Pesquisa Brasileira em Odontopediatria e Clínica Integrada 2024; 24:e230066
https://doi.org/10.1590/pboci.2024.072
ISSN 1519-0501 / eISSN 1983-4632

ORIGINAL ARTICLE

Clinical Presentation and Risk Factors for Molar-Incisor and Second Primary Molar Hypomineralization: A Cross-Sectional Study

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Academic Editor: Catarina Ribeiro Barros de Alencar

Received: April 06, 2023 / **Review:** September 14, 2023 / **Accepted:** November 22, 2023

How to cite: Rosa TC, Silva FMF, Vieira FGF, Vieira AR, Gonçalves AF, Costa MC, et al. Clinical presentation and risk factors for molar-incisor and second primary molar hypomineralization: A cross-sectional study. Pesqui Bras Odontopediatria Clín Integr. 2024; 24:e230066. https://doi.org/10.1590/pboci.2024.072

ABSTRACT

Objective: To identify the clinical presentation of molar incisor hypomineralization (MIH) and hypomineralization of second primary molars (HSPM), including the distribution patterns of presence and severity of lesions, and to investigate the association of risk factors during the pre-and postnatal period with the presence of lesions. **Material and Methods:** This cross-sectional study was conducted with 160 individuals (72 with MIH/HSPM and 88 without lesions). The symmetry analysis regarding the presence and severity of MIH/HSPM was evaluated in pairs of homologous and opposite teeth. Sociodemographic and medical information was obtained using a detailed questionnaire. Data were analyzed by means of chi-square tests, Student's t-test, and logistic regression ($p<0.05$). **Results:** Symmetry of presence and severity of hypomineralization lesions were present in homologous permanent teeth in 53.8% and 70.5% of cases, respectively, with statistically significant results only for the symmetrical pattern of severity of MIH lesions in the maxillary first molars ($p=0.016$) and mandibular first molars ($p=0.02$). Otherwise, a non-symmetric presence was statistically significant in homologous second primary molars ($p=0.002$) and opposite primary and permanent teeth ($p\leq0.001$). An association between MIH/HSPM and systemic diseases during pregnancy and children medication was found ($p<0.05$); however, no evidence was found between these and MIH/HSPM severity. **Conclusion:** The symmetric pattern of severity of MIH lesions was statistically significant in permanent homologous teeth. Risk factors during pre and postnatal periods may be related to MIH/HSPM; however, these do not seem to interact with severity.

Keywords: Dental Enamel; Tooth Demineralization; Developmental Defects of Enamel.

Introduction

The perceived increase in the prevalence of developmental defects of enamel (DDE) has prompted research to identify possible related etiological factors and more appropriately characterize these conditions [1,2]. Molar incisor hypomineralization (MIH) is one of the most common enamel defects [3,4]. Its global prevalence is estimated at 14.2% [5], and its functional and aesthetics consequences to individuals can currently be considered an important oral health problem [6].

MIH is defined as a qualitative developmental enamel defect affecting at least one permanent molar but may also affect permanent incisors [1]. Similar hypomineralized lesions have been identified in primary teeth, known as hypomineralized second primary molars (HSPM) [7]. Depending on the severity, the affected teeth are characterized by demarcated opacities varying from white/yellowish to brown color and post-eruptive enamel breakdown [8]. Another reported characteristic of MIH is the asymmetric distribution of lesions regarding presence and phenotypes (color of the opacities), corresponding to different degrees of severity [9].

Theories on the occurrence of the different clinical phenotypes are related to gene expression and/or environmental factors [10]. There is already some evidence indicating that polymorphisms in genes involved in enamel formation are implicated in the occurrence of MIH [11]. Environmental factors have also been related to the etiology of MIH, such as the use of medication and severe infections in the pre/perinatal or childhood period [12,13]. Thus, it is important to explore further associations of possible etiological factors related to MIH since this information may help to understand the clinical characteristics and distribution of affected teeth.

Therefore, the aims of this study were to identify the clinical presentation of MIH and HSPM, including the location and severity of lesions and to investigate the association of risk factors during pre- and postnatal period with presence of lesions.

Material and Methods

This study was reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [14].

Study Design

This cross-sectional study was approved by the local Research Ethics Committee (Protocol no. 1.130.443). The caregivers and the participants received information regarding the purpose of the study and provided written informed consent.

Setting

The sample was gathered between July 2015 and September 2019. Individuals aged 7-14 years old, living in the urban area of the city of Rio de Janeiro, Brazil, who were referred for dental care at the Pediatric Dental Clinic of the Federal University of Rio de Janeiro were selected. The data were collected from the dental files from July 2020 to December 2020.

Participants and Sample Size

The inclusion criteria were individuals aged between 7-14 years old, presenting for dental examination with the four erupted first permanent molars (FPMs). Participants were divided in "case group", for those showing at least one FPM or second primary molar affected by MIH/HSPM or included in the "control group" if no signs of MIH/HSPM were noted. The exclusion criteria were medically compromised individuals, those

presenting with syndromes, other enamel defects (such as fluorosis, amelogenesis imperfecta and hypoplasia), those undergoing orthodontic treatment (with banded first permanent molars) and those whose caregivers could not provide information on the prenatal and postnatal period until the first four years of the child's life.

As a service evaluation, this study included all records of patients seen at the university pediatric dentistry service during the selected time period, using a convenience sampling approach. Initially, 407 records of children and adolescents, with complete information were selected. With the application of the inclusion criteria, a total of 160 individuals between 7 and 14 years of age were selected (72 for the case group and 88 for the control group), as seen in Figure 1.

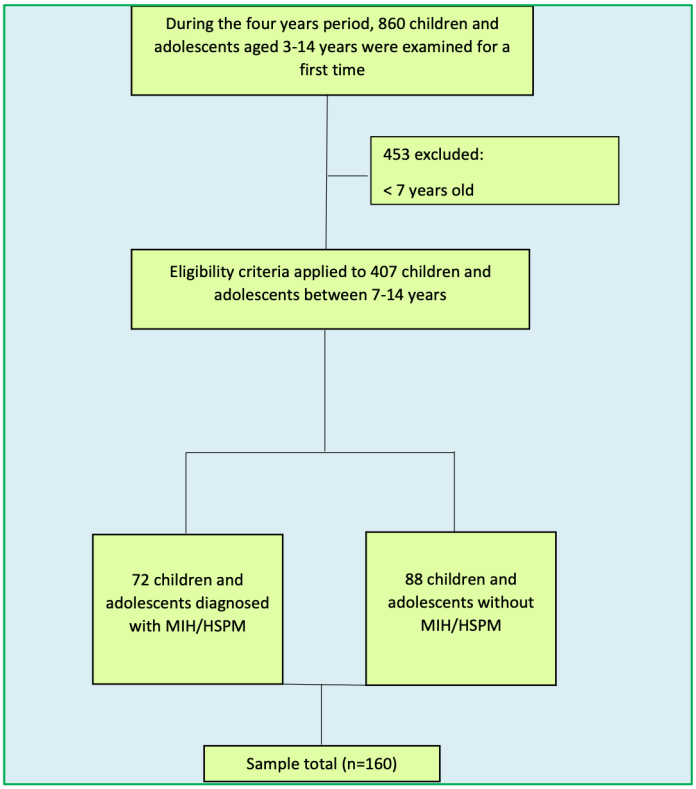

Figure 1. Flowchart of study participants.

Calibration

A calibration exercise was carried out in two stages, including theoretical and practical activities to assess intra and inter-examiner reliability for the diagnosis of MIH/HSPM. The theoretical step consisted of discussing the clinical characteristics and the differential diagnosis between the different enamel defects and sound teeth. The practical step was performed with 27 clinical images of enamel defects, including fluorosis, hypoplasia, amelogenesis imperfecta, MIH and HSPM with different locations, discoloration, and severity of breakdown. The main investigator (F.M.F.) examined these images independently and after one week of the first examination. The intra-examiner and inter-examiner kappa reached were 0.90 and 0.84, respectively.

Outcome Variables

The clinical examination was conducted by a calibrated pediatric dentist (F.M.F), with the child positioned in the dental chair and facing the examiner, using artificial lighting (Olsen, Palhoça, Santa Catarina). The examination involved the use of a dental mirror (Golgran Indústria e Comércio de Instrumental Odontológico, São Caetano do Sul, SP, Brazil) and WHO probe (Trinity Ind. e Com. Ltda., São Paulo, SP, Brazil),

along with sterile gauze (Dental Cremer Produtos Odontológicos, Blumenau, SC, Brazil). Prior to the examination, prophylaxis was performed using a pumice stone (Biodinâmica, Ibiporã, PR, Brazil) and a Robinson brush (Preven Ind. e Com. de Produto Odontológicos, Guapirama, PR, Brazil). In cases where no symptoms of sensitivity were present, compressed air (Olsen, Palhoça, SC, Brazil) was used to dry the tooth surfaces. The diagnosis of MIH/HSPM was based on the criteria established by the European Academy of Paediatric Dentistry [8]. In brief, all present teeth were examined and those presenting demarcated opacities, post-eruptive enamel breakdown, atypical restorations, atypical dental caries or were extracted due to MIH/HSPM were reported. The severity of the lesions was considered as mild when the tooth presented demarcated opacities ≥ 1.0mm, without enamel breakdown or severe, if the tooth showed enamel breakdown, atypical dental caries, or restorations (Figure 2). Demarcated opacities ≤ 1.0mm were not included in the study.

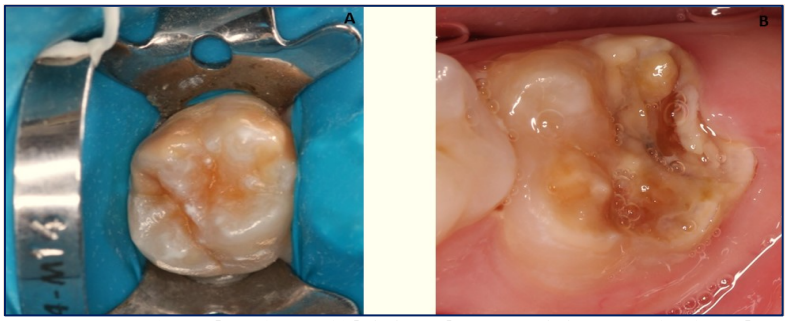

Figure 2. First permanent molars showing mild (A) and severe (B) molar incisor hypomineralization.

For the analysis of symmetry of presence and severity of MIH, six pairs of homologous permanent teeth were evaluated in each patient: maxillary first permanent molars (16 and 26), mandibular first permanent molars (36 and 46), maxillary central permanent incisors (11 and 21), mandibular central permanent incisors (31 and 41), maxillary lateral permanent incisors (12 and 22), and mandibular lateral permanent incisor (32 and 42). When the participant was in the mixed dentition, two pairs of teeth were also evaluated for the presence of HSPM: maxillary primary second molars (55 and 65) and mandibular primary second molars (75 and 85). The same was performed for evaluation of opposite teeth: maxillary and mandibular first permanent molars (16 and 46; 26 and 36), maxillary and mandibular permanent central incisors (11 and 41; 21 and 31), maxillary and mandibular permanent lateral incisors (12 and 42; 22 and 42) and maxillary and mandibular second primary molars (55 and 85; 65 and 75).

For each pair of evaluated teeth, the symmetry of presence was first determined (yes/no). If the symmetry of presence was detected, the symmetry of severity was then investigated (yes – both teeth showing the same severity; no – each tooth showing a different degree of severity). Pairs of teeth without MIH/HSPM were not included in this analysis.

Collection of Medical History

General health data were collected for both groups using a structured questionnaire formulated by the authors through an interview with the patient's mother. This questionnaire included sociodemographic data and possible risk factors during the patient's prenatal and postnatal periods. Prenatal factors included information on the mother's health during pregnancy (presence of diabetes and hypertension), medications taken, and complications during childbirth (premature birth and hypoxia). Postnatal factors included history of

hospitalization, medications taken up to four years of age (antibiotic, corticoid and/ or other medications), records of severe infections, fever, and breathing problems (asthma, bronchitis, or pneumonia).

Statistical Analysis

The data were organized in Excel® (Microsoft Corporation, Redmond, Washington) and analyzed using the software SPSS (Statistical Package for Social Science for Windows, version 21.0, SPSS Inc., Chicago, Illinois). The chi-square test and student's t-test were used to compare groups in relation to the sociodemographic data ($p<0.05$). Descriptive statistics was carried out to observe the frequency of affected teeth by MIH/HSPM. The chi-square test was used to assess the association of symmetry for the presence and severity of MIH/HSPM lesion for each homologous and opposite pair of teeth ($p<0.05$). Finally, bivariate logistic regression and odds ratio were performed to assess the chances between the variables (risk factors during pregnancy period and child up to four years of life) in relation to the groups (with and without MIH/HSPM) ($p<0.05$). The backward stepwise procedure was used to include or exclude variables in the fitting of models in logistic regression analyses. In addition, the chi-square test also assessed the association between risk factors and MIH/HSPM severity ($p<0.05$).

A power calculation was obtained for the case-control comparisons using a value of 0.4 (40%) of exposure in the control group, a 0.35 (35%) relative risk of disease associated with exposure, alfa value of 5% and a minimal sample of 72 individuals, with a resulting power of 0.8.

Results

The final sample consisted of 160 individuals, divided into case (n=72) and control group (n=88) (Figure 1). The overall prevalence of MIH/HSPM in the population evaluated in this study was 17.7%. There was no association and statistical significance between the groups in relation to demographic characteristics (Table 1).

Table 1. Characteristics of the sample.

Variables	Case Group N (%)	Control Group N (%)	Total N (%)	p-value
Gender				
Male	39 (54.8)	49 (55.7)	88 (55.0)	0.874*
Female	33 (45.2)	39 (44.3)	72 (45.0)	
Total	72 (100.0)	88 (100.0)	160 (100.0)	
Mean Age (SD)	10.8 (±1.8)	9.9 (±1.5)	10.1 (±1.6)	0.601**
Ethnicity				
White	23 (26.1)	22 (30.6)	45 (28.1)	0.707*
Mixed Background	51 (58.1)	13 (18.1)	88 (55)	
Black	14 (15.9)	37 (51.4)	27 (16.9)	
CCEB[a]				
High	4 (5.6)	5 (5.7)	9 (5.6)	0.999*
Middle Income	63 (87.5)	77 (87.5)	140 (87.5)	
Low Income	5 (6.9)	6 (6.8)	11 (6.9)	

*Chi-square test; **Student's t-test; [a]Family income was obtained by the Brazilian Economic Classification Criteria (*Critério de Classificação Econômica Brasil* – CCEB).

Distribution of MIH/HSPM Lesions

From the 72 patients of the MIH/HSPM case group, 1.840 teeth were examined. Of these, 30 (1.63%) were primary teeth diagnosed with HSPM and 311 (16.9%) were permanent teeth with MIH. Most affected teeth were the maxillary and mandibular first permanent molars (n=188; 60.5%) followed by the maxillary central

incisors (n=49; 15.8%). Considering the severity of MIH/HSPM lesions, 76.2% (n = 260) of teeth were mildly affected (Table 2).

Table 2. Distribution of teeth with MIH/HSPM by dentition, groups of teeth and frequency of severity.

Dentition	Groups of Teeth	Affected Teeth	Severity	
			Mild	Severe
		N (%)	N (%)	N (%)
Primary	Maxillary Second Molars	18 (60.0)	12 (60.0)	6 (60.0)
	Maxillary Canine	1 (3.3)	1 (5.0)	--
	Mandibular Canine	1 (3.3)	1 (5.0)	--
	Mandibular Second Molars	10 (33.4)	6 (30.0)	4 (40.0)
	Total Primary Teeth Affected	30 (8.8)	20 (66.7)	10 (33.3)
Permanent	Maxillary Second Molar	1 (0.33)	1 (0.42)	--
	Maxillary First Molars	94 (30.2)	66 (27.5)	28 (39.5)
	Maxillary Second Premolar	1 (0.33)	1 (0.42)	--
	Maxillary Canine	3 (0.97)	2 (0.83)	1 (1.4)
	Maxillary Lateral Incisor	19 (6.3)	18 (7.5)	1 (1.4)
	Maxillary Central Incisors	49 (15.7)	45 (18.8)	4 (5.6)
	Mandibular Central Incisors	25 (8.0)	25 (10.1)	--
	Mandibular Lateral Incisor	22 (7.0)	22 (9.2)	--
	Mandibular Canine	3 (0.97)	2 (0.83)	1 (1.4)
	Mandibular First Molars	94 (30.2)	58 (24.3)	36 (50.7)
	Total Permanent Teeth	311 (91.2)	240 (77.2)	71 (22.8)
	Total	341 (100.0)	260 (76.2)	81 (23.8)

Regarding the distribution of MIH lesions in each dental arch (Table 3), from the 197 pairs of homologous permanent teeth evaluated, no statistically significant difference was seen regarding symmetry of occurrence of MIH lesions, with 53.8% of pairs showing symmetry and 46.2% with asymmetric lesion presence. Symmetry of lesion severity between pairs of homologous permanent teeth was statistically significantly higher for mandibular first permanent molars and maxillary first permanent molars compared to the other tooth groups ($p \leq 0.05$). For the primary dentition, asymmetric presence of hypomineralization lesions was identified in homologous second primary molars ($p=0.002$) (Table 3).

There was a clear tendency for asymmetric presence of lesions among pairs of opposite teeth (n=233 pairs; 75.6% asymmetric presence), especially for anterior teeth ($p<0.05$). For posterior opposite teeth, asymmetric presence of lesions was also identified, although associations were only disclosed for the comparison between primary teeth (65 *versus* 75). No statistically significant tendency of symmetry was seen regarding the severity of the lesions in pairs of opposite teeth presenting MIH/HSPM ($p \geq 0.05$) (Table 4).

Association Between Risk Factors and the Presence and Severity of MIH/HSPM

The presence of MIH/HSPM was associated with some risk factors during the prenatal period, including systemic disease during pregnancy (OR=2.43; 95% CI=1.60-5.10, p=0.019) and complications during childbirth (OR=4.20; 95% CI=1.29-13.65, p=0.017) and in the postnatal period, including medication taken in childhood up to four years of age (OR=3.26; 95% CI 1.52-6.97, p=0.002) and systemic diseases (OR=3.04; 95% CI=1.16-7.97, p=0.017). After adjusting the model for risk factors, only a few variables remained associated with MIH/HSPM ($p< 0.05$) (Table 5). In addition, risk factors were not associated with the degree of severity of MIH/HSPM (Table 6).

Table 3. Distribution of pairs of homologous teeth according to symmetry of MIH/HSPM presence and severity.

Type of Teeth	Presence of MIH/HSPM Lesions				Severity of MIH/HSPM Lesions				
	Asymmetry[1] N (%)	Symmetry[1] N (%)	Total Pairs of Teeth N (%)	p-value*	Asymmetry[2] N (%)	Symmetry[2] Mild +Mild N (%)	Symmetry[2] Severe+Severe N (%)	Total Pairs of Teeth N (%)	p-value*
Permanent Teeth									
11 *versus* 21	15 (46.8)	17 (53.2)	32 (100.0)	0.724	5 (29.5)	11 (64.7)	1 (5.9)	17 (100.0)	0.090
12 *versus* 22	9 (64.3)	5 (35.7)	14 (100.0)	0.295	1 (20.0)	4 (80.0)	--	5 (100.0)	-
16 *versus* 26	26 (43.4)	34 (56.6)	60 (100.0)	0.304	10 (29.5)	21 (61.8)	3 (8.8)	34 (100.0)	0.016
31 *versus* 41	11 (61.1)	7 (38.9)	18 (100.0)	0.346	1 (42.8)	6 (57.2)	--	7 (100.0)	0.254
32 *versus* 42	8 (53.3)	7 (46.7)	15 (100.0)	0.796	4 (57.2)	3 (42.8)	--	7 (100.0)	0.705
36 *versus* 46	22 (37.9)	36 (62.1)	58 (100.0)	0.066	11 (30.6)	19 (52.8)	6 (16.7)	36 (100.0)	0.020
Total Permanent Teeth	91(46.2)	106 (53.8)	197 (100.0)	0.285	31 (29.5)	64 (61.0)	10 (9.5)	105 (100.0)	0.006
Primary Teeth									
55 *versus* 65	16 (88.8)	2 (11.2)	18 (100.0)	0.005	-	2 (100.0)	--	2 (100.0)	-
75 *versus* 85	8 (80.0)	2 (20.0)	10 (100.0)	0.058	2 (100.0)	-	--	2 (100.0)	-
Total Primary Teeth	24 (85.7)	4 (14.2)	28 (100.0)	0.002	2 (50.0)	2 (50.0)	--	4 (100.0)	-

[1]Symmetry = Presence of MIH/HSPM lesion in both teeth of homologous pair; [1]Asymmetry = Presence of MIH/HSPM lesion in only one teeth of homologous pair; [2]Symmetry = Presence of MIH/HSPM lesion in homologous teeth with the same degree of severity; [2]Asymmetry = Presence of MIH/HSPM lesion in homologous teeth with different degree of severity; *Chi-square test.

Table 4. Distribution of pairs of opposite teeth according to symmetry of MIH/HSPM presence and severity.

Type of Teeth	Presence of MIH/HSPM Lesions				Presence and Severity of MIH/HSPM Lesions				
	Asymmetry[1] N (%)	Symmetry[1] N (%)	Total Pairs of Teeth N (%)	p-value*	Asymmetry[2] N (%)	Symmetry[2] Mild +Mild N (%)	Symmetry[2] Severe+Severe N (%)	Total Pairs of Teeth N (%)	p-value*
Permanent Teeth									
11 *versus* 41	20 (74.1)	7 (25.9)	27 (100.0)	0.012	--	7		7 (100.0)	--
21 *versus* 31	26 (81.2)	6 (18.8)	32 (100.0)	≤0.001	--	6	--	6 (100.0)	--
12 *versus* 42	13 (81.2)	3 (18.8)	16 (100.0)	0.008	--	3		3 (100.0)	--
22 *versus* 32	13 (81.2)	3 (18.8)	16 (100.0)	0.012	--	3	--	3 (100.0)	--
16 *versus* 46	41 (59.4)	28 (40.6)	70 (100.0)	0.151	9 (32.1)	15 (53.6)	4 (14.3)	28 (100.0)	0.059
26 *versus* 36	34 (59.6)	23 (40.4)	57 (100.0)	0.145	9 (39.1)	9 (39.1)	5 (22.8)	23 (100.0)	0.221
Total Permanent Teeth	219 (75.7)	70 (24.3)	289 (100.0)	≤0.001	18 (35.2)	24 (47)	9 (17.6)	51 (100.0)	≥0.05

Primary Teeth									
55 versus 85	8 (66.6)	4 (33.4)	12 (100.0)	0.248	2 (50.0)	2 (50.0)	--	4 (100.0)	--
65 versus 75	6 (85.7)	1 (14.3)	7 (100.0)	0.044	--	1 (100.0)	--	1 (100.0)	-
Total Primary Teeth	14 (73.6)	5 (26.4)	19 (100.0)	≤0.001	2 (40.0)	3 (60.0)	--	5 (10.00)	-

[1]Symmetry = Presence of MIH/HSPM lesion in both teeth of opposite pair; Asymmetry = Presence of MIH/HSPM lesion in only one teeth of opposite pair; [2]Symmetry = Presence of MIH/HSPM lesion in opposite teeth with the same degree of severity; [2]Asymmetry = Presence of MIH/HSPM lesion in opposite teeth with different degree of severity.; *Chi-square test.

Table 5. Interaction between risks factors and presence of MIH/HSPM during in the prenatal and postnatal period (n=160).

Variables	MIH/HSPM		Crude OR (95% CI)	p-value*	Adjusted OR (95% CI)	p-value**
	Absence N (%)	Presence N (%)				
Prenatal Characteristic						
Systemic Diseases						
No	73 (60.3)	48 (39.7)				
Yes	15 (38.5)	24 (61.5)	2.43 (1.60 - 5.10)	0.019	2.17 (1.08- 4.67)	0.048
Medication Taken						
No	74 (59.2)	51 (40.8)				
Yes	14 (40.0)	21 (60.0)	2.17 (1.01 - 4.67)	0.046	***	----
Complications During Childbirth						
No	84 (58.3)	60 (41.7)				
Yes	4 (25.0)	12 (75.0)	4.20 (1.29-13.65)	0.017	2.58 (0.72- 9.24)	0.144
Postnatal Characteristics						
History of Hospitalization up to 4 Years of Age						
No	84 (57.1)	63 (42.9)				
Yes	4 (30.8)	9 (69.2)	3.0 (0.98-1.13)	0.078	***	--
Medication Taken in Early Childhood (Until 4 Years)						
No	75 (62.0)	46 (38.0)				
Yes	13 (33.3	26 (66.7)	3.26 (1.52- 6.97)	0.002	2.36 (1.03 – 5.41)	0.042
Systemic Diseases (Until 4 Years)						
No	81 (58.7)	57 (41.3)				
Yes	7 (31.8)	15 (68.2)	3.04 (1.16- 7.94)	0.017	***	--

*p-value in bivariate regression analysis p<0.05; **p-value in backward stepwise adjusted model regression analysis p<0.05; ***Variables not included in adjusted analysis.

Table 6. Relationship between MIH/HSPM severity and risk factors during pre and postnatal period (n=72).

Variables	Mild N (%)	Severe N (%)	p-value*
Prenatal Characteristics			
Systemic Diseases During Gestational Period			
No	25 (52.1)	23 (47.9)	0.867
Yes	13 (61.9)	11 (45.8)	
Medication Taken Period Gestational Period			
No	25 (49.0)	26 (51.0)	0.320
Yes	13 (61.9)	8 (38.1)	
Complications During Childbirth			0.354
No	30 (50.0)	30 (50.0)	
Yes	8 (66.7)	4 (33.3)	
Postnatal Characteristics			
History of Hospitalization up to 4 Years of Age			0.592
Yes	34 (54.0)	29 (46.0)	
No	4 (44.4)	5 (55.6)	
Medication Taken in Early Childhood (Until 4 Years)			
No	24 (52.2)	22 (47.8)	0.891
Yes	14 (53.8)	12 (46.2)	
Systemic Diseases (Until 4 Years)			
No	15 (57.7)	11 (42.3)	0.530
Yes	23 (50.0)	23 (50.0)	

*Chi-square test.

Discussion

Some of the most recently studied topics on MIH have been the pattern of distribution of lesion severity among the dentition and the possible associated etiologic factors [15]. Our study focused on the clinical characteristics and distribution of teeth affected by hypomineralization defects and the possible association of environmental factors occurring during the prenatal and postnatal periods with its presence. Regarding lesion presence and distribution, the present study agrees with the literature, which reports that the majority of hypomineralization lesions are present in the maxillary arch [16,17].

An interesting observation in the present work was that hypomineralization lesions were not limited to FPMs, permanent incisors and primary second molars, with lesions also present in other groups of teeth, such as permanent canines, second premolars and second molars, albeit with lower prevalence, in accordance with other observations [18]. On the other hand, our sample consisted of individuals with an average age of 10 years, which may explain the lower prevalence of MIH in canines and permanent second molars, since complete eruption of these teeth usually occurs after 10 years of age.

MIH is cited, in most of the studies as an asymmetric defect, since the same patient may present the condition in different teeth with varying severity and this has been influenced by gene expression and/or environmental factors [10]. In fact, MIH may present variable clinical presentations in relation to number of affected surfaces, color, and loss of structure [19]. Biondi et al. [9] reported 49.9% of permanent homologous teeth with symmetry of presence (both teeth in a pair showing lesions) and from these, 82.6% showed similar severity. The present study has shown similar results, with 53.8% of pairs of homologous permanent teeth showing symmetry for presence, especially among the first permanent molars and 70.5% showing similar severity. An additional point of our study was the analysis between pairs of opposite teeth, which showed only higher prevalence of symmetric lesions among anterior teeth.

Regarding severity, most affected teeth in our study showed mild lesions (260; 76.2%). In fact, it has been observed that lesion severity increases with patient's age [20] in association with decreased mechanical properties of MIH affected teeth, resulting in post-eruptive enamel breakdown over time [3]. Regarding the distribution of lesion severity in the present study, most lesions were also symmetric, both for homologous (70.5%) and opposite permanent teeth (64.6%), but these results should be analyzed in view of the dichotomous diagnostic criteria used in this study, which used only mild (demarcated opacity) or severe (loss of structure, atypical restorations, and dental caries) classification. Data such as color and numbers of surfaces affected by MIH/HSPM, were not included in the classification of severity.

The literature reports no association between the prevalence of enamel hypomineralization and sex [3,21] or socioeconomic condition [22]. These data are in line with the results of this study, although most individuals with MIH belonged to the middle socioeconomic group. Some studies suggested an association of MIH presence with socioeconomic status, especially in families considered middle and high-income [23,24]. Considering ethnicity and MIH, no association was found in the present study. Future multicenter studies should be undertaken to unveil potential differences between such genetically heterogeneous populations.

MIH has been recently considered a multifactorial disease [1]. Risk factors such as use of medication and occurrence of systemic diseases during pregnancy and in the first years of life have been associated with this condition [12,13]. A recent systematic found similar results [25], although it reported that peri- and postnatal etiological factors are more likely to increase the odds of causing MIH than prenatal factors. In addition, more recently, a potential interaction between genes and environmental factors related to enamel development defects has also been reported, mainly as medication use in the first three years of life [26,27]. In fact, in this study, we found a significant association with using medications in a child's first four years of life and presence of MIH.

Regarding the degree of severity, there was no association between risk factors during pre and postnatal period with severity of MIH lesions. This could be attributed to the fact that the severity of MIH/HSPM lesions is also probably related to genetic influences, resulting in the different phenotypes such as lesion color, structure loss and groups of affected teeth [10]. Thus, future research should consider investigating the potential impact of genetic-environmental interactions on both the development and severity of MIH.

A larger sample size could have enabled definitive comparisons of the association between pre- and postnatal risk factors and the presence of MIH. Therefore, the results of this study should be only considered as pathways for further investigations. Other limitations of the present study include the use of a restrictive dichotomous severity variable and the common memory bias observed in retrospective studies. Finally, a significant part of the enrolled patients received treatment at a university clinic and were referred for this specific condition, what could bring some selection bias. On the other hand, this study used a detailed and validated clinical criterion, employed by an experienced pediatric dentist and included mothers as the main source of the medical history data, increasing the confidence of the obtained results.

Conclusion

No clear preference for presence of symmetric/asymmetric lesion presence in pairs of homologous teeth were observed. In opposite tooth pairs, a tendency for asymmetric lesion presence were found, especially in anterior teeth. Regarding the severity of lesions, a tendency for symmetric distribution was observed in all tooth pairs studied. In addition, the study concluded that risk factors during the pre and postnatal periods may be related to the development presence of MIH/ HSPM; however, it was not possible to identify interactions of these factors with the severity of this condition.

Authors' Contributions

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All authors declare that they contributed to critical review of intellectual content and approval of the final version to be published.

Financial Support

This study was financed in part by the Coordination for the Improvement of Higher Education Personnel – Brazil (CAPES) – Finance Code 001 and Rio de Janeiro State Agency for Research Support—FAPERJ (Grant number: E-26/202.035/2020).

Conflict of Interest

The authors declare no conflicts of interest.

Data Availability

The data used to support the findings of this study can be made available upon request to the corresponding author.

References

[1] Lygidakis NA, Garot E, Somani C, Taylor GD, Rouas P, Wong FSL. Best clinical practice guidance for clinicians dealing with children presenting with molar-incisor-hypomineralisation (MIH): An updated European Academy of Paediatric Dentistry policy document. Eur Arch Paediatr Dent 2022; 23(1):3-21. https://doi.org/10.1007/s40368-021-00668-5

[2] Schwendicke F, Elhennawy K, Reda S, Bekes K, Manton DJ, Krois J. Global burden of molar incisor hypomineralization. J Dent 2018; 68(1):10-18. https://doi.org/10.1016/j.jdent.2017.12.002

[3] Costa-Silva CM, Jeremias F, de Souza JF, Cordeiro Rde C, Santos-Pinto L, Zuanon AC. Molar incisor hypomineralization: Prevalence, severity, and clinical consequences in Brazilian children. Int J Paediatr Dent 2010; 20(6):426-434. https://doi.org/10.1111/j.1365-263X.2010.01097.x

[4] Mejía JD, Restrepo M, González S, Álvarez LG, Santos-Pinto L, Escobar A. Molar incisor hypomineralization in Colombia: Prevalence, severity, and associated risk factors. J Clin Pediatr Dent 2019; 43(3):185-189. https://doi.org/10.17796/1053-4625-43.3.7

[5] Zhao D, Dong B, Yu D, Ren Q, Sun Y. The prevalence of molar incisor hypomineralization: evidence from 70 studies. Int J Paediatr Dent 2018; 28(2):170-179. https://doi.org/10.1111/ipd.12323

[6] Leal SC, Oliveira TRM, Ribeiro APD. Do parents and children perceive molar-incisor hypomineralization as an oral health problem? Int J Paediatr Dent 2017; 27(5):372-379. https://doi.org/10.1111/ipd.12271

[7] Elfrink ME, Ten Cate JM, Jaddoe VW, Hofman A, Moll HA, Veerkamp JS. Deciduous molar hypomineralization and molar incisor hypomineralization. J Dent Res 2012; 91(6):551-555. https://doi.org/10.1177/0022034512440450

[8] Ghanim A, Silva MJ, Elfrink MEC, Lygidakis NA, Marino RJ, Weerheijm KL, et al. Molar incisor hypomineralisation (MIH) training manual for clinical field surveys and practice. Eur Arch Paediatr Dent 2017; 18(4):225-242. https://doi.org/10.1007/s40368-017-0293-9

[9] Biondi AM, Córtese SG, Babino L, Toscano MA. Molar incisor hypomineralization: Analysis of asymmetry of lesions. Acta Odontol Latinoam 2019; 32(1):44-48.

[10] Vieira AR, Manton DJ. On the variable clinical presentation of molar-incisor hypomineralization. Caries Res 2019; 53(4):482-488. https://doi.org/10.1159/000496542

[11] Jeremias F, Pierri RA, Souza JF, Fragelli CM, Restrepo M, Finoti LS, et al. Family-based genetic association for molar-incisor hypomineralization. Caries Res 2016; 50(3):310-318. https://doi.org/10.1159/000445726

[12] Alaluusua S. Aetiology of molar-incisor hypomineralisation: A systematic review. Eur Arch Paediatr Dent 2010; 11(2):53-58. https://doi.org/10.1007/BF03262713

[13] Silva MJ, Scurrah KJ, Craig JM, Manton DJ, Kilpatrick N. Etiology of molar incisor hypomineralization - A systematic review. Community Dent Oral Epidemiol 2016; 44(4):342-353. https://doi.org/10.1111/cdoe.12229

[14] von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: Guidelines for reporting observational studies. Lancet 2007; 370(9596):1453-1457. https://doi.org/10.1016/S0140-6736(07)61602-X

[15] Rosa TC, Pintor AV, Magno MB, Marañón-Vásquez GB, Maia LC, Neves AA. Worldwide trends on molar incisor and deciduous molar hypomineralisation research: A bibliometric analysis over a 19-year period. Eur Arch Paediatr Dent 2022; 23(1):133-146. https://doi.org/10.1007/s40368-021-00676-5

[16] Lygidakis NA, Dimou G, Briseniou E. Molar-incisor-hypomineralisation (MIH). Retrospective clinical study in Greek children. I. Prevalence and defect characteristics. Eur Arch Paediatr Dent 2008; 9(4):200-206. https://doi.org/10.1007/BF03262636

[17] Soviero V, Haubek D, Trindade C, Da Matta T, Poulsen S. Prevalence and distribution of demarcated opacities and their sequelae in permanent 1st molars and incisors in 7 to 13-year-old Brazilian children. Acta Odontol Scand 2009; 67(3):170-175. https://doi.org/10.1080/00016350902758607

[18] de Farias AL, Rojas-Gualdrón DF, Girotto Bussaneli D, Santos-Pinto L, Mejía JD, Restrepo M. Does molar-incisor hypomineralization (MIH) affect only permanent first molars and incisors? New observations on permanent second molars. Int J Paediatr Dent 2021; 32(1):1-10. https://doi.org/10.1111/ipd.12780

[19] Oliver K, Messer LB, Manton DJ, Kan K, Ng F, Olsen C, et al. Distribution, and severity of molar hypomineralisation: trial of a new severity index. Int J Paediatr Dent 2014; 24(2):131-151. https://doi.org/10.1111/ipd.12040

[20] Americano GC, Jacobsen PE, Soviero VM, Haubek D. A systematic review on the association between molar incisor hypomineralization and dental caries. Int J Paediatr Dent 2017; 27(1):11-21. https://doi.org/10.1111/ipd.12233

[21] Petrou MA, Giraki M, Bissar AR, Basner R, Wempe C, Altarabulsi MB, et al. Prevalence of molar-incisor-hypomineralisation among school children in four German cities. Int J Paediatr Dent 2014; 24(6):434-440. https://doi.org/10.1111/ipd.12089

[22] Fatturi AL, Menoncin BL, Reyes MT, Meger M, Scariot R, Brancher JA, et al. The relationship between molar incisor hypomineralization, dental caries, socioeconomic factors, and polymorphisms in the vitamin D receptor gene: A population-based study. Clin Oral Investig 2020; 24(11):3971-3980. https://doi.org/10.1007/s00784-020-03263-y

[23] Balmer R, Toumba J, Godson J, Duggal M. The prevalence of molar incisor hypomineralisation in Northern England and its relationship to socioeconomic status and water fluoridation. Int J Paediatr Dent 2012; 22(4):250-257. https://doi.org/10.1111/j.1365-263X.2011.01189.x

[24] Goyal A, Dhareula A, Gauba K, Bhatia SK. Prevalence, defect characteristics and distribution of other phenotypes in 3- to 6-year-old children affected with hypomineralised second primary molars. Eur Arch Paediatr Dent 2019; 20(6):585-593. https://doi.org/10.1007/s40368-019-00441-9

[25] Garot E, Rouas P, Somani C, Taylor GD, Wong F, Lygidakis NA. An update of the aetiological factors involved in molar incisor hypomineralisation (MIH): A systematic review and meta-analysis. Eur Arch Paediatr Dent 2022; 23(1):23-38. https://doi.org/10.1007/s40368-021-00646-x

[26] Bezamat M, Souza JF, Silva FMF, Corrêa EG, Fatturi AL, Brancher JA, et al. Gene-environment interaction in molar-incisor hypomineralization. PLoS One 2021; 16(1):e0241898. https://doi.org/10.1371/journal.pone.0241898

[27] da Silva FMF, de Carvalho FM, Franco ALMM, Soares TRC, Fonseca-Gonçalves A, Vieira AR, et al. Association between molar hypomineralization, genes involved in enamel development, and medication in early childhood: A preliminary study. Int J Paediatr Dent 2023; 34(3):211-218. https://doi.org/10.1111/ipd.13094