Association Between Frequency and Severity of Dental Fluorosis and Molar Incisor Hypomineralization

Manuel Restrepo*/ Diego Fernando Rojas-Gualdrón**/ Aline Leite de Farias***/ Diego Girotto-Bussaneli****/ Lourdes Santos-Pinto*****

Objective: *To assess the association between the frequency and severity of dental fluorosis (DF) and molar incisor hypomineralization (MIH) in a fluoridated salt region.* ***Study design:*** *In this retrospective cross-sectional study, we evaluated the buccal, occlusal/incisal, and palatal/lingual surfaces of first permanent molars and permanent incisors of 453 patients aged 13–16 years through intraoral standardized photographs. Two standardized examiners evaluated DF and MIH independently, utilizing the Thylstrup-Fejerskov (TF) index and the MIH index. The statistical analysis was performed using a generalized linear model and logistic regression adjusted for age, sex, and dental caries experience.* ***Results:*** *The MIH frequency at the surface level was lower in the presence of DF (PR= 0.03; P= 0.00, 95% CI: 0.01–0.08). At the surface level, MIH severity was lower among those presenting mild DF (aOR= 0.02; 95% IC: 0.01–0.07). Regarding severe DF, we found no significant difference in MIH severity (P= 0.174).* ***Conclusion:*** *MIH frequency and severity tend to be lower in the presence of DF.*

Keywords: *MIH, Fluorosis, Hypomineralization, Pediatric dentistry.*

INTRODUCTION

While we have seen a decrease in the dental caries experience, developmental defects of enamel (DDE) are increasingly evident in clinical practice.

Dental development is a slow, complex, multidimensional, and multilevel genetically-controlled process.[1] DDE are caused by interactions of local, systemic, genetic, and environmental factors, which can affect the functional ameloblast. Hence, the type of defect will depend on when the damage occurred during amelogenesis. If the damage occurs during the secretory phase, when the matrix is deposited, a hypoplasia type DDE can occur. In contrast, if the damage occurs during the maturation phase when the matrix is removed and the mineral content incorporated, a hypomineralization type DDE can occur, which can be diffuse or demarcated.[2]

It is widely accepted that fluoride effectively controls dental caries.[3] However, it has been suggested that fluoride excess can stress the ameloblast affecting the synthesis of proteins responsible for the organic matrix removal,[4] clinically resulting in a diffuse hypomineralization named dental fluorosis (DF). This type of DDE varies from thin, white, and fuzzy lines to a completely white surface. The most severe cases may display pigmentations and loss of structure.[5] DF affects symmetrically groups of teeth, especially the permanent maxillary premolars, second molars, and incisors.[6] Due to the increase in porosity, fluorotic enamel is less resistant to demineralization, and therefore more susceptible to dental caries.[7]

Molar incisor hypomineralization (MIH) is a type of DDE of multifactorial origin with a possible genetic component[8] that

* Manuel Restrepo, DDS, MSc, Ph.D. Professor. Basic and Clinical Research Group in Dentistry, School of Dentistry, CES University, Medellín, Colombia.

** Diego Fernando Rojas-Gualdrón, MSc, Ph.D. Professor. School of Medicine, CES University, Medellín, Colombia.

*** Aline Leite de Farias, DDS, MSc, PhD student. Department of Pediatric Dentistry and Orthodontics, São Paulo State University (Unesp), Araraquara School of Dentistry, Araraquara, São Paulo, Brazil.

**** Diego Girotto-Bussaneli, DDS, MSc, PhD. Postdoc student. São Paulo State University (Unesp), Araraquara School of Dentistry, Araraquara, São Paulo, Brazil.

***** Lourdes Santos-Pinto, DDS, MSc, Ph.D. Professor. Department of Pediatric Dentistry and Orthodontics, São Paulo State University (Unesp), Araraquara School of Dentistry, Araraquara, São Paulo, Brazil.

Send all Correspondence to:
Manuel Restrepo
School of Dentistry, CES University
Calle 10 A # 22 – 04
Medellín, Colombia
E-mail: mrrestrepo@ces.edu.co

asymmetrically affects the first permanent molars and permanent incisors.[9] Clinically, well-demarcated white, yellow, or brown opacities can be seen, which may be associated with post-eruptive fractures, atypical dental caries lesions, and atypical restorations. The MIH affected enamel presents significant structural and componential alterations, which may result in hypersensitivity and dental caries.[10]

The studies that have evaluated the association between DF and MIH in fluoridated water regions have found lower MIH frequencies.[11-13] However, data from fluoridated salt regions are lacking. Also, the available studies have used the modified DDE index (mDDE), which according to Elfrink *et al* presents disadvantages since it does not consider classic MIH characteristics such as post-eruptive fractures, atypical dental caries lesions, atypical restorations, and dental extraction.[14] Thus, for the first time in a fluoridated salt region and using specific and validated indexes, we aimed to evaluate the association between the frequency and severity of DF and MIH.

MATERIALS AND METHOD

This study is described according to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) statement.

Study design, setting, and participants

This retrospective cross-sectional study was approved by the Institutional Committee of Research Ethics of CES University (project code Ae-401; act 141; 2019) and followed the Council for International Organizations of Medical Sciences (CIOMS) guidelines related to the use of clinical records for research. Informed consent was obtained from all participants.

We examined intraoral photographic records of adolescents aged 13–16 years, born and residing in Medellín, Colombia, who attended the dental clinic of CES University's School of Dentistry. Since 1989 and as public health policy, the Colombian population has access to fluoridated salt (180–220 mg F/kg). According to the National Study of Oral Health (ENSAB IV, 2014),[15] the prevalence of DF in 15-year-old Colombian adolescents is 56%.

The data was collected between February and April 2020. The intraoral photographic records of patients with craniofacial syndromes, and those wearing fixed appliances or dental prostheses were excluded.

The inclusion criteria were as follows: patients with permanent dentition and complete digital (JPG format), high-resolution (1280x853 pixels per inch) photographic records, consisting of 5 photographs, i.e., upper arch, lower arch, right lateral, left lateral, and occlusal.

Variables

The presence of MIH was defined as the primary outcome. DF was considered an explanatory variable, and age, sex, and dental caries experience were considered confounding variables.

Measurements and bias

DF was classified according to the Thylstrup-Fejerskov (TF) index.[5] This index allows to record DF based on histopathological characteristics and includes the mildest to the most severe stages (ordinal scale from 0 to 9). Based on the loss of structure, teeth with TF 1–4 were classified as mild DF, and those with TF ≥ 5 were classified as severe DF. An independent and standardized (Kappa= 0.89) examiner made the DF classification.

MIH was classified according to the MIH index.[16,17] This index classifies the defect's clinical state (demarcated opacity, post-eruptive enamel fracture, atypical restoration, atypical dental caries lesion, or absent tooth due to MIH) and extension by thirds in the buccal, occlusal/incisal, and palatal/lingual surfaces. The surfaces showing opacities only were classified as mild, and the surfaces showing loss of structure, atypical restorations, atypical dental caries lesions, and extracted teeth were classified as severe.[18] MIH evaluation was performed by another standardized examiner (Kappa= 0.87), who also evaluated the dental caries experience using the decayed, missing, and filled teeth (DMFT) and decayed, missing, and filled surfaces (DMFS) indices proposed by the World Health Organization (WHO) (Kappa= 0.91).[19]

The photographs were taken by a single operator with the same photographic equipment (Nikon D3400 24 mp with a 90mm macro lens and a Dine Mini Ring and Point Flash) and processed with Adobe Photoshop Lightroom (version 2017 for Mac). The photographs were evaluated on a desktop computer with an integrated 21.5-inch screen (1920x1080 pixels per inch) and an Intel HD Graphics 6000 1536 MB graphic card, using Preview (version 11, Apple Inc., CA, USA) in full-screen mode.

Sample size and statistical analysis

This study presents a secondary analysis of an existing sample consisting of 453 photographic records (Farias *et al* unpublished) in which the association of MIH with other permanent teeth was analyzed with an 80% statistical power and a prevalence ratio (PR) ≥ 1.9.

DF and MIH were calculated as an affectation percentage at patient, tooth, and surface level. A generalized linear model with a binomial family and logarithmic link function was used to analyze the association between DF and MIH at the surface level. The results are presented as PR with P-values and 95% confidence intervals (CI). Ordinal logistic regression was used to analyze the association between the DF's and MIH's severity. The results are presented as ordinal odds ratios (OR) with P-values and 95% CI. In both cases, the adolescents-teeth-surfaces conglomerate was considered through a robust estimation of the variances. The results are presented as crude estimations adjusted for age, sex, and dental caries experience. Also, statistical power post hoc estimates were made for the OR. The data were analyzed using STATA® (version 16.1; College Station, TX, USA).

RESULTS

The final sample consisted of 453 patients, of whom 228 (50.33 %) were females. The mean age was 14.49 ± 1.19 years. Figure 1 shows the frequency of DF's and MIH's involvement per tooth.

The percentage of patients with DF was 28.70% (n= 130); 23.07% presented at least one tooth with severe DF. The premolar was the most frequently affected tooth (18.15%), with the maxillary (20.84%) being more commonly affected than the mandibular (15.45%). The first permanent maxillary molars (4.09%) were the less affected teeth. The permanent maxillary incisors (7.88%) and canines (9.07%) were more frequently affected by DF than the mandibular (3.37% and 5.03%, respectively). The most commonly

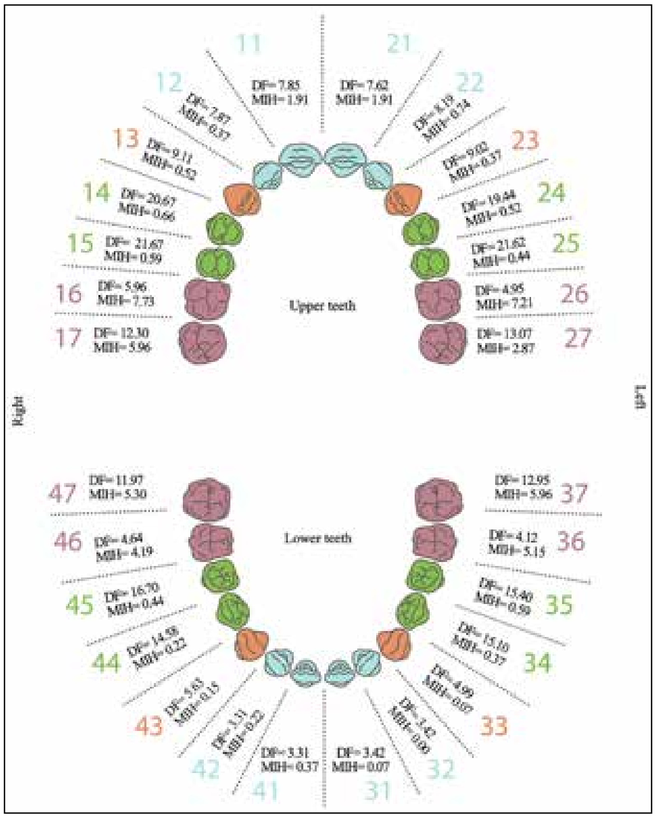

Figure 1. Frequency of Dental Fluorosis (DF) and Molar-Incisor Hypomineralization (MIH) involvement per tooth.

affected surface was the occlusal (13.03%), followed by the buccal (12.71%) and palatal/lingual (8.10%). Considering all the evaluated permanent teeth surfaces (n= 32441), the most frequently encountered score was TF2 (3.74%). No teeth/surfaces presented with TF ≥ 7.

The percentage of patients with MIH was 31.06% (n= 141); 38.3% presented at least one tooth (first permanent molar or permanent incisor) with severe MIH. 32.62% of the patients presented MIH in one tooth, 36.17% in two teeth, 18.44% in three teeth, 6.38% in four teeth, 3.55% in five teeth, and 2.84% in six teeth. The first permanent right maxillary molar was the most frequently affected tooth (7.73%), followed by the first permanent left maxillary molar (7.21%), the first permanent left mandibular molar (5.15%), and the first permanent right mandibular molar (4.19). Among the permanent incisors, the maxillary were the most frequently affected. The buccal was the most commonly affected surface (3.73 %), and the palatal was the least commonly affected (0.51%).

Table 1 shows the distribution of DF and MIH in first permanent molars and permanent incisors at surface level. TF2 was DF's most frequent score, and white or cream demarcated opacities were the most frequent MIH defect.

Table 2 shows the presence of MIH, according to the presence of DF at surface level. The frequency of MIH frequency at surface level was higher in the absence of DF (PR= 0.03; 95% CI: 0.01–0.08) and presence of dental caries (PR= 3.80; 95% CI: 2,39–6.03). Age, sex, and dental caries experience did not influence the association between MIH's and DF's presence (aPR= 0.03; 95% CI: 0.01–0.08). However, we observed heterogeneity in the association's strength between DF and MIH, being higher in the absence of dental caries

Table 1 Distribution of dental fluorosis and molar incisor hypomineralization (surfaces, n= 19818)

Thylstrup-Fejerskov (TF) index	n	%
TF0 (normal, smooth and translucent enamel)	17276	87.17
TF1 (fine horizontal opaque white lines)	599	3.02
TF2 (thick horizontal opaque white lines)	887	4.48
TF3 (Opaque white lines of greater amplitude that accentuate with white and opaque areas in the perikymata)	564	2.85
TF4 (Chalky white, totally opaque surface)	396	2.00
TF5 (totally opaque surface with <2 mm rounded pits)	84	0.42
TF6 (totally opaque surface; merged, rounded pits <2 mm in vertical height)	12	0.06
TF7 (loss of the dental enamel < 50%)	-	-
TF8 (loss of the dental enamel > 50%)	-	-
TF9 (loss of most of the dental enamel)	-	-
Molar incisor hypomineralization (MIH) index		
No enamel defect (healthy)	16589	83.71
Other enamel defects	2554	12.89
White or creamy demarcated opacity	374	1.89
Yellow or brown demarcated opacity	153	0.77
Post-eruptive enamel fracture	46	0.24
Atypical restoration	73	0.37
Atypical dental caries	9	0.05
Absent due to MIH	6	0.03
Cannot be classified	14	0.07

Table 2 Presence of molar incisor hypomineralization according to the presence of dental fluorosis

		Crude			
		Frequency	**PR**	***P*-value**	**95% CI**
DF	Absent	3.81	1	-	-
	Present	0.12	0.03	0.00	0.01, 0.08
		Adjusted for age, sex, and dental caries experience			
DF	Absent	3.83	1	-	-
	Present	0.11	0.03	0.00	0.01, 0.08
		Heterogeneity according dental caries, adjusted			
DF	Dental caries				
Absent	Absent	3.68	1		
Present	Absent	0.08	.022	0.000	0.01, 0.09
Absent	Present	12.30	1		
Present	Present	5.00	0.41	0.375	0.06, 2.98

DF, dental fluorosis

(aPR= 0.022; 95% CI: 0.01–0.09). No statistically significant difference was observed in the presence of dental caries (aPR= 0.41; 95% CI: 0.06–2.98).

Table 3 shows the association between MIH and dental fluorosis according to severity at surface level. After adjusting for age, sex, and dental caries experience, the severity of MIH was lower among those with mild DF than those without DF (aOR= 0.02; 95% CI: 0.01–0.07). Regarding severe DF, no significant difference was observed in the severity of MIH (*P*= 0.174).

Table 3 Association between molar incisor hypomineralization and dental fluorosis according to severity at surface level

	Crude			Adjusted		
DF	OR	*P*-value	95% CI	OR	*P*-value	95% CI
Absent	1	-	-	-	-	-
Mild	0.02	0.00	0.01, 0.08	0.02	0.00	0.01, 0.07
Severe	0.27	0.171	0.04, 1.76	0.27	0.174	0.04, 1.79

DF, dental fluorosis

DISCUSSION

This study showed that the frequency and severity of MIH are lower in the presence of DF.

One of the strengths of this study is that the observation bias was controlled, as two different researchers evaluated DF and MIH independently. This is one of the advantages of using photographs in research since conducting such evaluations clinically can be challenging and time-consuming. The use of photographs in research also prevents patients from being subject to multiple clinical examinations performed by various examiners.

This is one of the first studies to utilize valid criteria to independently classify DF (TF index) and MIH (MIH index), a crucial methodological feature that strengthens our study's internal validity. According to Thylstrup and Fejerskov, the TF index has high precision and sensitivity and accurately characterizes DF even in populations with different severities (Thylstrup and Fejerskov 1987). It also allows relating the clinical characteristics with the histologic characteristics, a particular and crucial feature for clinicians, researchers, and epidemiologists.[5] On the other hand, the MIH index includes validated criteria that classify the clinical status and extent of this type of DDE.[16,18] Although it also allows differentiation of MIH from other enamel defects, the severity can only be determined for MIH. Other studies have used the mDDE index to evaluate DF and MIH;[11-13] however, this index does neither allow evaluating the defects' severity nor consider common MIH characteristics such as post-eruptive fractures, atypical restorations, atypical dental caries lesions, and atypical dental extractions.[14]

As the examination was based on photographic records, this study's limitation is that the history of fluoride exposure could not be identified. However, to control this information bias, we established that all participants should have born and resided in the same city (as obtained from the medical record) as one of the inclusion criteria. The use of photographs could represent a methodological limitation due to the risk of under- or overestimating the frequency and severity of enamel defects. As for MIH and dental caries, the use of standardized photographs for the diagnosis of DF is a reliable and reproducible method compared to clinical diagnosis.[20,21]

DF's pathologic mechanism has been widely discussed in the scientific literature. Chronic fluoride intake during amelogenesis affects the dental enamel's structure and composition.[22] In this study, the permanent premolars and second permanent premolars were the most frequently affected teeth by DF (Figure 1). The frequency and severity of DF tend to be higher in permanent teeth with delayed eruption because fluoride exposure increases with age.[23] According to Bårdsen's meta-analysis, fluoride exposure duration seems to be more critical than specific risk periods during amelogenesis.[24] In contrast, the first permanent molar was the least affected tooth by DF. This is interesting since the first permanent molar is the most frequently affected tooth in MIH.

Similar to other studies conducted in fluoridated water regions,[11-13, 25-29] we found that the frequency and severity of MIH was lower in the presence of DF (Table 2). Balmer *et al* (2012)[11] suggest that fluoride could be a MIH protective factor, while Koch (2003)[25] affirms that MIH cannot be related to fluoride intake. Based on our findings, we hypothesize that DF and MIH "compete" with each other; thus, studies are needed that evaluate the temporality of these defects. We also believe that the difference in fluoride exposure between regions/populations could explain the variability in the prevalence and severity of MIH.

Contrary to what one might believe, enamel affected by DF is more susceptible to dental caries' demineralization.[7] It should also be considered that the fluorotic enamel presents higher porosity and, thus, a greater mineral area to be dissolved by acids, which facilitates its penetration into the dental enamel.[7] Likewise, the enamel affected by MIH presents significant alterations in its structure and composition, such as increased porosity, a greater amount of carbon and carbonate, and a decreased mineral content.[10] These characteristics have been associated with a higher dental caries experience.[10,30] Hence, it is crucial for the clinician to know the source of exposure to fluoride of individual and collective use, determine the patient's individual risk, and implement effective measures for the control of dental caries in patients with DF or MIH.

CONCLUSION

Our findings showed that in a fluoridated salt region, the MIH frequency and severity tends to be lower in the presence of DF.

REFERENCES

1. Brook AH, O'Donnell MB, Hone A, et al. General and craniofacial development are complex adaptive processes influenced by diversity. Aust Dent J. 2014; 59(Suppl. 1):13-22.
2. Seow WK. Developmental defects of enamel and dentine: challenges for basic science research and clinical management. Aust Dent J. 2014;59(Suppl. 1):143-154.
3. Cury JA, Tenuta LM. Enamel remineralization: controlling the caries disease or treating early caries lesions? Braz Oral Res. 2009;23(Suppl. 1):23-30.
4. Suzuki M, Shin M, Simmer JP, Bartlett JD. Fluoride affects enamel protein content via TGF-β1-mediated KLK4 inhibition. J Dent Res. 2014; 93:1022-1027.
5. Thylstrup A, Fejerskov O. Clinical appearance of dental fluorosis in permanent teeth in relation to histologic changes. Community Dent Oral Epidemiol. 1978; 6:315-328.
6. Ramires I, Pessan JP, Levy FM, et al. Prevalence of dental fluorosis in Bauru, São Paulo, Brazil. J Appl Oral Sci. 2007;15:140-143.
7. Marín LM, Cury JA, Tenuta LM, Castellanos JE, Martignon S. Higher Fluorosis Severity Makes Enamel Less Resistant to Demineralization. Caries Res. 2016;50:407-413.
8. Vieira AR, Kup E. On the Etiology of Molar-Incisor Hypomineralization. Caries Res. 2016; 50:166-169.
9. Weerheijm KL, Jälevik B, Alaluusua S. Molar-incisor hypomineralisation. Caries Res. 2001; 35:390-391.
10. Elhennawy K, Manton DJ, Crombie F, et al. Structural, mechanical and chemical evaluation of molar-incisor hypomineralization-affected enamel: A systematic review. Arch Oral Biol. 2017; 83:272-281.
11. 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; 22:250-257.
12. Balmer R, Toumba KJ, Munyombwe T, Duggal MS. A comparison of the presentation of molar incisor hypomineralisation in two communities with different fluoride exposure. Eur Arch Paediatr Dent. 2015; 16:257-264.
13. Balmer RC, Laskey D, Mahoney E, Toumba KJ. Prevalence of enamel defects and MIH in non-fluoridated and fluoridated communities. Eur J Paediatr Dent. 2005; 6:209-12.
14. Elfrink ME, Ghanim A, Manton DJ, Weerheijm KL. Standardised studies on molar incisor hypomineralisation (MIH) and hypomineralised second primary molars (HSPM): a need. Eur Arch Paediatr Dent. 2015; 16:247-255.
15. Ministry of Health and Social Protection–Ministerio de Salud y Protección Social. [Internet]. IV Estudio Nacional de Salud Bucal. ENSAB IV: Situación en Salud Bucal. Para Saber cómo estamos y saber qué hacemos. Colombia 2014. [cited 2021 Jan 15]. Available from: https://www.minsalud.gov.co/sites/rid/Lists/BibliotecaDigital/RIDE/VS/PP/ENSAB-IV-Situacion-Bucal-Actual.pdf
16. Ghanim A, Elfrink M, Weerheijm K, et al. A practical method for use in epidemiological studies on enamel hypomineralization. Eur Arch Paediatr Dent. 2015; 16:235-246.
17. Ghanim A, Mariño R, Manton DJ. Validity and reproducibility testing of the Molar Incisor Hypomineralization (MIH) Index. Int J Paediatr Dent. 2019; 29:6-13.
18. Ghanim A, Silva MJ, Elfrink MEC et al. Molar incisor hypomineralisation (MIH) training manual for clinical field surveys and practice. Eur Arch Paediatr Dent. 2017; 4:225-242.
19. World Health Organization. Oral Health Surveys: basic methods. Geneva, Switzerald: WHO; 2013:125.
20. Martins CC, Chalub L, Lima-Arsati YB, et al. Agreement in the diagnosis of dental fluorosis in central incisors performed by a standardized photographic method and clinical examination. Cad Saude Publica. 2009; 25:1017-1024.
21. Dye BA, Goodwin M, Ellwood RP, Pretty IA. Digital epidemiology–Calibrating readers to score dental images remotely. J Dent. 2018;74(Suppl. 1):S27-S33.
22. Aoba T, Fejerskov O. Dental fluorosis: chemistry and biology. Crit Rev Oral Biol Med. 2002;13:155-170.
23. Bhagavatula P, Levy SM, Broffitt B, et al. Timing of fluoride intake and dental fluorosis on late-erupting permanent teeth. Community Dent Oral Epidemiol. 2016; 44:32-45.
24. Bårdsen A. "Risk periods" associated with the development of dental fluorosis in maxillary permanent central incisors: a meta-analysis. Acta Odontol Scand. 1999; 57:247-256.
25. Koch G. Prevalence of enamel mineralization disturbances in an area with 1-1.2 ppm F in drinking water. Review and summary of a report published in Sweden in 1981. Eur J Paediatr Dent. 2003;4:127-128.
26. da Costa-Silva CM, Jeremias F, de Souza JF, et al. Molar incisor hypomineralization: prevalence, severity and clinical consequences in Brazilian children. Int J Paediatr Dent. 2010; 20:426-434.
27. Krishnan R, Ramesh M, Chalakkal P. Prevalence and characteristics of MIH in school children residing in an endemic fluorosis area of India: an epidemiological study. Eur Arch Paediatr Dent. 2015; 16:455-460.
28. Ahmad SH, Petrou MA, Alhumrani A, et al. Prevalence of molar-incisor hypomineralisation in an emerging community, and a possible correlation with caries, fluorosis and socioeconomic status. Oral Health Prev Dent. 2019;17:323-327.
29. Tagelsir Ahmed A, Soto-Rojas AE, Dean JA, et al. Prevalence of molar-incisor hypomineralization and other enamel defects and associated sociodemographic determinants in Indiana. J Am Dent Assoc. 2020; 151:491-501.
30. 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; 27:11-21.