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Original Article

Prevalence of Molar Incisor Hypomineralization Among Children Treated with Asthmatic Drugs During Their First Three Years of Life (A Cross-Sectional Study)

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Abstract

Aim: This present study aims to assess the prevalence of Molar Incisor Hypomineralization among a group of children treated with asthmatic drugs during their first three years of life.

Subjects and methods: The study included 160 asthmatic patients (aged 8 to 12 years old) attending the outpatients' pediatric pulmonary unit of two Pediatric Hospitals. A clinical examination was performed to diagnose the presence or absence of Molar Incisor Hypomineralization and its severity. Data about medical history, duration, and types of asthmatic drugs were obtained from the parents and the hospital's medical records

Results: Among the study population, 23.1 % had Molar Incisor Hypomineralization, where 15% were mild, 4.4% were moderate, and only 3.8 % were severe cases. The prevalence of Molar Incisor Hypomineralization was higher in males (25.2 %) than in females (19.3 %). However, all the severe cases were found among females. All cases took corticosteroids in combination with beta-2-agonist and/or antihistamines.

Conclusion: Children treated with asthmatic drugs - especially corticosteroid inhalers-during their first three years of life showed an increased risk for MIH with a higher prevalence among males than females.

Keywords: MIH, Asthma, Asthmatic drugs, Asthmatic Children

Introduction

Molar-Incisor Hypomineralization (MIH) is classified as a qualitative defect in the development of the enamel of uncertain etiology. The European Academy of Pediatric Dentistry (EAPD) proposed its first terminology in 2003 to describe a condition with an indefinite etiology that affects one or more permanent molars and may also involve permanent incisors. [1]

Epidemiological studies from diverse parts of the world show an extensive variation in the prevalence of MIH, ranging between 2.8 to 40.2%. However, this variation may be due to a deficiency of standardized tools for recording MIH, which causes the prevalence to be underestimated. [2]

The characteristic feature of MIH-affected teeth is the presence of porous enamel, which can be damaged easily under regular masticatory forces leading to cavities with

rough, irregular margins that facilitate the development of caries. Therefore, MIH poses a significant problem for both the patient and the clinicians because of the hypersensitive teeth that are difficult to be anesthetized due to chronic pulp irritation and challenging to be restored. [3,4]

To explain the possible etiological factors, it is essential to consider that the mineralization of the first permanent molars (FPMs) and permanent incisors commences at the end of the gestation period and is accomplished throughout the first three years of life. Thus, abnormalities in this period affect the function of ameloblasts resulting in the occurrence of MIH. [5,6,7]

The etiological factors of MIH are thought to be systemic in origin. Many studies have claimed that postnatal problems and diseases during the first three years of life were more commonly seen in children with MIH than those without. Respiratory diseases such as pneumonia, Asthma, and asthmatic drugs, affect the pH of the tooth enamel during its formation, which inhibits the action of the proteolytic enzymes and affects the development of the hydroxyapatite crystal resulting in enamel hypomineralization .[8,9]

One of the most important routes of asthma drug administration is aerosol therapy; the drugs most often used in aerosol therapy are corticosteroids, beta-2 agonists, anticholinergics, and mucolytics. Studies have demonstrated that corticosteroids interfere with amelogenesis in the same way they disturb bone formation. Therefore, it may also affect tooth mineralization and hypothetically cause MIH. Besides, both corticosteroids and beta-2 agonists, especially in powder formulations, have an acid pH that can damage the enamel .[10, 11]

Although an increasing number of studies worldwide have assessed the potential etiological factors involved in the occurrence of MIH, there is insufficient evidence regarding neonatal and childhood diseases associated with MIH etiology. Moreover, many potential factors are highly associated, and most researchers failed to account for confounding variables.[7,12] Therefore, this study aimed to assess the prevalence of Molar Incisor Hypomineralization and its severity among a group of children who have been treated with asthmatic drugs early in their lives.

Subjects and Methods

The study was designed to be an observational cross-sectional study which was carried out in Pediatric pulmonary units of Agouza Police Hospital and Abu Rish Japanese Pediatric Hospital in Cairo, Egypt.

The target participants consisted of asthmatic children aged 8-12 attending the Pediatric Pulmonary Clinics and taking asthmatic drugs during their first three years of life. The participant having fully erupted permanent first molar and permanent incisors were included in the study. Children with chronic diseases other than asthma were excluded. Children with an orthodontic appliance or extensive caries lesions were also excluded from the study.

Sample size calculation:

The sample size was determined by the Centre of Evidence-Based Dentistry at the Faculty of Dentistry, Cairo University. By adopting a confidence interval of (95%), and a margin of error of (5%) with finite population correction; The predicted sample size (n) was a total of (160) cases. The sample size was calculated using Epi info for windows version 7.2. The sample size calculation was reviewed and approved by the Medical Biostatistics Unit (MBU), Faculty of Dentistry, Cairo University.

Data source management:

Data were collected through clinical examination to detect MIH's presence and severity. Also, a written questionnaire was used to collect information regarding the child's prenatal, perinatal, and postnatal circumstances to eliminate confounders.

Data collection through the questionnaire:

Data about medical history and onset, duration, and types of asthmatic drugs the participants have been taking early in their lives were obtained from the parents and the medical records at the Pulmonary Clinics.

The data were collected through one single sheet, self-administered, structured questionnaire in the Arabic language, answered by the child's guardians. This questionnaire was based on five validated previously published questionnaires performed in Saudi Arabia, Greece, Turkey, Germany, and Lebanon.[7,8,9,14,15]

The questionnaire was only to collect data about the medical history of the participants in a way to eliminate the effect of confounders that may results in MIH.

The questionnaire was carefully addressing questions concerned with possible etiological factors that might be associated with MIH and related to prenatal circumstances (mother's medical history during pregnancy and medication administrated), birth complications (conditions during delivery, birth weight, the necessity for incubator and breastfeeding), and postnatal conditions and child medical history during his first three years of life.

Clinical examination:

A clinical examination was performed by the principal investigator in the pediatric pulmonary clinic to identify the presence or absence of MIH. The clinical examination was carried out using a mirror and probe to examine each first permanent molar & permanent incisors following the diagnostic criteria of MIH set by the European Academy of Pediatric Dentistry (EAPD). [16]

In case of a positive diagnosis, the severity of MIH was classified, according to Mathu-Muju & Wright, 2006, into three categories Mild, Moderate, and Severe MIH [2]:

a- Mild MIH: demarcated opacities, color changes only (creamy white or yellow-brown).

b- Moderate MIH: loss in enamel substance with normal dental sensitivity.

c- Severe MIH: loss in enamel substance with affected dentine or atypical restoration and usually associated with dental hypersensitivity.

Bias:

- Selection bias: avoided by the selection of all presented patients that follow the eligibility criteria.
- Information bias: prevented by explaining the aim of the study to the parents and not guiding them through answering the questionnaire.
- Detection bias: all data collected were accurately recorded and detected.

Statistical methods:

Statistical analysis was performed with SPSS 20®1, Graph Pad Prism®1, and Microsoft Excel 2016. All qualitative data were presented as frequency & percentages. All comparisons were performed using the Chi-square test to assess the difference in proportions of answers to questions with more than two responses. It was verified at $P \leq 0.05$. The results are considered statistically significant if the p-value was less than 0.05. Different associations were analysed using spearman's correlation coefficient test.

Results:

Demographic data of the participants

The present study included 160 asthmatic children. Out of them, 64.4 % (n=103) were males, and 35.6 % (n= 57) were females.

Prevalence and severity of MIH

The total prevalence of MIH among the population was 23.1% (n= 37). Following the diagnostic criteria set by the EAPD, the presence of Demarcated opacities of enamel was the highest finding with 23.1% (n=37), while only 1.3% (n=2) of the population presented with atypical restorations. On the

other hand, the criteria of an extracted tooth due to MIH and failure of tooth eruption due to MIH were completely absent in the study population as shown in Table (1).

Regarding MIH severity, 15% (n=24) had Mild MIH, 4.4% (n=7) had Moderate MIH, and 3.8% (n=6) had severe MIH. In the present study, MIH cases were higher in males 25.2 % (n=26), than in females 19.3 % (n=11). However, all the severe MIH cases were only found among females as shown in Tables (2) and (3).

Responses to the questionnaire

The frequency and percentages of yes and no answers to general medical questions are presented in Table (4). Most children's mothers did not take medications during pregnancy, 91.9% (n= 147), nor had complications during labor, 99.4% (n= 159). Most of the participants, 82.5% (n= 132), had received breastfeeding, and their mothers were not taking any medication during the breastfeeding period, 98.1% (n= 157).

Regarding the incubation necessity and duration, only 15% (n=24) of the whole population needed an incubator after birth. The Incubation duration ranged from 1day to one month, with an insignificant statistical difference between different durations at P-value = 0.45. The frequency and percentages of MIH severity distribution among results of medical history questions are presented in **Error! Reference source not found.**).

The beginning and type of asthmatic drug intake and their correlation with the prevalence of MIH were assessed as shown in **Error! Reference source not found.**). Comparison between different answers revealed a significant statistical difference between different answers at P<0.0001, where 57.9% of children (n=92) started their asthmatic drugs at age 1-2 years old. However, there was a weak positive insignificant correlation between the age of starting the asthmatic drugs and MIH with [r (P) = 0.12 (0.1)].

In addition, a comparison between different types of asthmatic drugs have been taken by the child revealed a significant statistical difference between different types at P < 0.0001, where most of the population 62.5% (n= 100), were taking Corticosteroid inhalers, in addition to beta 2 agonists, and 13.1% (n= 21) were taking them in addition to antihistamines. Only 4.4 % (n=7) were taking beta-2-agonist without corticosteroids, and 19.4 % (n=31) were taking corticosteroids without beta-2 agonists. It was found through the distribution of MIH severity among types of asthmatic drugs that all the participants who developed MIH were taking corticosteroids either with beta-2-agonist or with antihistamines, or with both of them with the combination between corticosteroids and beta-2-agonist being significantly the highest in all MIH severity levels. Table (7) presents the frequency and percentages of MIH severity distribution among starting asthmatic medications and their type.

Table (1): Frequency and percentages of presence or absence of MIH diagnostic criteria among children taking asthmatic drugs:

MIH	Absent		Present		P-value
	N	%	N	%	
Presence of demarcated opacities	123	76.9%	37	23.1%	<0.0001*
Presence of enamel breakdown	154	96.3%	6	3.8%	<0.0001*
Presence of atypical restoration	158	98.8%	2	1.3%	<0.0001*
Presence of extracted tooth due to MIH	160	100.0%	0	0.0%	<0.0001*
Presence of failure of eruption	160	100.0%	0	0.0%	<0.0001*

N: count %: percentage P: probability level which is significant at P ≤ 0.05

Table (2): Frequency and percentages of MIH severity among children taking asthmatic drugs:

severity of MIH	N	%	P-value
No MIH	123 a	76.9%	<0.0001*
Mild	24 b	15.0%	
Moderate	7 c	4.4%	
Severe	6 c	3.8%	

N: count %: percentage P: probability level which is significant at P ≤ 0.05
Counts with the same superscript letters were insignificantly different as P > 0.05
Counts with different superscript letters were significantly different as P <0.05

Table (3): Frequency and percentages of MIH severity distribution among gender

MIH severity	Total N	Male (n=103)		Female (n=57)		P-value
		N	%	N	%	
Normal cases	123	77 [a]	74.8%	46 [a]	80.7%	0.39
Mild MIH	24	20 [b]	19.4%	4 [b]	7.0%	0.03*
Moderate MIH	7	6 [c]	5.8%	1 [c]	1.8%	0.23
Severe MIH	6	0 [d]	0.0%	6 [b]	10.5%	0.0008*
P value		<0.0001*		<0.0001*		

N: count %: percentage P: probability level which is significant at P ≤ 0.05
Counts with the same superscript letters were insignificantly different as P > 0.05
Counts with different superscript letters were significantly different as P < 0.05

Table (4): Frequency and percentages of yes and no answers to general medical questions

	Q	No		Yes		P-value
		N	%	N	%	
Q1	Did the mother take any medications during pregnancy?	147	91.9%	13	8.10%	<0.0001*
Q2	Were there any complications during labor?	159	99.4%	1	0.6%	<0.0001*
Q3	Was the baby within the normal weight range at birth?	12	7.5%	148	92.5%	<0.0001*
Q4	Was it necessary to put the baby in an incubator after birth and what was its duration?	136	85.0%	24	15%	<0.0001*
Q5	Was it breastfeeding or formula feeding? and if it was breastfeeding what was its duration?	28	17.50%	132	82.50%	<0.0001*
Q6	Did the mother take any medication during the period of breastfeeding?	157	98.1%	3	1.9%	<0.0001*
Q7	Did the child suffer from any other illness during the first three years of life?	160	100.0%	0	0.0%	<0.0001*
Q8	Was the child subjected to Prolonged use of antibiotics early in life?	152	95.0%	8	5.0%	<0.0001*
Q10	Did the child suffer from asthma from the first three years of life?	0	0.0%	160	100.0%	<0.0001*
Q11	Was the child required to be hospitalized and placed on a ventilator as a result of asthma?	114	71.3%	46	28.70%	<0.0001*

N: count %: percentage P: probability level which is significant at P ≤ 0.05

Table (5): Frequency and percentages of MIH severity distribution among results of medical history questions

Question	Answer	Normal (n=123)		Mild (n=24)		Moderate (n=7)		Severe (n=6)	
		N	%	N	%	N	%	N	%
Q1 Medication intake during pregnancy	No	112	91.1	22	91.7	7	100	6	100
	Yes	11	8.9	2	8.3	0	0	0	0
	P value	<0.0001*		<0.0001*		<0.0001*		<0.0001*	
Q2 Complications during labor	No	123	100	23	95.8	7	100	6	100
	Yes	0	0	1	4.2	0	0	0	0
	P value	<0.0001*		<0.0001*		<0.0001*		<0.0001*	
Q3 Normal weight at birth	No	5	4.1	5	20.8	2	28.6	0	0
	Yes	118	95.9	19	79.2	5	71.4	6	100
	P value	<0.0001*		<0.0001*		0.12		<0.0001*	
Q4 Incubation necessity and duration	No	107	87.0	16	66.7	7	100	6	100
	Yes	16	13.0	8	33.3	0	0	0	0
	P value	<0.0001*		0.02*		<0.0001*		<0.0001*	
Q5 Breast feeding or formula feeding and its duration	No	23	18.7	4	16.7	1	14.3	0	0
	Yes	100	81.3	20	83.3	6	85.7	6	100
	P value	<0.0001*		<0.0001*		0.01*		<0.0001*	
Q6 Medications taken by mother during breast feeding	No	120	97.6	24	100	7	100	6	100
	Yes	3	2.4	0	0	0	0	0	0
	P value	<0.0001*		<0.0001*		<0.0001*		<0.0001*	
Q7 Any other illness of the child during first three years of life	No	123	100	24	100	7	100	6	100
	Yes	0	0	0	0	0	0	0	0
	P value	<0.0001*		<0.0001*		<0.0001*		<0.0001*	
Q8 Prolonged use of antibiotics	No	115	93.5	24	100	7	100	6	100
	Yes	8	6.5	0	0	0	0	0	0
Q8 Prolonged use of antibiotics (cont.)	P value	<0.0001*		<0.0001*		<0.0001*		<0.0001*	
Q10 Suffering from asthma during first	No	0	0.0	0	0.0	0	0	0	0
	Yes	123	100.0	24	100.0	7	100	6	100
	P value	<0.0001*		<0.0001*		<0.0001*		<0.0001*	
Q11 Hospitalization and ventilation	No	91	74.0	15	62.5	4	57.1	4	66.7
	Yes	32	26.0	9	37.5	3	42.9	2	33.3
	P value	<0.0001*		0.06		0.58		0.27	

N: count %: percentage

P: probability level which is significant at $P \leq 0.05$

Table (6): Frequency and percentages of different answers to Q9 (starting asthmatic medications and their type)

Q9: starting asthmatic medications and their type		N	%	P-value
Age	<1 year	54 a	34.0%	<0.0001*
	1-2 years	93 b	57.8%	
	2-3 years	13 c	8.2%	
Type	Corticosteroid's inhaler	5 ad	3.1%	<0.0001*
	Antihistamine	1 a	0.6%	
	Corticosteroid's inhaler + beta 2 agonist	100 b	62.5%	
	Corticosteroid's inhaler + antihistamine	26 c	16.3%	
	Beta 2 agonist + antihistamine	7 d	4.4%	
	Corticosteroid's inhaler + beta 2 agonist+ antihistamine	21 b	13.1%	

N: count %: percentage P: probability level which is significant at P ≤ 0.05
Counts with the same superscript letters were insignificantly different as P > 0.05
Counts with different superscript letters were significantly different as P <0.05

Table (7): Frequency and percentages of MIH severity distribution among starting asthmatic medications and its type

Q9: starting asthmatic medications and its type		Total N	Normal (n=123)		Mild (n=24)		Moderate (n=7)		Severe (n=6)		r(P)
			N	%	N	%	N	%	N	%	
Age	<1 year	54	42 a	34.4%	8 a	33.3%	2 a	28.6%	2 a	33.3%	0.12(0.1)
	1-2 years	93	77 b	62.3%	10 a	41.7%	2 a	28.6%	4 b	66.7%	
	2-3 years	13	4 c	3.3%	6 b	25.0%	3 a	42.9%	0 c	0.0%	
	P value		< 0.0001*		0.04*		0.59		0.01*		
Type	Corticosteroid's inhaler	5	4 a	3.3%	1 a	4.2%	0 a	0.0%	0 a	0.0%	
	anti-histamine	1	1 b	0.8%	0 a	0.0%	0 a	0.0%	0 a	0.0%	
	Corticosteroid's inhaler + beta 2 agonist	100	74 c	60.2%	15 b	62.5%	7 b	100.0%	4 b	66.7%	
	Corticosteroid's inhaler + anti-histamine	26	22 d	17.9%	2 a	8.3%	0 a	0.0%	2 c	33.3%	
	Beta 2 agonist + anti-histamine	7	7 a	5.7%	0 a	0.0%	0 a	0.0%	0 a	0.0%	
	Corticosteroid's inhaler + beta 2 agonist + anti-histamine	21	15 d	12.2%	6 c	25.0%	0 a	0.0%	0 a	0.0%	
	P value		< 0.0001*		< 0.0001*		<0.001*		0.01*		

N: count %: percentage P: probability level which is significant at P ≤ 0.05
Counts with the same superscript letters were insignificantly different as P > 0.05
Counts with different superscript letters were significantly different as P < 0.05

Discussion

Molar Incisor Hypomineralization is a relatively unknown entity with an incompletely defined etiology.[12,17]

Respiratory disease, mainly Asthma during the first three years of life, is considered to be one of the etiological factors of MIH mostly because of the frequently used corticosteroids in the treatment of asthmatic children, which may also affect the tooth mineralization process causing MIH.[7]

Few studies have studied the association between Asthma and MIH. Nevertheless, those studies differ in their study design and population size. Therefore, it isn't easy to obtain a final agreement based on their results.[11] Therefore, this study aimed to determine the prevalence of MIH among asthmatic children treated with asthmatic drugs in their first three years of life.

The eligibility criteria included children treated with asthmatic drugs during their first three years. Since the mineralization of the first permanent molars and permanent incisors occurs during the late gestation period and lasts during the first three years of childhood, therefore, abnormalities in this period might affect ameloblasts leading to the occurrence of MIH. [6, 15]

The study population was aged from 8 to 12 years old, which is the optimal age when all permanent first molars and most incisors have erupted. In addition, the permanent first molars will be in relatively good condition without extensive post-eruptive breakdown or caries. [5,9, 18]

Regarding the gender of the participants, the number of males (64.4%, n=103) was significantly higher than females (35.6 %, n= 57), although studies showed that Asthma tends to be more common among girls compared to boys; however, Asthma is more diagnosed among boys before puberty and then the "gender-shift" toward females after puberty .[19]

In the present study, out of 160 clinically examined asthmatic children, 23.1% (n= 37) were diagnosed with MIH, where 15% (n=24) had Mild MIH, 4.4% (n=7) had Moderate MIH, and 3.8% (n=6) had severe MIH. That percentage is much lower than that set by **Guergolette et al., 2009** [20]**,** whose study revealed that (89.7%) of the asthma group presented dental enamel defects, compared with only (38.2%) of those in the control group**.** Also, **Visweswar et al., 2012** [21] found that the asthma group (76.9%) presented with dental enamel defects, compared with only (26.9%) of those in the control group**.** This broad difference in the prevalence might be due to the effect of confounders like birth complications, prolonged use of antibiotics, and early chronic diseases.

On the other hand, the results of the present study were nearly similar to those found by **Mastora et al., 2017** [14], who found the overall prevalence of MIH among the asthmatic children (case group) to be 24 children (34.3%).

Following the diagnostic criteria of MIH set by EAPD, all the MIH cases had demarcated enamel opacities, and 3.8% (n=6) of the whole population developed post-eruptive enamel breakdown in addition to the enamel opacities. Only 1.3% (n=2) had atypical restoration, and no one in the population had an extracted tooth or a tooth that failed to erupt due to MIH. This is consistent with other studies where the demarcated opacities were the most frequent pattern among MIH cases .[18,22]

In the present study, MIH cases were higher in males 25.2 % (n=26) than in females 19.3 % (n=11). That was in accordance with the results of the previous studies of **Wogelius et al., and Abdalla et al., 2021** [11, 18], which showed that boys had slightly higher MIH prevalence than girls.

Although Mild MIH was significantly higher in males 19.4% (n=20) than in females 7% (n=4), all the severe MIH cases were only found among females. This is in agreement with **Abo ElSoud and Mahfouz, 2019** [23] study conducted in Egypt where the severity of MIH was higher in girls 32.14%, than in

boys 5.33%. This could be because girls are more advanced in dental development than boys. Hence the affected first permanent molars are more advanced in their eruption. Hypomineralized molars would be exposed to masticatory stresses, causing post-eruptive degradation earlier than in boys. [24]

The participants' weight at birth and the necessity of incubator usage affected the final results to some extent, where 20.8% (n=5) of the mild MIH cases and 28.6 %(n=2) of the moderate MIH cases had low birth weight. In comparison, 33.3 % (n=8) of the mild MIH cases required an incubator after birth for different periods. That was following a recent systematic review of **Garot et al., 2021** [25], which demonstrated that; low birth weight and complications, including hypoxia, increased the possibility of MIH**.**

Regarding the age at which the child started his asthmatic drugs, there was a weak positive insignificant correlation between that age of starting the asthmatic drugs and MIH. This was similar to **Mastora et al., 2017** [14] results, where no difference between the occurrence of enamel defects and the duration of drug use occurred.

Corticosteroids were considered in many studies to be a causative factor for ameloblastic activity disturbance resulting in MIH. [14] In the present study, the type of asthmatic drugs taken during the first three years of life was recorded according to the questionnaire filled out by the parents and the child's medical record whenever possible. It was revealed that most of the population were taking corticosteroid inhalers with beta-2-agonist 62.5% (n=100), and 13.1% (n= 21) were taking them in addition to antihistamines. Only 4.4 % (n=7) were taking beta-2-agonist without corticosteroids, and 19.4 % (n=31) were taking corticosteroids without beta-2 agonists.

It was shown that all the participants who developed MIH were taking corticosteroids either with beta -2-agonist or with antihistamines, or with both of them with the combination between corticosteroids and beta-2-agonist being significantly the highest in all MIH severity levels. This was reinforced by the fact that corticosteroid medication is frequently used with asthmatic children and is known to inhibit osteoblast activity and development, resulting in reduced bone production. There could be a comparable impact on ameloblasts, which could help to explain how Asthma can increase an individual's risk of developing MIH. [8]

This was in agreement with a systematic review conducted by **Serna et al., 2016** [26], assessing the drugs that may cause MIH. That review acknowledged that the association between the use of asthma drugs with enamel defects had been documented. However, those drugs couldn't be recognized as a reason for such defects because no study researchers have used a control group of children who have Asthma but have not taken medication.

Limitations of the study:

Because some participants' prenatal, perinatal, and postnatal medical histories were not documented in medical records, data gathering depended mainly on parents'/guardians' memory to fill out the questionnaire, which could generate reporting biases. However, mothers accurately remembered perinatal factors such as birth weight, route of delivery, and gestational age, even many years after the events.

Conclusion:

Children treated with asthmatic drugs during their first three years of life showed an increased risk for Molar Incisor Hypomineralization with a higher prevalence among males than females. The present study revealed that it might be a correlation between asthmatic drugs, especially corticosteroids, and the prevalence of MIH. However, further prospective studies on the etiology of MIH are needed.

Abbreviations:

Molar Incisor Hypomineralization (MIH), European Academy of Pediatric Dentistry (EAPD).

Conflict of Interest:

The authors declare no conflict of interest.

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Ethics:

This study protocol was approved by the ethical committee of the faculty of dentistry-Cairo university on the 30th of April,2020, approval number: 9420

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