

# Etiological Factors Involved in Molar-Incisor Hypomineralization in 7 to 12-Year-Old Children in Tehran

# Razieh Khanmohammadi<sup>1</sup>, Bahman Seraj<sup>1,2</sup>, Ahmadreza Salari<sup>3</sup>, Firoozeh Alipour<sup>1\*</sup>

- 1. Department of Pediatric Dentistry, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran
- 2. Dental Research Center, Dentistry Research Institute, Tehran University of Medical Sciences, Tehran, Iran
- 3. Private Practice, Tehran, Iran

Article Info	ABSTRACT
<i>Article type:</i> Original Article	<b>Objectives:</b> Molar-incisor hypomineralization (MIH) lesions are common in children. The prevalence of MIH is variable in different communities. However, information regarding the prevalence of MIH in the Iranian population is limited. This study sought to assess the prevalence and etiological factors of MIH in 7-12-year-old children in Tehran.
<i>Article History:</i> Received: 27 Nov 2021 Accepted: 23 May 2022 Published: 27 Jun 2022	<b>Materials and Methods:</b> This descriptive, cross-sectional study evaluated 1028 elementary students between 7-12 years, selected from different districts of Tehran in 2017. The frequency of MIH in the maxillary and mandibular molars and incisors was determined by clinical examination. In order to assess the role of different factors in the development of MIH, a questionnaire was filled out by the mothers regarding problems during their pregnancy, medical history of children, and age of occurrence of systemic conditions (if any). The effect of different factors on the development of MIH was analyzed by the logistic regression test.
* Corresponding author: Department of Pediatric Dentistry, School of Dentistry, Tehran University of Medical Sciences, Tehran, Iran Email: alipour.firoozeh@yahoo.com	<b>Results:</b> The prevalence of MIH was found to be 25.6%. The delivery condition of the mother (P<0.001), history of urinary tract infection (P<0.011), history of chickenpox (P<0.018), and frequent use of amoxicillin during childhood (P<0.041) significantly affected the occurrence of MIH. The most commonly involved teeth were the mandibular left first molars.
	<b>Conclusion:</b> The prevalence of MIH in our study population was within the range reported in the literature. Considering the relatively high prevalence of MIH in 7-12-year-old children, pediatric dentists should pay special attention to treatment of MIH. <b>Keywords:</b> Students; Iran; Dental Enamel Hypoplasia

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## **INTRODUCTION**

Enamel hypomineralization is a developmental anomaly, which may occur alone or in association with dysplasia in other tissues, some systemic conditions, or genetic/ environmental factors [1]. Molar-incisor hypomineralization (MIH) refers to enamel defects in one or more permanent molars with/without incisors[2]. According to another definition, MIH often involves one or more permanent first molars with a minimum of one hypomineralized incisor [3]. MIH of molars is not related to fluoride and the teeth are referred to as cheese molars [4]. Localized enamel opacities in MIH are different from the more diffuse opacities related to fluorosis [5]. The involved porous teeth have higher susceptibility to plaque accumulation and are at higher risk of caries and fracture after eruption. The influential factors in the etiopathology of MIH include medical problems (before, during and after birth), environmental pollutants, and genetic factors.

Copyright © 2022 The Authors. Published by Tehran University of Medical Sciences. This work is published as an open access article distributed under the terms of the Creative Commons Attribution 4.0 License (http://creativecommons.org/licenses/by-nc/4). Non-commercial uses of the work are permitted, provided the original work is properly cited. The term MIH was first used in 2001 to describe permanent first molars with white or vellow-brown discoloration, which were often associated with hypomineralized permanent incisors[6]. Enamel defects in MIH have a systemic origin and can affect a number of teeth. Unlike tetracycline discoloration or linear enamel hypoplasia, MIH does not have chronological manifestations. Unlike amelogenesis imperfect it does not affect the entire dentition [7]. In MIH, the enamel structure is soft and porous. Thus, unusual cavities may develop, and enamel destruction may occur in the occlusal surface. Defective enamel structure also results in development of hypersensitivity, secondary caries, suboptimal restorative treatments, restoration loss, and eventual tooth loss [8,9].

The reported prevalence of MIH varies from 4% to 25%. However, most previous studies on this topic have been conducted in European countries [10,11]. Ahmadi et al. [12] evaluated the prevalence of MIH and its correlation with systemic conditions in a group of Iranian children and showed that the prevalence of this condition was 12.7%. Mehran et al. [13] studied 1400 elementary students in Tehran and reported that 34.2% of females and 30.1% of males had enamel defects in their permanent incisors and first molars.

Despite the significance of MIH, studies regarding its prevalence in Iran are limited. Thus, we sought to assess the prevalence and etiological factors of MIH in 7-12 year-old children in Tehran.

# MATERIALS AND METHODS

This descriptive cross-sectional study was conducted on 7-12 year-old children residing in Tehran, who were selected from elementary schools in different municipal districts by cluster sampling. The parents signed informed consents prior to the participation of their children in the study.

The sample size was calculated to be 1028 students considering the prevalence range of MIH to be 0.5% to 40.2% and its global prevalence of 14.2% [14], and assuming P=0.12, d=34\%, power of 90% and effect size of 2. The students were selected by random cluster sampling such that one girls' school

and one boys' school were chosen from different municipal districts of Tehran. For sample selection, first male and female students were separated by stratified sampling, and the required number of males and females was calculated. We categorized Tehran into 5 areas of north, west, south, and center, and one district was randomly selected from each area. By doing so, the obtained results could be generalized to the entire population of Tehran. Ten schools were randomly selected from each district (5 girls' schools and 5 boys' schools). One class was chosen from each school (with averagely 20 students in each class). Prior to clinical examination, the examiner (a senior dental student) received instructions regarding the clinical manifestations of MIH and other enamel defects, and the kappa coefficient of agreement was calculated to assess the intraobserver agreement, which was found to be 0.9, indicating good agreement. Students in the first school were examined by both the senior dental student and a faculty member pedodontist. Their results were compared and disagreements were resolved the bv discussion until the inter-observer agreement reached 1. The students in the remaining schools were examined by the senior dental student alone.

The inclusion criteria were age range of 7-12 years, willingness for participation in the study, and cooperation during clinical examination. The exclusion criteria were presence of enamel or dentin defects in all teeth, chronological hypoplasia, history of trauma, and history of infection in primary incisor teeth.

For clinical examination, first the surface of maxillary and mandibular permanent first molar and incisors was cleaned with a gauze and then wetted and inspected for presence of opaque spots, surface destruction, and caries using a dental explorer and cap flashlight.

Also, in order to determine the possible predictive factors for MIH, a questionnaire was filled out by the mothers to collect information regarding the health status of their children in the preschool years, their demographics, possible confounders related to development of MIH such as the delivery method, problems during pregnancy and delivery such as pregnancy diabetes, difficult vaginal delivery, etc. The questionnaire also asked some questions regarding birth weight, febrile infectious diseases, antibiotic use, renal diseases, asthma, respiratory problems, diabetes mellitus, etc. This information was collected from the mothers by asking them to fill out a form in this respect.

Data were analyzed using SPSS version 23 (SPSS Inc., IL, USA). The frequency and percentage of variables were calculated and reported. The prevalence of MIH was calculated in general, and separately for each maxillary and mandibular molar and incisor tooth. The binary logistic regression (backward step-wise LR model) was applied to assess the effect of different variables on the occurrence of MIH in general, and separately for each tooth. Type 1 error was considered to be 0.05.

# RESULTS

Among the 1028 patients, 520 (50.6%) were males and 508 (49.4%) were females and 263 (25.6%) had MIH. Of the mothers, 62 (6%) had preeclampsia (systolic blood pressure >140 mmHg or diastolic blood pressure >90 mmHg, often associated with hematuria), 47 (4.6%) had hypertension, 105 (10.2%) had pregnancy diabetes and 67 (6.5%) had respiratory problems and asthma. Duration of breast-feeding was less than 6 months for 85 children (8.3%), between 6-12 months for 181 (17.6%), between 12-18 months for 689 (67%) and over 18 months for 73 children (7.1%). A total of 809 (87.7%) had been delivered vaginally while 129 (12.5%) were delivered by the cesarean section. Also, 31 (3%) mothers reported difficult delivery and 59 children (5.7%) had low birth weight (<2.5 kg).

Table 1 reports the history of different medical conditions in children. Involvement with MIH was noted in mandibular permanent first molars in 129 patients (12.5%), maxillary permanent first molars in 74 children (7.2%), maxillary incisors in 48 patients (4.7%) and mandibular incisors in 10 children (1%). No other tooth was involved with MIH.

**Table 1.** Frequency of different medicalconditions in children

History of disease	Number	Percentage
Ear infection	290	28.2
<b>Respiratory problems</b>	98	9.5
Urinary tract infection	89	8.7
Febrile diseases	117	11.4
Chickenpox	520	50.6
Use of amoxicillin	210	20.4
Chronic renal diseases	86	8.4
Long-term jaundice	113	11
History of allergy	99	9.6
Asthma	60	5.8
Diabetes mellitus	43	4.2
Celiac disease	7	0.7
Cleft lip ± palate	3	0.3
Cystic fibrosis	10	1
Cardiac problems	25	2.4
History of anesthesia	5	0.5
Seizure	12	1.2

Table 2 shows the frequency of involvement of teeth with MIH. Mandibular left first molars had the highest frequency of involvement (n=271, 26.4%) followed by mandibular right first molars (n=256, 24.9%), maxillary right first molars (n=240, 23.3%) and maxillary left first molars (n=195, 19%). Regression analysis was applied to assess the effect of different variables on the occurrence of MIH.

As shown in Table 3 the results of the regression test for prediction of development of MIH in 7-12 year-olds revealed that among the assessed variables, only the delivery condition of the mother (P<0.001), history of urinary tract infection (P<0.011), history of chickenpox (P<0.018), and history of frequent use of amoxicillin during childhood (P<0.041) significantly affected the development of MIH, and other variables had no significant effect.

Involved tooth	Number	Percentage
Mandibular right first molar	256	24.9
Mandibular left first molar	271	26.4
Maxillary right first molar	240	23.3
Maxillary left first molar	195	19
Maxillary right central incisor	41	4
Maxillary left central incisor	32	3.1
Maxillary right lateral incisor	23	2.2
Maxillary left lateral incisor	19	1.8
Mandibular left central incisor	15	1.5
Mandibular left canine	7	0.7
Mandibular right canine	7	0.7
Mandibular right central incisor	6	0.6
Mandibular right lateral incisor	4	0.4
Mandibular left lateral incisor	3	0.3

Table 2. Freq	uency of molar	-incisor hyp	omineralization
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On the other hand, the results of regression analysis in prediction of development of hypomineralization in the maxillary incisors revealed that preeclampsia (P<0.0001), pregnancy diabetes (P<0.04), and history of asthma and respiratory problems during pregnancy had significant effects on the development of hypomineralization in maxillary incisors while other variables had no significant effect.

Also, delivery condition of the mother (P<0.042) and development of chickenpox (P<0.041) had significant effects on development of hypomineralization in mandibular incisors of 7-12-year-olds. Other variables had no significant effect. Preeclampsia (P<0.0001), history of asthma and respiratory problems during pregnancy (P<0.0001), frequent use of amoxicillin (P<0.007) and history of diabetes in children (P<0.01) had significant effects on hypomineralization of maxillary permanent **Table 3.** Regression analysis for prediction of molar-incisor

 hypomineralization development in 7–12-year-old children

Variable	Р
Gender	0.216
Age	0.387
Preeclampsia	0.989
Pregnancy hypertension	0.983
Pregnancy diabetes	0.988
Asthma and respiratory problems during pregnancy	0.991
Duration of breastfeeding	0.226
Delivery condition of the mother	0.001*
History of ear infection	0.132
Age of ear infection	0.131
Respiratory problems	0.999
Age of respiratory problem development	1
Development of urinary tract infection	0.011*
Age of urinary tract infection	0.847
development	0 5 0 4
Age of fobrile disease development	0.504
Age of febrine disease development	0.301
Age of development of chickenpox	0.010
Frequent use of amovicillin	0.174
Ago of froquent use of amovicillin	0.041
Age of nequent use of amovicinin	0.090
Ago of affliction with chronic ronal discassos	0.990
Age of annound white the onic renar diseases	0.990
Age of affliction with coliac disease	0.372
Cleft lin and nalate	0.545
Age of affliction with cleft lin + nalate	1
Long-term jaundice	0 3 2 9
Age of affliction with long-term jaundice	0.925
Development of cystic fibrosis	0.701
Development of cardiac problems	0.549
Age of affliction with cardiac problems	0.701
Development of allergy	0.981
Age of affliction with allergy	0.982
History of general anesthesia	1
Age receiving general anesthesia	1
Development of asthma	1
Age of onset of asthma	0.999
Development of diabetes mellitus	0.254
Age of onset of diabetes mellitus	0.171
Development of seizure	0.991
Age of onset of seizure	0.991

\* Significant

**Table 4.** Results of the regression model regardingthe effect of different factors on the occurrence ofmaxillary permanent first molar hypomineralization

Variable	В	SE	Р	Exp(B)
Preeclampsia	2.637	0.607	0.0001	13.97
Asthma or respiratory diseases during pregnancy	3.151	0.613	0.0001	23.358
Frequent use of amoxicillin	2.961	1.105	0.007	19.324
Diabetes mellitus	2.576	0.993	0.01	13.143

B: estimated coefficient; SE: standard error; Exp (B): exponential value of B or odds ratio

Preeclampsia (P<0.0001), history of asthma and respiratory problems during pregnancy (P<0.0001), delivery condition of the mother (P<0.016), development of chickenpox (P<0.007) and affliction with cystic fibrosis (P<0.015) had significant impact on the development of hypomineralization in mandibular permanent first molars. Other variables had no significant effect (Table 5).

**Table 5.** Results of the regression model regarding theeffect of different factors on the occurrence ofmandibular permanent first molar hypomineralization

Variable	В	SE	Р	Exp(B)
Preeclampsia	3.938	0.518	0.0001	51.33
Asthma or respiratory diseases during pregnancy	3.34	0.572	0.0001	28.212
Delivery conditions	0.66	0.274	0.016	1.934
Chicken pox	1.671	0.619	0.007	5.317
Cystic fibrosis	-3.565	1.467	0.015	0.028

B: estimated coefficient; SE: standard error; Exp (B): exponential value of B or odds ratio

#### DISCUSSION

This study assessed the prevalence and etiological factors of MIH in 7–12-year-old children in Tehran. According to the results, the prevalence of MIH in 7-12-year-old students in Tehran was 25.6%. The reported prevalence

rates for MIH vary from 0.5% to 40.2% in previous studies and its global prevalence rate is reportedly 14.2% [14]. Thus, the value obtained in our study was within the previously reported range.

In total, our results revealed higher prevalence of MIH in our study population compared with most other populations. The prevalence of MIH in our study was close to the value reported in 6-11-year-olds by Lucheng district, Wenzhou city, China, which was 25.5% [15]. Other reported values were mostly lower than that found in the present study. Ahmadi et al. [12] reported the prevalence of MIH to be 12.7% in a group of Iranian children, which was lower than our value while Mehran et al. [13] evaluated 1400 elementary students in Tehran and reported that 34.2% of females and 30.1% of males had enamel defects in their permanent incisor and first molar teeth. Difference in the prevalence of MIH in different geographical areas is probably due to the effect of environmental (before and after birth), sociodemographic, and behavioral factors (socioeconomic status, and lactation). method nutrition, of assessment (examination under light. retrospective, prospective or longitudinal study design), and rate of caries in the study population [16,17]. Genetics and age may also play a role in development of MIH [18]. By an increase in age over 10 years, a significant drop is noted in the prevalence of MIH [19]. Also, children younger than 10 years have higher prevalence of MIH compared with those over 10 years of age; however, since aging increases the rate of destruction of teeth, older children may show more severe signs and symptoms [20]. Also, higher rate of utilization of preventive and therapeutic dental care services by older children may decrease the prevalence of MIH in them.

The results of regression test in our study revealed that the delivery condition of the mother, history of urinary tract infection, history of chickenpox, and history of frequent use of amoxicillin during childhood had significant impacts on development of MIH. The risk factors of MIH in previous studies included the use of penicillin or macrolides in the first year of life, use of amoxicillin in the first 3 years of life, history of acute earache [21], Prenatal and postnatal factors such as systemic diseases of the mother, medication intake during pregnancy, birth-related complications or premature birth, history of fever, asthma, or respiratory infections during infancy, alcohol consumption by the mother, race [22], history of infectious diseases before and after birth, [20]low birth weight, history of urinary tract infection, chickenpox or allergy [23], age [19], preterm delivery and respiratory disorders at birth [24], history of asthma, fever or antibiotic intake during childhood [25], low socioeconomic class [26], medical problems of the mother and child before, during or after birth [12], teenage pregnancy [27], and use of amoxicillin [28].

In the present study, gender and age had no significant impact on development of MIH. However, some previous studies found a difference in the prevalence of MIH in males and females, which was attributed to the difference in time of development and complete formation of tooth crowns, time of tooth eruption, and oral hygiene practice between males and females [16,26].

No consensus has been reached regarding the possible causes of MIH [18,29]. Genetics may play a role in this respect. However, epidemiological studies with a standardized methodology in different countries are required to confirm this theory [16,30]. During fetal development, infection [20], psychological stresses of the mother, and frequent ultrasound exposures [31] have been shown to significantly increase the risk of MIH. During birth, the cesarean section and the complications of vaginal delivery can both increase the risk of MIH in children [32]. al. [33] showed Alaluusua et that developmental defects in teeth were correlated with long-term breastfeeding. Also, evidence shows that use of beta-2 agonists and corticosteroids increases the frequency of severe MIH [34]. Respiratory diseases are also correlated with MIH [35]. Also, respiratory diseases in the first year of life can influence tooth formation by oxygen deprivation[36]. Chickenpox, caused by Varicella zoster affects the epithelial surface and can attack the

ameloblasts derived from the epithelium in enamafel development phase and influence their activity [28,36]. Treatment with antibiotics especially amoxicillin in the first 3 vears of life is also correlated with development of MIH. It may be due to the direct impact of amoxicillin on active ameloblasts or the infective nature of disease for which, antibiotics have been prescribed [37]. The correlation of some systemic conditions with development of MIH highlights the role of pediatricians in early detection of MIH and early referral of patients to pediatric dentists for in-time management of these lesions.

In the present study, mandibular left first molars had the highest rate of involvement with MIH (26.4%) followed by mandibular right first molars (24.9%), maxillary right first molars (23.3%) and maxillary left first molars (19%). In the study by Buchgraber et al, [38] in south Austria, maxillary and mandibular molar teeth were equally involved while maxillary incisors had a higher rate of involvement than mandibular incisors. Subramaniam et al. [39] reported that mandibular molars had a higher rate of involvement with MIH than maxillary molars (29.41% versus 27.94%). Their results were almost in line with our findings. de Lima et al. [24] reported that maxillary molars had the highest prevalence of MIH (36.1%). Cho et al. [11] evaluated Chinese children in Hong Kong and reported that maxillary permanent first molars were more commonly involved with MIH followed by mandibular permanent first molars and maxillary central incisors.

The results of studies regarding the prevalence of MIH in the maxilla and mandible have been controversial. Some studies found no significant difference between the maxilla and mandible while some other reported higher prevalence of MIH in the maxilla [4, 40]. The reason for this difference has not been clearly understood. However, development of mandibular molars starts later than maxillary molars. Thus. factors affecting tooth development during this period may be responsible for development of MIH [11,17].

Considering our adequately large sample size and reliable method of examination, it seems that our results are generalizable to the entire population of elementary schoolers regard MIH children aged 7 to 10 years old in Tehran. One limitation of this study was absence of a data bank regarding the medical history of children. Thus, we had to ask the mothers to fill out a questionnaire to collect information in this regard. According to the European Academy of Pediatric Dentistry, the best age for clinical examination of teeth for MIH is 8 vears of age since the eruption of target teeth is almost complete and the possibility of not detecting MIH lesions due to tooth-colored restorations would be minimal at this age [30]. Thus, we selected patients in the age range of 7 to 12 years. Considering the high prevalence of MIH in our study population, further attempts should be made for detection and restoration of MIH defects. Moreover, this study was conducted in Tehran. There is a lack of validity, as the respondent may be forgetful or not be thinking within the full context of the situation. Further studies on children residing in other cities of Iran are recommended.

### CONCLUSION

The prevalence of MIH in our study population was within the range reported in the literature and delivery condition of the mother, history of urinary tract infection, history of chickenpox, and history of frequent use of amoxicillin during childhood, significantly affected the development of MIH. Considering the relatively high prevalence of MIH in 7-12 year-old children, pediatric dentists should pay special attention to treatment of MIH.

#### CONFLICT OF INTEREST STATEMENT None declared.

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