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Increase in severity of molar–incisor hypomineralization and its relationship with the colour of enamel opacity: a prospective cohort study

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Background. Predicting risk of posteruptive enamel breakdown (PEB) of molar–incisor hypomineralization (MIH) opacity is a difficult but important clinical task. Therefore, there is a need to evaluate these aspects through longitudinal studies.
Objective. The aim of this longitudinal study was to analyse the relationship between colours of MIH opacity of children aged 6–12 (baseline) and other clinical and demographic variables involved in the increase in severity of MIH.
Materials and methods. A blinded prospective 18-month follow-up was conducted with 147 individuals presenting mild MIH. Tooth-based incidence of increase in severity of MIH (PEB or atypical restorations) was used as dependent measurement. Enamel opacities were recorded according to colour shades of white, yellow and brown, allowing assessment of susceptibility to structural loss over time, according to colour of MIH opacity. Poisson regression models were used to adjust the results for demographic and clinical variables.
Results. Brown and yellow MIH opacities were at higher risk for PEB and atypical restorations than those of white ones, even after adjustment for clinical and demographic variables.
Conclusion. Teeth presenting mild MIH severity associated with yellow and brown enamel opacities were at high risk for increase in severity of MIH than lighter ones. This result could help clinicians determine a risk-based treatment for children with MIH.

Introduction

Cases of permanent first molars and incisors with idiopathic enamel hypomineralization have been described in the literature since the 1970s[1–7]. In 2001, Weerheijm *et al.*[8] suggested the term molar–incisor hypomineralization (MIH) to define it as hypomineralization of systemic origin of one to four permanent first molars, frequently associated with affected incisors. Several factors have been involved in the aetiology of MIH. In literature, MIH has been linked to environmental changes such as pre- and perinatal problems, respiratory disease, high fever diseases such as chicken pox, and the frequent use of antibiotics in early childhood[9–13].

Clinically, the enamel defects of MIH can vary in colour shade from white to yellow/brownish, but always show a sharp demarcation between the affected and sound enamel[8,14]. The tooth surface enamel initially develops with a normal thickness, but it can easily fracture under masticatory forces[8] predisposing it to unexpectedly fast caries development[14].

Several previous cross-sectional studies[6,15–18] have shown that hypomineralized enamel was associated with posteruptive enamel breakdown (PEB). This fact may be connected with the level of porosity of hypomineralized enamel, onset and duration of the influence of masticatory forces and other agents, such as bacterial plaque and acid beverages, on hypomineralized enamel[9]. The influence of posteruptive time on the increase in severity of MIH was suggested by Leppäniemi *et al.*[6].

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Data from cross-sectional studies reinforce this statement, because more severe defects were found among older children[6,18,19]. Prevalence studies however provide data only about the proportion of a population with severe defects at a single moment in time. To assess the progressive condition of MIH and thereby the threat to health of the dentition, it is necessary to have data from longitudinal studies.

Hardness measurements[20–24] revealed that hypomineralized areas in enamel were associated with a reduction in the mechanical properties of the regions affected by MIH. When the clinical and histological appearances of MIH were compared by polarization microscopy[5], yellow/brown opacities were shown to be more porous than lighter opacities. Furthermore, hardness values[25] and mineral density[26] were related to colour change in hypomineralized demarcated opacities, with yellow lesions being softer than white[25]. The higher porosity of darker opacities may contribute to lower mechanical resistance that facilitates PEB. There are however no prospective data available yet to provide evidence of the higher risk for structural loss from areas of darker enamel opacity.

Therefore, the aims of this prospective cohort study were to evaluate the hypothesis that darker opacities of MIH have a higher susceptibility to PEB over time than lighter ones. The influences of demographic variables and clinical characteristics of teeth on the increase in severity of MIH over time were also examined.

Materials and methods

Approval for this assessment was obtained from the Ethics Committee of the Piracicaba Dental School, São Paulo, Brazil. Parents of the participants in the study gave their informed consent before the study began.

Study design

This was a prospective cohort study, based on two clinical examinations of the same children at 6–12 and 8–14 years of age, respectively, residents of the city of Botelhos, Minas Gerais, Brazil.

Subjects

Baseline. In a previous population-based study, conducted in October, 2008[18], all children aged 6–12 years old, from public schools in Botelhos, Minas Gerais, Brazil, were invited to participate (n = 1315).The exclusion criteria were children whose parents did not agree to their participation in the study (n = 189), those who did not have their four-first permanent molars fully erupted (n = 102), with dental fluorosis (n = 36), generalized enamel hypoplasia (n = 13) or amelogenesis imperfecta (n = 1), and those who were undergoing orthodontic treatment at the time of the assessment (n = 56). Overall, 918 children were eligible, and the percentage of children who had at least one-first permanent molar with MIH was 19.8%.

Follow-up. The follow-up was performed in April 2010. All children, previously diagnosed with MIH (n = 182) at baseline, aged 8–14 years, were invited to participate. Children not diagnosed with MIH were excluded.

Calibration and reproducibility

Examiner training methods and the reliability of the clinical recordings were described at Baseline[18]. Briefly, a calibration exercise was conducted using 37 clinical photographs of patients from the Department of Paediatric Dentistry. All patients had enamel defects (15 with MIH). One month after this exercise, the clinical photographs were re-examined and Kappa statistics were used to measure the agreement. The inter- and intra-examiner agreement for dental caries and MIH were both above 0.91.

Before the follow-up examination, a new calibration exercise was conducted, in which the criteria for examinations were revised using the same photographs. Moreover, to determine intra-examiner agreement, about 10% of the examined children were randomly selected and re-examined during the fieldwork, on a separate occasion, 24 h apart and with no access to the previous records.

The intra-examiner agreement for both dental caries and MIH was above 0.92. For MIH severity, the overall proportion of identical diagnoses was 94% for demarcated enamel opacity, 95% for PEB and 97% for atypical restoration.

Assessment of dental caries, MIH prevalence and severity

Children were examined in the school environment, according to the WHO guidelines[27] under natural light in an outdoor setting by two calibrated dentists (CMCS and FJ). The first dentist (CMCS) evaluated the children for dental caries. The second (FJ) evaluated the first permanent molars and permanent incisors of the same children for prevalence, severity and colour of demarcated enamel opacity of MIH.

Teeth were gently dried with a piece of gauze, and a calibrated dentist examined them using a dental mirror and dental probe. Caries was charted by the decayed, missing and filled surfaces (DMFS) index[27], and no radiographs were taken either at baseline or at follow-up.

Molar–incisor hypomineralization was charted by the criteria proposed by the European Academy of Paediatric Dentistry[28]. Only demarcated opacities larger than 1.0 mm in diameter were considered. Enamel opacities were also recorded according to colour shades of white, yellow and brown[1].

Demarcated enamel opacities were differentiated from early caries lesions (white spot), according to their locations on the teeth. Noncavitated carious lesions were often associated with plaque retention, and these are usually located adjacent to the gingival margin and extend along the buccal or lingual surfaces. In contrast, demarcated enamel opacities have no preferential localization on the tooth[29].

Teeth that presented only demarcated opacities, with no structural loss or atypical restorations, were considered to have mild MIH. Moderate MIH included enamel opacities associated with PEB limited to enamel. Severe defects were classified as the presence of hypomineralized lesions associated with loss of dental structure affecting enamel and dentin, and/or atypical restorations replacing affected hard tissue[6]. The grade of hypomineralization for each individual tooth was defined by the most severe defect seen on its surfaces.

Assessment of increase in severity of MIH

At follow-up, one blinded calibrated dentist (CMCS) evaluated the children for increase in severity of MIH. Only teeth with mild MIH at baseline were reassessed for severity according the same criteria presented above. Teeth that presented moderate or severe MIH at baseline were excluded from this analysis because some atypical restorations and severe PEB associated with dental caries may have masked the colour of enamel opacity at baseline. This fact makes it difficult to analyse the susceptibility to structural loss over time according to the colour of MIH opacity.

The follow-up was performed under the same conditions as the initial examination allowing direct comparisons of MIH severity to be made after a period of 18 months. An increase in severity of MIH was considered the presence of PEB on the affected teeth in comparison with the previous demarcated enamel opacity existent at baseline. PEB was also divided into mild structural loss, when it was limited to enamel and extensive structural loss, when it affected both enamel and dentin[3]. Extensive structural loss was differentiated from dental caries because it was often associated with pre-existent opacity, showing a demarcated enamel opacity surrounding the border of the lesions[9,28]. On the other hand, dental decay was detected as visible evidence of cavitations into dentin, with a detectably softened floor or wall[27].

Atypical restorations performed on previously demarcated enamel opacity were also considered as an increase in severity of MIH, because several studies consider atypical restorations as severe defects of MIH[6,15,18]. The examiner carefully considered and recorded differential reasons for the increase in severity of MIH as they occurred, and subsequently reclassified the severity of MIH before that point by reviewing the clinical record.

Assessment of Decayed and filled surfaces increment

The DFS of children were reassessed at follow-up, and caries increment was calculated as increases in decayed surfaces and/or filled surfaces (FS) by one calibrated dentist (CMCS). Because almost all children were at the mixed dentition stage, the permanent canines, premolars and second permanent molars had not normally erupted in all children. For this reason, these teeth were excluded from the analysis[30]. Therefore, the analysis of caries increment was limited to permanent first molars and permanent incisors.

Demographic variables

Demographic variables (children's residential area, years of age and gender) were also investigated to evaluate their relationship with increase in severity of MIH.

Statistical analysis

Increase in severity of MIH at follow-up (yes/no) was analysed as a dependent variable. To evaluate the hypothesis that darker enamel opacities (yellow and brown) had higher susceptibility to structural loss over time than light ones (white), the association of colour shade of MIH opacities (white, yellow and brown) with increase in the severity of MIH over time was assessed.

Relative risk (RR) and confidence intervals (CI) were calculated, and *P*-values were obtained using the Chi-square test. To adjust the RR for the effects of covariates, a Poisson regression model with robust variance was used. Only variables with $P \leq 0.2$ in the bivariate analyses were selected for the model. The variables that remained in the Poisson regression model at $P < 0.05$ were considered as risk indicators for an increase in the severity of enamel opacity of MIH. All statistical analyses were performed with SAS software 9.1 for Windows (SAS Institute Inc. Cary, NC, USA).

Results

In this cohort study, there was a high rate of participation of children in the follow-up assessment; 80.7% (147 of 182) of all children initially recruited were re-examined. The causes of children's nonparticipation were their absence on examination days (27%), they had moved from the city (41%), they were not interested (21%) and other reasons (11%). At baseline, the number of teeth with mild MIH was 398 (100% of all tooth that were re-evaluated at follow-up) being 262 (65.8%) first permanent molars and 136 (34.2%) permanent incisors. Colours of MIH opacity ranged from white ($n = 154$), yellow ($n = 191$) to brown ($n = 53$).

Table 1 shows the distribution of increase in the severity of MIH, according to the colour of enamel opacity at baseline and after 18 months, by tooth type. After the period of 18 months, 48 teeth presented an increase in severity of MIH, 8.3% being associated with white opacities, 60.4% with yellow and 31.3% with brown opacities. Among the molars that presented increase in MIH, PEB was found

Table 1. Increase in severity of MIH according to the colour of enamel opacity after 18 months.

		Increase in severity of MIH at follow-up		
Type of teeth	**Colour of MIH (baseline) *n* (%)**	**Mild PEB (limited to enamel) *n* (%)**	**Extensive PEB (enamel + dentine) *n* (%)**	**Atypical restorations *n* (%)**
Molars	White – 83 (31.5)	4 (3.6)	–	–
	Yellow – 148 (57.4)	8 (4.1)	9 (6.2)	11 (7.6)
	Brown – 31 (11.2)	–	6 (14.3)	4 (17.8)
Incisors	White – 71 (56.2)	–	–	–
	Yellow – 43 (29)	1 (2.1)	–	–
	Brown – 22 (14.8)	–	–	5 (20.8)

PEB, posteruptive enamel breakdown; MIH, molar–incisor hypomineralization.

more frequent than atypical restorations. On the other hand, among permanent incisors, atypical composite resin restorations were more found than PEB.

Among permanent first molars, the occlusal tooth surface represented 75.5% of the all surfaces that showed an increase in severity of MIH in 2010, followed by the lingual (12.3%) and buccal surfaces (10.7%). The approximal surfaces of molars accounted for around 1.5%. For permanent incisors, the buccal surface comprised 100% of all faces that presented an increase in severity of MIH.

The bivariate analyses at tooth level using the increase in severity of MIH as the exploratory factor are shown in Table 2. Teeth that presented mild MIH associated with brown and yellow enamel opacities were at higher risk of increase in severity of MIH than those with white opacities over time. Among the demographic variables, children under the age of 10 were at higher risk for increase in severity of MIH than older children. For clinical variables, type of tooth (molars) and increment in DFS (DFS increment >0) were the risk factors for increase in severity of MIH after 18 months.

Table 3 shows the result of Poisson regression model performed with regard to the occurrence of increase in severity of MIH at follow-up. The model also showed that brown and yellow enamel opacities were at higher risk for increase in severity of MIH when compared with white ones. Further adjustment for years of age, and DFS increment at follow-up, slightly attenuated this association.

Discussion

In this cohort study, a positive association was found between the colour of enamel opacity and increase in severity of MIH after 18 months. Several previous cross-sectional studies[6,9,15–18] have shown that hypomineralized enamel was associated with PEB and atypical restorations. This is however the first prospective study that has demonstrated the higher risk of darker enamel opacity for PEB over time.

Table 2. Relative risk for increase in severity of MIH at tooth level after 18 months' follow-up.

Variables	Baseline *n*	Increase in MIH severity (FE) *n* (%)	Crude values* RR	95% CI	*P*
Colour of MIH opacity					
White	154	4 (2.6)	1.00		<0.0001**
Yellow	191	29 (15.2)	5.84	2.10–16.27	
Brown	53	15 (28.3)	10.90	3.78–31.38	
Residential area					
Rural	99	11 (11.1)	1.00	0.59–2.10	0.7379
Urban	299	37 (12.4)	1.11		
Gender					
Male	192	23 (12.0)	1.00	0.60–1.72	0.9617
Female	206	25 (12.1)	1.01		
Years of age***					
≥10 years	223	19 (8.5)	1.00	1.13–3.35	0.0144**
<10 years	175	29 (16.6)	1.94		
Type of tooth					
Incisor	136	6 (4.4)	1.00	1.58–8.33	0.0007**
Molar	262	42 (16.0)	3.63		
DMFTS at baseline					
>0	279	28 (12.3)	0.95	0.55–1.61	0.8464
0	171	20 (11.7)	1.00		
Caries increment					
>0	172	39 (17.3)	3.33	1.61–6.67	0.0003**
0	226	9 (5.2)	n1.00		

*Chi-square test, α = 5%.
***Dichotomized by median.
**Statically significant.
RR, Relative Risk; MIH, molar–incisor hypomineralization.

Table 3. Adjusted RR for increase in severity of MIH at tooth level after 18 months' follow-up.

Variables	Baseline (*N*)	Increase in MIH severity (FE) *N* (%)	Adjusted values* RR	95% CI	*P*
Colour of MIH opacity					
White	154	4 (2.6)	1.00		
Yellow	191	29 (15.2)	5.37	1.72–16.76	0.0037
Brown	53	15 (28.3)	9.46	2.94–30.44	0.0002
Years of age					
≥10 years	223	19 (8.5)	1.00	1.01–3.06	0.0443
<10 years	175	29 (16.6)	1.76		
Caries increment					
>0	172	39 (17.3)	3.22	1.28–8.33	0.0129
0	226	9 (5.2)	1.00		

*Poisson regression.
RR, Relative Risk; MIH, molar–incisor hypomineralization.

In this study, brown and yellow enamel opacities were at higher risk for PEB and atypical restorations than white ones. This relationship remained even after adjustment for years of age, type of tooth and DFS increment at follow-up. Laboratory studies may explain the relationship between colour of enamel opacity and trend towards PEB. Hypomineralized areas in enamel showed a reduction in mechanical properties and in mineral density[20–26], which facilitates PEB. Moreover, it has been shown that there is a relationship between hardness values, mineral density and the colour of the hypomineralized enamel, with yellow/brown opacities being softer than white ones[25,26]. Jälevik and Noren[5] showed that yellow/brown opacities were more porous than lighter opacities. This finding could also contribute to the reduction in the mechanical properties of dark enamel opacities.

Other variables were also related to the increase in severity of MIH after 18 months. Among the demographic variables, the children's age was associated with PEB and atypical restorations. Previous cross-sectional studies[6,18,19] have shown that as age increased, there was higher prevalence of clinical severity of the affected teeth, probably because of the presence of masticatory forces for long periods. This study however showed that children under 10 years of age presented higher risk for an increase in severity of MIH than older children. An explanation for this finding could be the fact that a higher prevalence of moderate and severe defects was found among children older than 10 years of age at baseline[18], leaving few teeth for analysis among older children. A further explanation is that by the time children reached this age, most surfaces prone to enamel disintegration had already broken down. The remaining opacities were probably less porous or less exposed to masticatory forces.

Regarding clinical variables, the type of tooth and DFS increment at follow-up were associated with an increase in severity of MIH after 18 months. More cases of increase in severity of MIH were found among molars than incisors, although after adjustment by Poisson regression, this difference was no longer statistically significant. For molars, PEB was the main cause of increase in severity of MIH, probably because of the high incidence of masticatory forces on the opacities[14], especially considering that the occlusal surface was the one most frequently reported as having increase in severity of MIH. Among incisors, atypical restorations on the buccal surface were the main cause of increase in severity of MIH at follow-up. The high incidence of atypical restorations on incisors could be related to an aesthetic concern[31] rather than PEB, because there are generally no masticatory forces on the opacities in incisors[14]. Moreover, several cross-sectional studies have shown that in general, the defects in incisors are mild[18,19,32].

Atypical restorations performed on previously demarcated enamel opacity were considered an increase in severity of MIH; however, their potential causes were not determined in this study. This could be considered a limiting factor. Nevertheless, the reduction in mechanical properties and mineral content of the hypomineralized enamel[20–26] in addition to the high caries incidence in the studied population is probably the main cause of atypical restorations over time.

In this study, dental caries activity was measured as DS and FS increments, which contributed to an increase in severity of MIH. The relationship between the increase in dental caries activity and MIH severity may be explained by the porous nature of hypomineralized enamel. It is possible that PEB is increased by the action of cariogenic bacteria that initially invade intact hypomineralized enamel and subjacent dentin[24,33] and rapidly destroy the originally hypomineralized tissue[6].

In this study, MIH was classified into three levels of severity: mild, moderate and severe according to Leppäniemi et. al[6]. The aim was to show more details about the initial level and increase in severity of MIH over time. Other studies have classified MIH into two groups, in which severe and moderate defects were combined into one group named disintegrated or severe defects[16,19]. Size, location and extension of structural loss have been also considered in the classification criteria of severity [2,3,9]. Furthermore, Mathu-Muju and Wright[34] suggested that tooth sensitivity and aesthetic concerns expressed by children or their parents should be considered as additional criteria for assessing the severity of MIH.

In epidemiologic and clinical studies, the level of severity of MIH is important, because it reflects the treatment needs of affected children; however, because of the lack of a well-defined standard for the classification of MIH severity, it is difficult to make comparisons among studies. Therefore, it is important to report the severity of defects in a comparable manner, and as suggested by Jälevik[35], dividing the severity of MIH into two groups seems to lead to better reproducibility.

Clinically, it is challenging to estimate the risk of increase in severity of MIH. This study highlighted some risk factors involved at tooth level (such as the colour of MIH opacity and type of tooth) and personal level (children's age and caries activity, measured by DFS increment). The localization of lesions also interferes with the increase in severity of MIH, because the occlusal surfaces showed the highest increase in severity of MIH. After controlling for other potential factors, Poisson's regression model suggested that the colour of enamel opacity seems to be a good predictor for PEB and atypical restorations. The higher susceptibility of yellow and brown enamel opacity to PEB and atypical restorations implies that even if only a dark colour change is present, the defective enamel may be a locus of lowered resistance and therefore more prone to PEB and dental caries. This result confirms that the visually assessed colour of enamel opacity reflects the severity of MIH[26]. This finding must be highlighted, because it could help clinicians to predict and individualize early interventions to prevent and control possible future threats to the children's dentition.

Conclusions

This cohort study showed that MIH could be considered a progressive defect over time. Some tooth risks and personal characteristics are associated with the increase in severity of MIH. Among these factors, the colour of enamel opacity seems to be a good predictor for future PEB and atypical restorations. This result could help clinicians to determine an early risk-based treatment for children with MIH when a dark colour change is present in an erupting tooth.

What this paper adds?

- This study is the first cohort study evaluating clinical and demographic risk factors associated with an increase in severity of MIH.
- This paper showed that the colour of enamel opacities and dental caries activity are valuable clinical risk factors for increase in severity of MIH.

Why this paper is important to paediatric dentists?

- Paediatric dentists must be aware of the presence and colour characteristics of MIH opacity and its clinical consequences. This cohort study demonstrated that children presenting darker MIH opacities are at higher risk of developing enamel breakdown and requiring more atypical restorations than those presenting white opacities.

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