SPATIAL DISTRIBUTION OF MOLAR INCISOR HYPOMINERALIZATION (MIH) OPACITIES IN FIRST PERMANENT MOLARS.

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ABSTRACT

Aims: To evaluate, through intraoral photographs analysis, the spatial distribution of MIH opacities in first permanent molars (FPM).

Materials and Methods: An analysis of intraoral photographs of FPM with demarcated MIH opacities was conducted. Our sample was constituted of children and adolescent patients treated at the Pediatric Dentistry Clinic of the Federal University of Parana and at the Children's Clinic of Araraquara School of Dentistry from October 2018 to February 2020. The presence of opacity was computed in a digital matrix, discriminating the anatomical regions of the FPM surfaces. The frequencies of distribution of the opacities were descriptively analyzed through 227 FPM digital images of 89 children built in GIMP and Python and by Spearman correlation (**α** = 0,05).

Results: The occlusal surface was the most affected one (94% to 100%). In the upper FPM, the palatine surface was the second most affected one (84%-91%). In the lower FPM, the vestibular surface was the second most affected one (85%-80%). A similar pattern of opacity distribution was observed in the contralateral teeth. On smooth surfaces, opacities were more frequent in the regions closer to the occlusal surface than to the cervical one.

Conclusions: MIH opacities were mostly present on occlusal, vestibular, and lingual/palatine surfaces, respectively. There is a possibility that the occurrences are in accordance with the chronology of dental formation.

KEYWORDS: Molar Incisor Hypomineralization. First Permanent Molars. Dental photography. Intraoral photography.
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INTRODUCTION

According to the International Molar Incisor Hypomineralization (MIH) has been identified as a specific type of developmental enamel defect (DDE). It was defined in 2001 as a systemic hypomineralization that affects one to four first permanent molars (FPM) and often damages permanent incisors[1].

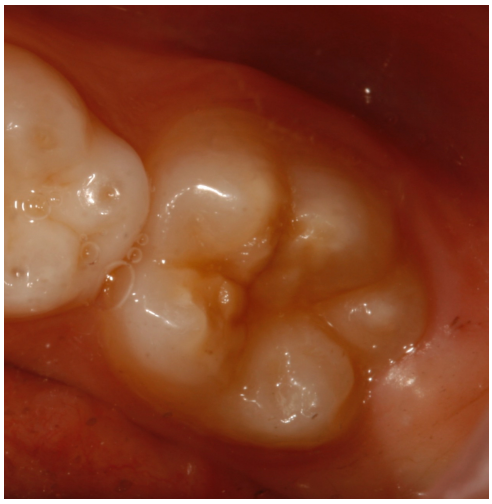

Figure 1. Example of clinical image of the sample.

MIH is considered a public health problem. In 2017, a systematic review study with meta-analysis estimated that the worldwide prevalence of MIH is 14.2%, which means it affects 878 million people. In Brazil, epidemiological studies report rates ranging from 9.12% to 18.4%[2-4].

Clinically, MIH is represented by demarcated opacities in tooth enamel, with defined boundaries between the healthy and the hypomineralized enamel. These opacities can be white, yellowish, or brownish[5]. Due to the porosity of the enamel, hypomineralized lesions can have different degrees of severity, and they also commonly cause enamel fractures or breakdowns[2,5,6]. These fractures can occur soon after tooth eruption, which results in dentin exposure and, consequently, hypersensitivity and a high risk of developing carious lesions[5].

Considering the distribution of the teeth affected by MIH, the greater the severity of the lesion in a first permanent molar, the greater the chance of it affecting the contralateral tooth[5]. Furthermore, the greater the number of first molars affected, the greater the probability that the upper incisors will present opacity[5,7]. The severity in the molars is greater than in the incisors, since the loss of enamel structure is not frequent in incisors[5]. Thus, although the appearance of lesions varies among the affected teeth, it is possible to observe a relationship between the severity of the defect and the number of affected teeth.

Regarding the clinical characteristics of hypomineralization, this defect occurs in the period of mineralization or maturation of the enamel matrix, which corresponds to a time period of two-thirds of the total amelogenesis cycle[8,9]. According to the chronology of dental development, incisors and first permanent molars have the mineralization and maturation phases between the last trimester of pregnancy and the child's third year of age[9], starting from the initial portions of the cusps towards the cervical region. In this period, it is possible that genetic factors and environmental exposures interfere in the etiology of DDE[8,10,11].

Thus, considering the chronology of dental formation and the particularities of each tooth, the hypothesis of this study considers that, regardless of the chronological variation of the development of FPM, they will be affected by hypomineralization with a spatial distribution in accordance with dental chronology. This would theoretically explain the similarity in the regions of development. Therefore, this observational study aimed to evaluate, through intraoral photographs analysis, the spatial distribution of MIH demarcated opacities among the dental surfaces of FPM.

MATERIALS AND METHODS

Ethical Aspects

This study was previously approved by the Human Research Ethics Committee (2.412.156/2017) of the Health Sciences Sector of the Federal University of Paraná, as well as by the Research Ethics Committee of the Araraquara School of Dentistry (protocol 11/09). To participate in the study, the guardians signed an Informed Consent Form (ICF) and the children signed an Assent Term. The study was conducted in accordance with the Declaration of Helsinki.

Study sample and design

This was a cross-sectional observational study carried out with teeth images from patients treated at the Pediatric Dentistry Clinic of the Federal University of Paraná (UFPR) and the Children's Clinic of the Araraquara School of Dentistry (UNESP). The study was conducted from October 2018 to February 2020.

The convenience sample was composed of images of first permanent molars (FPM) with MIH of children and adolescents aged 7 to 16 years under dental treatment at the Pediatric Dentistry Clinic of the Federal University of Paraná (UFPR). Images of teeth affected by MIH according to the European Academy of Pediatric Dentistry (EAPD) criteria[12] were selected, whereas images of teeth with previously restored, with loss of structure, under orthodontic treatment, and with associated cavitated carious lesions were excluded.

To map the appearance pattern of the stains, standardized intraoral occlusal photographs (6.25x, EOS Rebel XTI, Canon, USA) were used, as shown in **Figure 1**. To take the

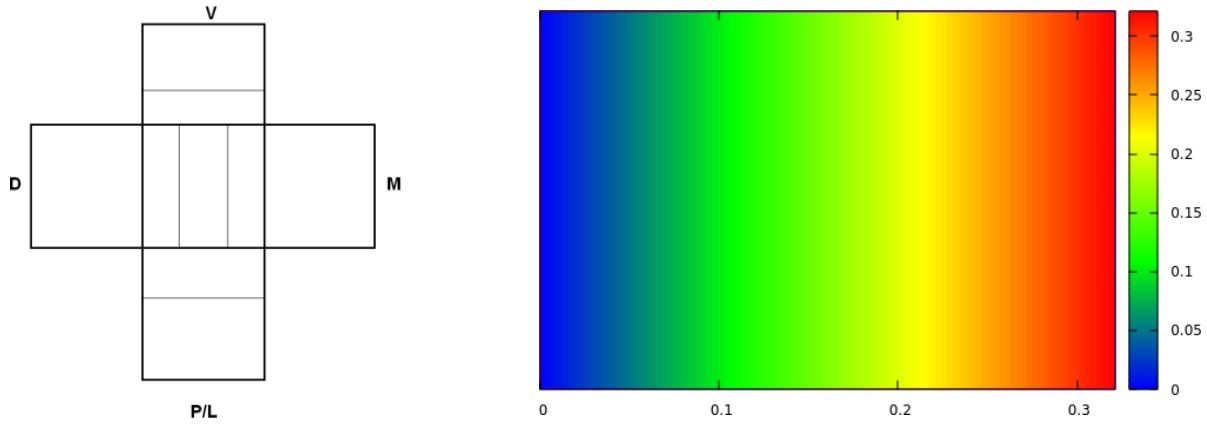

Figure 2. a. Graphic matrix of FPM, referencing the regions of each dental surface. **b**. Colour scale used to make the graphics.

photos, a lip retractor and an occlusal mirror were used, and the camera had the following settings: macro lens with a 100mm focal length, diaphragm with aperture of f/2.8 and ISO 100, and external ring flash with exposure of 1/200s.

MIH calibration and classification

The European Academy of Paediatric Dentistry (EAPD) criterion was used to diagnose MIH. It classifies the different severities of lesions in demarcated opacities, post-eruptive enamel loss, atypical restorations, atypical carious lesions, and MIH extracted tooth[12].

Examiner (B.S.) calibration for the MIH classification criterion[13] was performed by an independent researcher (J.F.S.) with extensive experience in epidemiological surveys that follow this criterion. The calibration process involved two phases: (1) a theoretical-practical training of the criterion involving images of the different severities of MIH and other enamel development defects for differential diagnosis; and (2) the calibration phase itself, which involved the projection of 40 images containing the various situations of the criterion. Kappa agreement values were calculated by comparing the scores of the examiner (B.S.) with those of the reference examiner (J.F.S.). The Kappa values obtained were 0.96 for intra-examiner agreement and 0.90 for inter-examiner agreement.

Analysis of photographic images

One examiner (B.S.) analyzed the images in two moments with a one-week interval between them using Adobe Photoshop 7.0. In order to systematically analyze dental areas affected by opacities and avoid possible observation biases, a graphic matrix of the first molars (**Figure 2A**) was created. In this matrix, the dental surfaces (vestibular, palatine/lingual, and occlusal) were subdivided as shown in **Figure 2A**. Two reference lines were established on the vestibular (V) and lingual (L) surfaces, which proportionally delimited the areas of the dental surface in occlusal (V1 and L1) and cervical (V2 and L2) regions. The occlusal surface (O) was divided into mesial (O1), middle (O2), and distal (O3) regions, as shown in **Figure 2A**. The proximal M and D, in turn, were considered in their entirety due to the difficulty of visualization in the cervical region (**Figure 2A**).

Thus, to map the surfaces, the examiner analyzed all the duplicate images, registering the presence or absence of MIH lesions in the graphic matrix. When there was any discrepancy between the examinations, a second examiner (J.F.S.) also performed the analysis in order to reach a consensus.

Statistical analysis

The data registered in the graphic matrix were transferred to a database in a dichotomized way and given the scores 0 (normal enamel, absence of MIH) and 1 (presence of MIH lesion) for each region.

In order to analyze the pattern of occurrence of MIH on the FPM surfaces, the percentages of the presence of MIH on the surfaces and regions were considered in two ways: (a) according to the number of each first molar (teeth 16, 26, 36, and 46), and (b) according to the total number of each surface (V, L, P, M, and D) evaluated in the sample.

These frequencies were represented in colour charts to show the relative frequency of occurrence on the affected surfaces and regions. The scale of the charts ranged from blue to red, according to frequency (**Figure 2B**). Subsequently, the color maps were transformed into three-dimensional FPM graphics in Paint 3D (USA).

Table 1. Frequency of opacities on the surfaces and regions of the FPM affected by MIH considering the total number of each FPM.

Dental Surfaces	Tooth 16		Tooth 26		Tooth 36		Tooth 46	
	Total N	Presence of MIH n (%)	Total N	Presence of MIH n (%)	Total N	Presence of MIH n (%)	Total N	Presence of MIH n (%)
V	55	44 (84.6%)	56	44 (86.3%)	55	41 (85.4%)	60	46 (80.7%)
L/P	61	49 (84.5%)	63	53 (91.4%)	36	18 (64.3%)	43	26 (63.4%)
O	61	59 (100%)	64	59 (100%)	58	47 (94%)	63	57 (95%)
M	56	34 (62.3%)	56	29 (56.9%)	53	16 (35.6%)	57	28 (51.9%)
D	33	19 (60%)	37	23 (71.9%)	35	13 (46.4%)	32	14 (45.2%)

RESULTS

Among the 242 FPM evaluated, 227 presented MIH. In total, 1015 surfaces were evaluated, which is equivalent to 89.86% of the sample. Some dental surfaces were not visible for opacity analysis; as a result, these surfaces were excluded from the analysis. The distal surfaces, along with the lingual or palatal surfaces of the upper teeth, exhibited the highest exclusion rate. **Table 1** presents the relative frequency of dental surfaces affected by MIH, considering the total number of each first molar (16, 26, 36, and 46). It is possible to observe that the occlusal surface was the one most affected by MIH in all FPM, ranging from 94% to 100% of the evaluated teeth.

In the upper FPM, the second most affected surface was the palatine (**Table 1**), whereas, in the lower FPM, the second most affected surface was the vestibular (**Table 1**).

Figures 3 to **6** show the relative frequencies of surfaces and regions affected by MIH, considering the total surfaces analyzed in the sample as a function of each FPM. The distribution of opacities was very similar between teeth 16 and 26. The occlusal surface was the most affected one, followed by the palatine, vestibular, mesial, and distal surfaces. It is possible to observe that the occurrence of opacity on the vestibular surface of teeth 16 is greater than on teeth 26 (**Figure 3**). Regarding the distribution of opacities, the upper teeth had a greater coincidence of occurrence when compared to the lower teeth (**Figures 3** and **4**).

As for the regions of the vestibular, lingual/palatine, and occlusal surfaces, the regions closer to the occlusal surface were more affected than those closer to the cervical surface in all affected teeth (**Figures 5** and **6**). The palatine/lingual surface showed a similar pattern in the upper teeth. In the lower teeth, the frequency was noticeably lower, but it was still possible to observe the same pattern (**Figures 5** and **6**). The regions of the occlusal surface were divided in the mesio-distal direction, and in these regions the occurrence of MIH did not vary much (**Figures 5** and **6**).

Table 2 shows the relationship between the frequencies of MIH involvement and the surfaces of each tooth. It is noted that, when the occlusal surface is affected, there is a coincidence of involvement in 81.5% to 86.3% of the vestibular surfaces, 64.1% to 91.4% of the lingual/palatine surfaces, 38.1% to 62.3% of the mesial surfaces, and 48.3% to 60% of the distal surfaces. This pattern of coincidence of appearance is seen on the occlusal, vestibular, lingual, mesial, and distal surfaces. Thus, when MIH

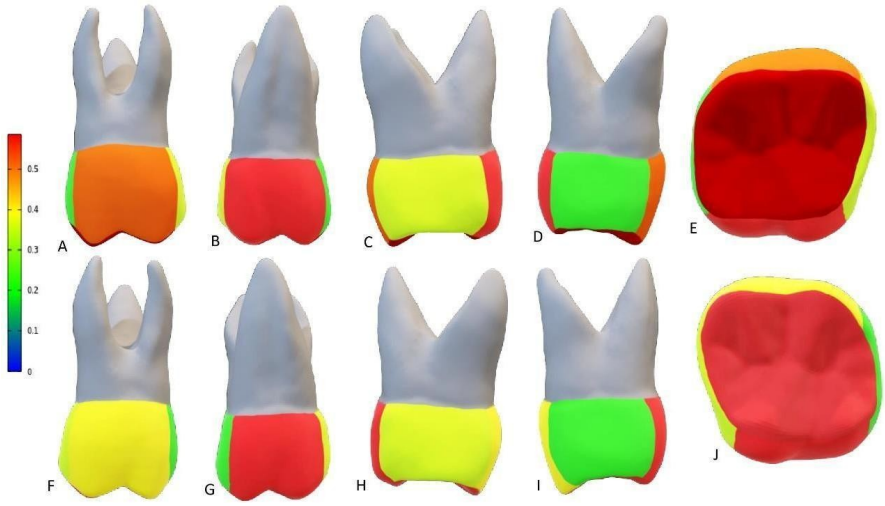

Figure 3. Three-dimensional images of teeth 16 and 26 with the frequency of occurrence of opacity per surface. Tooth 16: **A.** vestibular view **B.** palatine view **C.** mesial view **D.** distal view **E.** occlusal view. Tooth 26: **F.** vestibular view **G.** palatine view **H.** mesial view **I.** distal view **J.** occlusal view

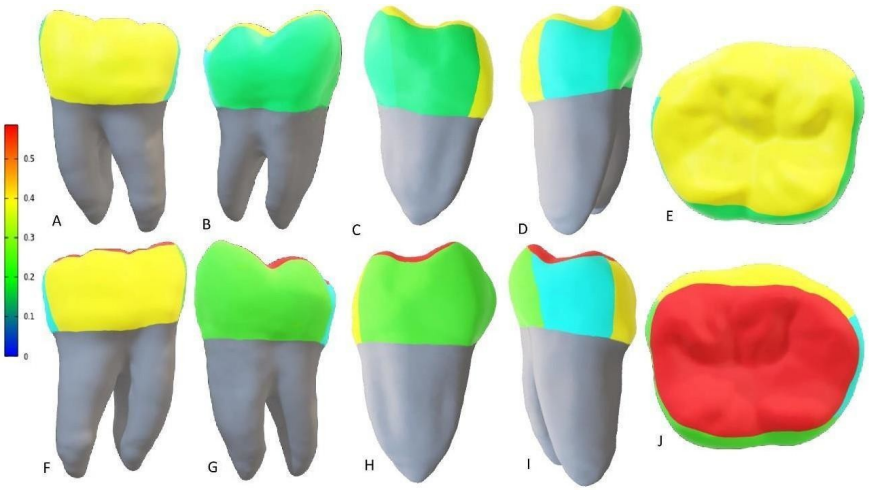

Figure 4. Three-dimensional images of teeth 36 and 46 with the frequency of occurrence of opacity per surface. Tooth 36: **A.** vestibular view **B.** palatine view **C.** mesial view **D.** distal view **E.** occlusal view. Tooth 46: **F.** vestibular view **G.** palatine view **H.** mesial view **I.** distal view **J.** occlusal view

occurs on the mesial surface, the distal surface is the most coincident one.

DISCUSSION

MIH has been defined as an asymmetric defect due to its varied expression among the FPM of an individual[5]. However, in the present study, it was possible to observe a pattern of occurrence of opacities in FPM affected by such defect. Vieira and Kup[14](2016) indicate a variability among the clinical characteristics of MIH, reaffirming its asymmetrical appearance related to its different severity levels[14]. However, the clinical consequences of this defect, such as the high risk of enamel fractures and caries, are also related to factors extrinsic to the appearance of MIH, for example, individual habits of the patient.

Weerheijm[5](2004) states that the greater the number of affected molars, the greater the risk of incisors also being affected. Moreover, it is possible that a FPM might be affected whereas its homologous might not[5,15]. This clinical variability can be justified by the temporal variability of dental development. Another important aspect is the environmental and systemic etiological factors associated with MIH, which are specific events in terms of duration, such as high fever, infections, occurrences during pregnancy, feeding, among others[8,14,16]. In the case of MIH, systemic exposures occur at a certain time of enamel formation in which the presence of variability of the homologous teeth formation stage may result in distinct degrees of severity, indicating clinical asymmetry[5]. This is different from other enamel defects of systemic origin, such as fluorosis, in which the enamel is exposed to a constant stimulus — ingestion of high concentrations of fluoride —, resulting in a defect with an apparent symmetry[17]. Also, it can be observed that the MIH pathogenesis can occur in different ways, which may also explain the clinical differences between the lesions[18].

In their radiographic study, Sahlstrand et al.[19](2013) pointed out differences in the time of enamel formation in permanent homologous teeth. They evaluated the chronology of dental development in children aged 7 to 11 years using panoramic radiographs. The premolars, as well as the second and third molars, were radiographically monitored and compared to their homologous. The results showed differences in dental development between homologous teeth. The authors suggested that these differences may explain the different expressions of MIH in an individual.

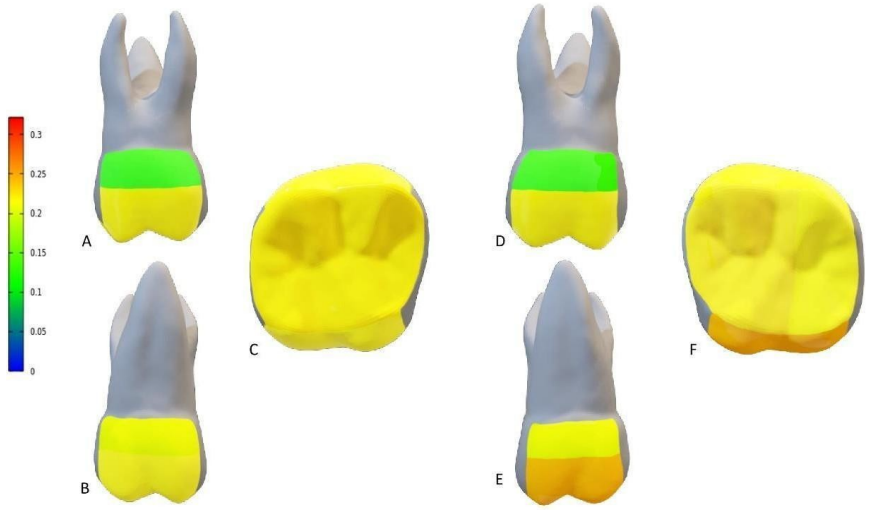

Figure 5. Three-dimensional images of teeth 16 and 26 with the frequency of occurrence of opacity per regions. Tooth 16: **A.** vestibular view: regions V1 and V2 (occlusal vestibular and cervical vestibular) **B.** palatine view: regions P1 and P2 (occlusal palatine and cervical palatine) **C.** occlusal view: regions O1, O2 and O3 (mesial occlusal, middle occlusal, distal occlusal). Tooth 26: **D**. vestibular view: regions V1 and V2 (occlusal vestibular and cervical vestibular) **E.** palatine view: regions P1 and P2 (occlusal palatine and cervical palatine) **F.** occlusal view: regions O1, O2 and O3 (mesial occlusal, middle occlusal, distal occlusal).

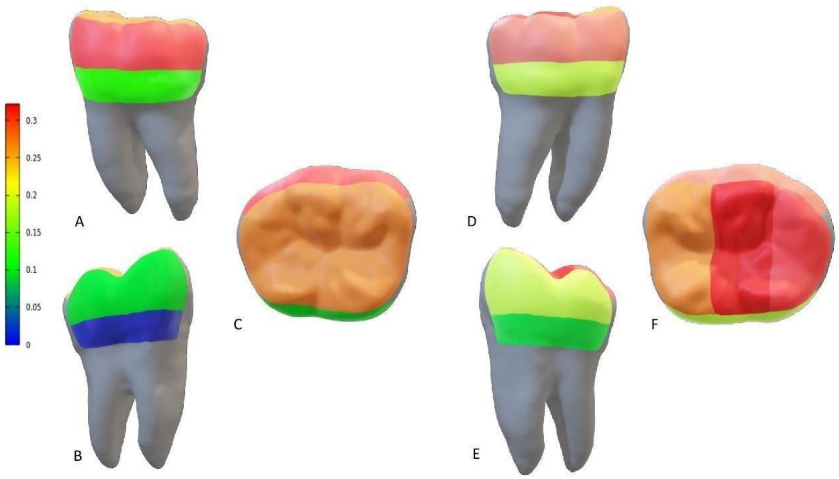

Figure 6. Three-dimensional images of teeth 36 and 46 with the frequency of occurrence of opacity per regions. Tooth 36: **A.** vestibular view: regions V1 and V2 (occlusal vestibular and cervical vestibular) **B.** palatine view: regions P1 and P2 (occlusal palatine and cervical palatine) **C.** occlusal view: regions O1, O2 and O3 (mesial occlusal, middle occlusal, distal occlusal). Tooth 46: **D**. vestibular view: regions V1 and V2 (occlusal vestibular and cervical vestibular) **E.** palatine view: regions P1 and P2 (occlusal palatine and cervical palatine) **F.** occlusal view: regions O1, O2 and O3 (mesial occlusal, middle occlusal, distal occlusal).

In the present study, the occlusal surface was the most affected, followed in order by the vestibular, palatine, mesial, and distal surfaces, suggesting that the occurrence of MIH is related to a pattern of coronary development. This result is in agreement with other studies that found a higher frequency of hypomineralized lesions on the occlusal and vestibular surfaces, respectively[7,20,21].

However, other studies have found greater occurrence of MIH on the vestibular surface, followed by the occlusal surface[2,22,23,24]. Garcia-Margarit et al.[25](2014) found higher frequencies on the occlusal surface of the upper teeth and on the vestibular surface of the lower teeth[25]. The variability of involvement among surfaces could be explained by the chronological window in which the process of amelogenesis was exposed. It is possible to note a greater occurrence of opacities on the occlusal and vestibular surfaces.

The results of the present study are in agreement with the literature regarding the lower involvement of the palatine/lingual surface when compared to the occlusal and vestibular ones[2,22,20,21,25,26]. No studies that included proximal surfaces in the analysis of lesion distribution were found.

It was also observed that the opacities are concentrated mainly in the region closer to the occlusal region, and not in the cervical region, on all surfaces analyzed. Although the reason why enamel defects are mainly concentrated on the occlusal and vestibular surfaces is still unclear[13], it suggests that its occurrence was in the child's first year of life, when there is greater susceptibility to interference in amelogenesis[8], which may justify the higher frequency of involvement in occlusal areas (**Figure 1**).

Studies show a relationship between hypomineralization in cusp tip of permanent canines and in second deciduous molars with MIH[27-29]. Considering that in the child's first year of life there is a coincidence of formation between these structures and the occlusal regions of the FPM and incisal regions of the permanent incisors, the results of this study corroborate the hypothesis of the chronological window: systemic exposures during the child's first year of life could interfere with the development of these structures.

Regarding the occurrence of MIH among dental surfaces, it was observed in this study that MIH occurs within a pattern and that there is a coincidence of occurrence on different surfaces. When the occlusal surface is affected, in most cases the vestibular surface is also affected, followed by the lingual/palatine, proximal, mesial, and distal surfaces. This pattern is confirmed when one surface is taken as reference for defining the percentage of occurrence of the others. This can be justified by the chronology of dental formation: the occlusal surface is the first to be formed, followed by the free and proximal surfaces[9,19].

One limitation of the present study is not showing the occurrence of MIH considering the individual level (patient) to investigate the asymmetric or symmetric occurrence. It should be evaluated in future studies. Another point is that although the photographic images are standardized, the lower frequency of involvement of MIH in proximal surfaces may be related to the difficulty of observing these surfaces in photographs, which constitutes a limitation of the present study. Therefore, future studies can analyze the pattern of occurrence of MIH through clinical examination.

CONCLUSION

In conclusion, MIH opacities showed a pattern of distribution in the first permanent molars. There was a higher frequency in the occlusal, vestibular, and lingual surfaces, followed by the mesial and distal surfaces in all FPM. The opacities were concentrated in the regions closer to the occlusal region, rather than to the cervical region.

Table 2. Relationship between the frequencies of MIH involvement and the surfaces of each tooth.

Affected surfaces	**Affected occlusal surface**			
	16 (n%)	**26 (n%)**	**36 (n%)**	**46 (n%)**
Vestibular	44 (84.6%)	44 (86.3%)	38 (84.4%)	44 (81.5%)
Lingual/palatine	49 (84.5%)	53 (91.4%)	18 (66.7%)	25 (64.1%)
Mesial	33 (62.3%)	29 (56.9%)	16 (38.1%)	26 (51%)
Distal	18 (60%)	23 (71.9%)	13 (50%)	14 (48.3%)
Affected surfaces	**Affected vestibular surface**			
	16 (n%)	**26 (n%)**	**36 (n%)**	**46 (n%)**
Occlusal	44 (84.6%)	44 (86.3%)	38 (84.4%)	44 (81.5%)
Lingual/palatine	38 (86.4%)	41 (95.3%)	15 (75%)	22 (73.3%)
Mesial	29 (70.7%)	26 (70.3%)	16 (41%)	27 (62.8%)
Distal	17 (70.8%)	18 (72%)	12 (54.5%)	13 (59.1%)
Affected surfaces	**Affected lingual/palatine surface**			
	16 (n%)	**26 (n%)**	**36 (n%)**	**46 (n%)**
Occlusal	49 (84.5%)	53 (91.4%)	18 (66.7%)	25 (64.1%)
Vestibular	38 (86.4%)	41 (95.3%)	15 (75%)	22 (73.3%)
Mesial	30 (66.7%)	28 (60.9%)	8 (47.1%)	17 (73.9%)
Distal	18 (64.3%)	21 (72.4%)	6 (50%)	8 (66.7%)
Affected surfaces	**Affected mesial surface**			
	16 (n%)	**26 (n%)**	**36 (n%)**	**46 (n%)**
Occlusal	33 (62.3%)	29 (56.9%)	16 (38.1%)	26 (51%)
Vestibular	29 (70.7%)	26 (70.3%)	16 (41%)	27 (62.8%)
Lingual/palatine	30 (66.7%)	28 (60.9%)	8 (41.1%)	17 (73.9%)
Distal	16 (84.2%)	15 (83.3%)	7 (63.6%)	10 (66.7%)
Affected surfaces	**Affected distal surface**			
	16 (n%)	**26 (n%)**	**36 (n%)**	**46 (n%)**
Occlusal	18 (60%)	23 (71.9%)	13 (50%)	14 (48.3%)
Vestibular	17 (70.8%)	18 (72%)	12 (54.5%)	13 (59.1%)
Lingual/palatine	18 (64.3%)	21 (72.4%)	6 (50%)	8 (66.7%)
Mesial	16 (84.2%)	15 (83.3%)	7 (63.6%)	10 (66.7%)

REFERENCES

1. Weerheijm KL, Jälevik B, Alaluusua S. Molar-incisor hypomineralisation. Caries Res. 2001; 35(5):390-391.

2. Da Costa-Silva CM, Jeremias F, De Souza JF, Cordeiro RDE C et al. Molar incisor hypomineralization: prevalence, severity and clinical consequences in Brazilian children. Int J Paediatr Dent. 2010; 20(6):426-434.

3. De Lima MDE D, Andrade MJ, Dantas-Neta NB, Andrade NS et al. Epidemiologic Study of Molar-incisor Hypomineralization in Schoolchildren in North-eastern Brazil. Pediatr Dent. 2015; 37(7):513-519.

4. Jeremias F, De Souza JF, Silva CM, Cordeiro RDE C et al. Dental caries experience and Molar-Incisor Hypomineralization. Acta Odontol Scand. 2013; 71(3-4):870-876.

5. Weerheijm KL. Molar incisor hypomineralization (MIH): clinical presentation, aetiology and management. Dent Update. 2004; 31(1):9-12, 2004.

6. Neves AB, Americano GCA, Soares DV, Soviero VM. Breakdown of demarcated opacities related to molar-incisor hypomineralization: a longitudinal study. Clin Oral Investig. 2019(2); 23:611-615.

7. Mittal NP, Goyal A, Gauba K, Kapur A. Molar incisor hypomineralisation: prevalence and clinical presentation in school children of the northern region of India. Eur Arch Paediatr Dent. 2014; 15(1):11-18.

8. Alaluusua S. Aetiology of Molar-Incisor Hypomineralisation: A

systematic review. Eur Arch Paediatr Dent. 2010(2);11: 53-58.

9. Nanci A. Ten Cate's Oral Histology: Development, Structure, and Function. 8th ed. Mobly; 2013.

10. Fatturi AL, Wambier LM, Chibinski AC, Assuncao L et al. A systematic review and meta-analysis of systemic exposure associated with molar incisor hypomineralization. Community Dent Oral Epidemiol. 2019(5); 47: 407-415.

11. Jeremias F, Koruyucu M, Küchler EC, Bayram M et al. Genes expressed in dental enamel development are associated with molar-incisor hypomineralization. Arch Oral Biol. 2013(10); 58:1434-1442.

12. Ghanim A, Elfrink M, Weerheijm K, Mariño R et al. A practical method for use in epidemiological studies on enamel hypomineralisation. Eur Arch Paediatr Dent. 2015(3); 16:235-246.

13. Lygidakis NA, Wong F, Jälevik B, Vierrou AM et al. Best Clinical Practice Guidance for clinicians dealing with children presenting with Molar-Incisor-Hypomineralisation (MIH): An EAPD Policy Document. Eur Arch Paediatr Dent. 2010; 11(2):75-81.

14. Vieira AR, Kup E. On the Etiology of Molar-Incisor Hypomineralization. Caries Res. 2016; 50(2):166-169.

15. Vieira AR, Manton DJ. On the Variable Clinical Presentation of Molar-Incisor Hypomineralization. Caries Res. 2019(4); 53:482-488.

16. Allazzam SM, Alaki SM, El Meligy OA. Molar incisor hypomineralization, prevalence, and etiology. Int J Dent. 2014; 2014:234508.

17. Rozier RG. Epidemiologic indices for measuring the clinical manifestations of dental fluorosis: overview and critique. Adv Dent Res. 1994; 8(1):39-55.

18. Manton DJ, Crombie FA, Silva MJ. The Pathogenesis and Aetiology of MIH: More Questions Than Answers. In: BEKES, K. (Ed.). Molar Incisor Hypomineralization: A Clinical Guide to Diagnosis and Treatment; 2020. 4 p. 33-41.

19. Sahlstrand P, Lith A, Hakeberg M, Norén JG. Timing of mineralization of homologues permanent teeth--an evaluation of the dental maturation in panoramic radiographs. Swed Dent J. 2013; 37(3):111-119.

20. Mulic A, Cehajic E, Tveit AB, Stenhagen KR. How serious is Molar Incisor Hypomineralisation (MIH) among 8- and 9-year-old children in Bosnia-Herzegovina? A clinical study. Eur J Paediatr Dent. 2017; 18(2):153-157.

21. Oyedele TA, Folayan MO, Adekoya-Sofowora CA, Oziegbe EO et al. Prevalence, pattern and severity of molar incisor hypomineralisation in 8- to 10-year-old school children in Ile-Ife, Nigeria. Eur Arch Paediatr Dent. 2015; 16(3):277-282.

22. Schmalfuss A, Stenhagen KR, Tveit AB, Crossner CG et al. Canines are affected in 16-year-olds with molar-incisor hypomineralisation (MIH): an epidemiological study based on the Tromsø study: "Fit Futures". Eur Arch Paediatr Dent. 2016; 17(2):107-113.

23. Fagrell T. Molar incisor hypomineralization. Morphological and chemical aspects, onset and possible etiological factors. Swed Dent J Suppl. 2011; 5(216):11-83.

24. Vlachou C. Distribution and morphology of hypomineralisation defects in primary teeth. Orientador: KOTSANOS, N. 2020. 74 f. (Postgraduate) - Paediatric Dentistr, Aristotle University of Thessaloniki, Thessaloniki.

25. Garcia-Margarit M, Catalá-Pizarro M, Montiel-Company JM, Almerich-Silla JM. Epidemiologic study of molar-incisor hypomineralization in 8-year-old Spanish children. Int J Paediatr Dent. 2014; 24(1):14-22.

26. Kevrekidou A, Kosma I, Arapostathis K, Kotsanos N. Molar Incisor Hypomineralization of Eight- and 14-year-old Children: Prevalence, Severity, and Defect Characteristics. Pediatr Dent. 2015; 37(5): 455-461.

27. Da Silva Figueiredo SE M J, Ribeiro APD, Dos Santos-Pinto LAM, De Cassia Loiola Cordeiro R et al. Are Hypomineralized Primary Molars and Canines Associated with Molar-Incisor Hypomineralization? Pediatr Dent. 2017; 39(7):445-449.

28. Garot E, Denis A, Delbos Y, Manton D et al. Are hypomineralised lesions on second primary molars (HSPM) a predictive sign of molar incisor hypomineralisation (MIH)? A systematic review and a meta-analysis. J Dent. 2018; 72:8-13.

29. Reyes MRT, Fatturi AL, Menezes J, Fraiz FC et al. Demarcated opacity in primary teeth increases the prevalence of molar incisor hypomineralization. Braz Oral Res. 2019; 15:33 e048.