intraoral photographs that were present in each patient's records. The identification of hypoplasia was carried out observing the presence of a quantitative defect in the tooth enamel with regular and smooth edges. Patients initially diagnosed with MIH via intraoral photographs were clinically reassessed to confirm the diagnosis, following the criteria defined by the EAPD and modified by Ghanim[9].

Patients in Group 1 were divided into two subgroups ("mild" and "severe"), according to the severity of their lesions. MIH was classified as "mild" when there were demarcated opacities without post-eruptive enamel breakdown, and "severe" when there were PEB, atypical caries or restorations, and/or an extraction(s) due to hypomineralization[10].

Hypomineralized lesions were classified according to the likely period of occurrence, based on the location of the defect, in accordance with Alalusua 2010[11]. Similarly, the possible period of occurrence of hypoplastic defects was evaluated following information from Logan *et al*, 2017[12].

Statistical analysis

Data were coded, set and analyzed using the Statistical Package for the Social Sciences (SPSS v23, IBM statistics). Descriptive data analysis was performed to obtain the prevalence rates. Chi-square test and t test were used to assess intergroup comparison regarding sex, age and race. Fisher's Exact test was used to qualitatively compare the groups regarding the presence of enamel hypoplasia. Adjusted Odds Ratios (OR) with 95 % test-based confidence intervals (CI) were calculated. The results were considered significant at $P < 0.05$.

RESULTS

The final study sample consisted of 311 orthodontic records of patients (158 females and 153 males), with a mean age of 14.6 years (SD=1.92).

Association between MIH and enamel hypoplasia

Among the 311 enrolled subjects, only seven had enamel hypoplasia (2.2%) and 109 had MIH (35.4%). As shown in Table 1, no significant difference was observed between the groups regarding sex, race and age. Compared to the control group, a higher proportion of MIH-affected patients had enamel hypoplasia (5.5% vs 0.49%, p=0.002) (Table 2).

Table 3 shows the binomial logistic regression to estimate the odds risk. The presence of MIH significantly increased the risk of enamel hypoplasia (OR = 12.45, 95 % CI 1.47–105.34, p =0.021), whereas the interaction of enamel hypoplasia rates with sex and race were nonsignificant. Descriptive analysis of enamel hypoplasia and MIH lesions are shown in Table 4.

DISCUSSION

This study tested the hypothesis that MIH is associated with enamel hypoplasia, based on the premise that some dental anomalies coexist with others in the same patient[13, 14]. To the best of our knowledge, this is the first study to evaluate the possible association between MIH and enamel hypoplasia.

The prevalence of MIH found in this study (35.4%) is twice the rate greater than reported by Zhao *et al* [15] (14.2%). However, literature shows that higher prevalence rates of MIH have been observed in South America[15]. Ethnic and environmental differences, in addition to variations in diagnostic criteria, can also explain for this great variability[4]. Therefore, the present study used the defined criteria by the EAPD and modified by Ghanim for the diagnosis of MIH[10], with the aim of synchronizing the methods and allowing for worldwide comparison.

With regard to the prevalence of enamel hypoplasia, only 2.2% of subjects presented this enamel defect, which confirms the low prevalence reported previously 0.8%[16] to 7.6%[17]. Higher rates of enamel hypoplasia have been observed in children from developing countries, who suffered from malnutrition and/or low birth weight[18].

The literature shows that the prevalence of developmental defects of enamel varies around 24.4%[19] and 52%[16]. However, it has been suggested that age, sex or race have an influence on the development of some enamel defects. A higher prevalence of DDE

Table 1. Intergroup comparison regarding sex, age and race.

	Sex		Age	Race			
Patients (N)	**Female**	**Male**	**Mean (SD) years**	**White**	**Brown**	**Asian**	**Black**
MIH-affected (109)	56 (51.4%)	53 (48.6%)	14.5 (1.92)	38 (34.9%)	40 (36.7%)	1 (0.9%)	30 (27.5%)
Non-MIH-affected (202)	102 (50.5%)	100 (49.5%)	14.7 (1.93)	85 (42.1%)	75 (37.1%)	0 (0.0%)	42 (20.8%)
Total (311)	158	153	14.6 (1.92)	123	115	1	72
P-VALUE	0.753*		0.371+	0.243*			

*Chi-square test + t test

Table 2. Intergroup comparisons regarding percentages of enamel hypoplasia.

	PREVALENCES			
	MIH-affected	**Non-MIH-affected**	**TOTAL**	**P-VALUE#**
Enamel hypoplasia	5.5% (6)	0.49% (1)	2.2% (7)	0.002*

*Chi-square test. # Statistically significant at P<0.05

Table 3. Adjusted Odds Ratio (95% confidence interval) for enamel hypoplasia.

Variables	**Enamel hypoplasia (N = 7) N (%)**	**Non enamel hypoplasia (N = 304) N (%)**	**Adjusted Odds ratio**	**95 % CI**		**P-VALUE#**
				Lower	***Upper***	
MIH						
Presence	6 (85.7)	103 (33.9)	12.45	1.47	105.34	0.021
Abscense	1 (14.3)	201 (66.1)				
Race						
Brown	3 (42.85)	112 (36.8)	0.933	0.185	4.72	0.934
Asian	0 (0.0)	1 (0.3)	1.28	0.000	Inf	0.993
Black	1 (14.3)	71 (23.4)	1.775	0.181	17.39	0.662
White (reference)	3 (42.85)	120 (39.5)				
Sex						
Male	4 (57.1)	151 (49.7)	1.38	0.295	6.42	0.685
Female (reference)	3 (42.9)	153 (50.3)				

Statistically significant at P<0.05

Table 4. Descriptive analysis of enamel hypoplasia and MIH lesions.

	Enamel Hypoplasia		MIH	
Patients	**Teeth**	**Enamel secretion**	**Teeth**	**Enamel mineralization**
Patient 1	13, 23	5 months (IU) to 4/5 months	16	Birth
Patient 2	31	5 months (IU) to 3/4 months	16,26,36,46	Birth to 6 months
Patient 3	15	10 months to 2 years	16,26	Birth to 6 months
Patient 4	22	5 months (IU) to 10/12 months	26,36,46	6 months to 1 year
Patient 5	41	5 months (IU) to 3/4 months	16,26,36	6 months to 1 year
Patient 6	31	5 months (IU) to 3/4 months	16,36	6 months to 1 year

in boys was reported by Robles *et al* in Spain [16], Li *et al* [20] in an Asian and Farsi[21] in an Arab population[16]. However, Chaves *et al* [22] did not find any difference in the occurrence of enamel defects in relation to sex. In the present study, the groups were comparable regarding sex, age and race.

Association studies involving enamel defects have been published[13, 23], even though most of them focused only on MIH and fluorosis. The studies that reported the coexistence between qualitative and quantitative enamel defects are descriptive in nature and do not provide information on the possible correlation between these two conditions[13, 24]. This association may be suggested, since all DDE are caused by complex interactions between genetic, systemic, and environmental factors that affect the structure of enamel during its formation[25]. Our results confirmed that patients with MIH have a higher prevalence of enamel hypoplasia. However, these defects did not affect the same tooth. The ameloblasts that caused the hypoplasic lesion were able to recover before the beginning of the mineralization phase. Furthermore, this same agent was able to damage the cells of other teeth that were in more advanced stages of amelogenesis, leading to hypomineralization lesions.

Amelogenesis is a complex process regulated by ameloblasts that occurs in two phases: secretory and mineralization. Any event that disturbs one of these phases may result in a qualitative or quantitative defect in tooth enamel[3]. Our results suggest that the

same threatening agent may affect ameloblasts at different phases of amelogenesis in different teeth. This is because, although the aetiology of MIH and enamel hypoplasia is not fully elucidated yet, there are several studies suggesting that these defects may be the result of the same threatening agents[3, 4].

The reason why only a few teeth are affected by defects is still unknown, however some studies suggest that the period of damage to the enamel may be short lived, meaning that the ameloblasts may be able to recover or just sensitizing[16, 25]. Furthermore, the minimum time period needed to cause abnormal ameloblast function depends on the sensitivity of the ameloblasts to the harming factor and the power of that factor. However, the late secretion and/or early mineralization stages seem to be more sensitive to the appearance of DDE[11].

It is noticeable that, although several systemic factors have been associated with MIH and enamel hypoplasia, it is difficult to isolate the relative contribution of each due to their potential synergistic effects[11]. However, hypomineralized areas in molars may reflect the approximate period in which the insult has happened[3]. The present study has shown that the period of mineralization in which the molar region was affected and the period of enamel secretion in teeth affected by hypoplasia were similar. These results suggest that DDE may have shared the same etiological factor, especially in the first year of life, which the most critical period for enamel defects as it coincides with early mineralization[11].

In addition to environmental and systemic factors, it was suggested that a genetic predisposition would play a role in the development of enamel defects. Genomic research shows that certain genes are directly related to amelogenesis[25]. While other studies evaluating concordance of identical twins have led researchers to suggest an underlying genetic predisposition to the development of enamel hypoplasia and MIH[25, 26].

Studies on dental anomalies pattern reinforce the role of the genetic factor in the emergence of various developmental anomalies[7, 14]. However, only one study evaluated the correlation between enamel defects and other dental anomalies[8]. The author found a greater prevalence of dental anomalies such as agenesis of second premolars, microdontia of maxillary lateral incisors, infraocclusion of primary molars and palatally displaced canine in patients with enamel hypoplasia. This result was credited to the genetic component, so that the same defect in one gene may produces different phenotypes.

Studies suggest that MIH-affected teeth can be explained by the duration and period of the insult during enamel formation[18, 27]. Therefore, injuries in other teeth could be expected in cases of large magnitude insults. This pattern has been previously reported, showing that the risk of incisor involvement seemed to increase with the number of affected molars[28]. Our results showed that MIH lesions increase 12.45-fold the risk of enamel hypoplasia. However, the findings showed that the presence of enamel hypoplasia is not related to race or sex. A similar result was observed in previous studies[29, 30].

The present study has some limitations that must be considered for an adequate interpretation of the results. This is because this work did not assess the possible etiological factors of DDE. Longitudinal researches are needed to elucidate the etiology and the temporal sequencing of the occurrence of defects. Knowledge of the contribution of genetic, systemic and environmental factors in enamel defects will help in the diagnosis and risk assessment of affected children and also in counseling families about associated complications[25].

CONCLUSION

Patients with MIH have a higher prevalence of enamel hypoplasia and these defects seem to be consequences of the same threatening agent acting at different stages of amelogenesis.

ACKNOWLEDGMENTS

This work was carried out with the support of the Coordination for the Improvement of Higher Education Personnel–Brazil (CAPES)–Financing Code 88887.486387/2020-00.

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