Do We Really Know the Prevalence of MIH?

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Aim: To analyze the existing variability on molar incisor hypomineralization prevalence in the literature; to distinguish the various molar incisor hypomineralization prevalence rates in different countries, areas, and regions of the world; and to know the valid diagnostic criteria used for the correct identification of molar incisor hypomineralization prevalence. Study design: A literature review from Medline® and Cochrane Library® online databases was performed using five terms individually or in combination. Articles not reporting diagnostic criteria employed and articles not written English were excluded. The results were analyzed by country, region, year of study, sample size, range of age, and prevalence rate. Results: A total of 37 articles in English were selected from 1987 to 2014 and from those only 14 employed the EAPD's 2003 diagnostic criteria. The reported age range varied from 5.5 to 17 years; the most frequently range used was 7 to 9 years. A wide prevalence range from 2.8% to 44% was found and 82.61% of the articles reported calibrated examiners. Conclusions: Comparison among the results of the studies is difficult due to the use of different indexes and diagnostic criteria, the analysis variability, selection methods, and different age groups. In reality, we are probably far from knowing the real MIH prevalence.

Key words: Molar incisor hypomineralization,, prevalence.

INTRODUCTION

he molar incisor hypomineralization (MIH) is a condition previously recognized and named with multiple terms, which could lead to confusion. Recently MIH has been defined as: "Hypomineralization of systemic origin from one to four first permanent molars frequently associated with affected incisors" ¹.

The hypomineralized enamel defect has its origin in the different stages of amelogenesis, with an ameloblast disturbance in the transitional or early maturation stage, resulting in a reduced mineral deposit; thus being a qualitative defect ^{2,3}.

The MIH etiological factors have not yet been well defined, although theories of combination of factors and its action in synergism have been proposed. A questionnaire sent to pediatric dentists throughout Europe in 2003 showed that this condition can be found all over Europe, but the prevalence rates are not entirely comparable ⁴.

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Previous studies have used different criteria to define this dental disorder, which has complicated the comparison of the resulting prevalence. Only one third of the investigations have been performed in all age cohorts or children randomly selected from the target population ⁵. Concerning MIH, in the sixth congress of the European Academy of Paediatric Dentistry (EAPD) it was concluded that there was a limited number of studies about MIH prevalence and thus it was necessary to modify the diagnostic criteria ⁶.

Weerheijm, et al. ⁽¹⁾, indicates that the MIH examination should be conducted on cleaned and moistened teeth (all clearly visible opacities should be recorded, regardless of their size) at the optimal age of 8 years old, since at this age all permanent molars and incisors have erupted. Currently the MIH prevalence rate varies from 2.8% to 44%. This condition is relatively frequent and can lead to serious problems for the affected children and their families by the consequences of pain, posteruptive breakdown, chewing and eating problems, esthetics, and treatment difficulties; for those reasons there is a growing concern for this entity, especially in Europe where it seems to be increasing.

In 2003 the EAPD ¹ defined the MIH characteristics and stated that permanent first molars and incisors should be examined (12 index teeth), this examination for MIH should be performed on wet teeth after cleaning and having established five criteria to be considered in epidemiological studies, based on 8-year-old population. Each tooth should be recorded for: absence or presence of demarcated opacities (white, yellow, or brown in color); posteruptive enamel breakdown (loss of initially formed enamel surface after tooth eruption, typically related to a pre-existent opacity); atypical restoration; extraction due to MIH and failure of eruption of a molar or incisor ¹.

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MIH affects first permanent molars that are often hypersensitive to normally innocuous thermal, mechanical and osmochemical stimuli, and decay rapidly; the presence of dental caries can mask the true diagnosis of MIH ^{7,8}. In order to classify the MIH severity, Mathu-Muju and Wright ⁹ proposed clinical criteria for severity levels.

Due to the wide prevalence range reported, a literature review has been conducted to analyze the existing variability on MIH prevalence in the literature; to find out about the various MIH prevalence rates in different countries, areas, and regions of the world; and to know the valid diagnostic criteria for the correct identification of the MIH prevalence.

MATERIALS AND METHOD

A literature review from Medline® and Cochrane Library® online databases was performed using the following terms: "MIH", "molar incisor hypomineralisation /hypomineralization", "prevalence", "epidemiological study", "enamel defects", "first permanent molars and incisors"; individually or in combination. The articles had to be in English specifying the diagnostic criteria employed, if the examiner performed a calibration for the study and the size and age of the sample. The results were analyzed by country, region, year of study, sample size, range of age, and prevalence rate.

RESULTS

From an initial selection in our search of 43 articles in English from 1987 to 2014, we finally selected 37 because there were six articles with unspecified diagnostic criteria. Most of the studies about MIH prevalence have been conducted in Europe, although we have found reports from many other countries. Currently, the prevalence varies among 2.8% and 44%. Table 1 includes the articles collected reporting MIH prevalence and the diagnostic criteria employed, but from the 37 studies presented in Table 1 only 14 studies employed the EAPD 2003 criteria (Table 2).

The continental prevalence for MIH was estimated with the data collected in Table 1. Results were: 8.3% in Africa ^{10,11}; 12.93% in Asia ¹²⁻¹⁷; 16.23% in Europe ¹⁸⁻⁴⁰; 24.92% in Oceania ^{26,41-43}, and 30% in South America ^{44,45}. The diagnostic criteria employed were: Koch ¹⁸, Alaluussa ¹⁹, mDDE (modified Developmental Defects of the Enamel index) ⁴⁶, and EAPD's 2003 ¹. In one case ³⁹ the authors evaluated all teeth according to a specific index developed in line with the diagnostic criteria defined by Weerheijm *et al* in 2003 ⁶.

The reported age range varied from 5.5 to 17 years and the most frequently range used was 7-9 years of age. A wide prevalence range was observed: from 2.8% to 44%. Calibrated examiners were reported in 86.21% of the publications.

DISCUSSION

Most of the MIH international studies have been conducted since the beginning of the 1980's to date in European countries and in children of European descent ¹⁵. In them, and due to the disparity of existing criteria at the beginning of the investigations, epidemiological studies presented before the establishment of the EAPD criteria in 2003 probably do not reveal the real prevalence of the defect ³².

Out of the 37 selected articles, 14 used the EAPD criteria of 2003 and the remaining 23 used other criteria such as Koch *et al* 18 , Alaluusua 19 and mDDE 46 . The evaluation of wet teeth was present

only in 46.4% of the studies. When the mDDE criteria were established, the wet teeth inspection was proposed by the FDI ⁴⁶. It is very important to fullfil these criteria, since there are studies of higher prevalence with dry teeth inspected ⁵. In one case ³⁹ the authors evaluated all teeth according to a specific index developed related to the diagnostic criteria defined by Weerheijm *et al* in 2003 ⁶.

It is worth to mention the existence of 15 studies from 2004 to 2013 that did not use the diagnostic criteria of the EAPD in their research. These data reflected the variability in diagnostic criteria, the deficiency in the calibration of the examiners and a poor agreement with EAPD's MIH diagnostic criteria. Large-scale studies on children samples are difficult to conduct, especially when a specific variable has to be determined. An accurate calibration of the examiners is required, which is complicated in countries without widely public dental health services established ³². The calibration and training of examiners with valid methods should be mandatory ⁵ to obtain more accurate results.

The clinical prevalence data currently available, mainly in Northern Europe, ranges between 3,6% and 25%, appearing the highest rates in children living in areas of low levels of fluoride and whose mothers had been encouraged to practice extensive and prolonged breastfeeding ⁴⁷. The wide prevalence range could be explained by differences in applying diagnostic criteria.

In other studies ^{42,43} neither socioecomical status nor ethnicity were modifiying factors in the occurrence of MIH. In a study performed in 2012 in Northern England ⁴⁰ prevalence of MIH was related to socioeconomic status but not to water fluoridation.

May be further noted that although recent studies have used the diagnostic criteria of the EAPD 2003, comparing them is difficult. Out of the 34 studies presented in Table 1, only 14 studies employed the EAPD 2003 criteria. In this group of investigations it is still difficult to compare prevalences due to the different age range studied and the performance of wet/dry teeth inspection.

CONCLUSIONS

The comparison between the results of the studies is difficult due to the use of different indexes and diagnostic criteria, the analysis variability and selection methods.

In this group of studies it is still difficult to compare prevalences due to the age range employed and the performance of wet/dry teeth inspection.

Worldwide epidemiological studies for MIH prevalence following the same diagnostic criteria are required.

In reality, we are probably far from knowing the real MIH prevalence.

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Table 1. MIH prevalence and diagnostic criteria employed (mDDE: modified Developmental Defects of the Enamel index; NR: not reported).

Region Country		Author	Year	Size	Age in years	Prevalence (%)	Diagnostic criteria	Calibr.
Europe	Sweden	Koch et al	1987	2226	8-13	15.4	Koch et al 1987 (Colour and surface changes. Exclusion of hypomineralisation of known origin, Al or fluorosis).	yes
Europe	Finland	Alaluusua et al	1996	102	6-7	17	Exclusion of hypoplasia, fluorosis and defects related to major disturbances in general health.	NR
Europe	Finland	Alaluusua et al	1996	97	12	25	Exclusion of hypoplasia, fluorosis and defects related to major disturbances in general health.	NR
Europe	Sweden	Jälevik et al	2001	516	8	18.4	mDDE	yes
Europe	Finland	Leppäniemi et al	2001	488	7-13	19.3	Exclusion of hypoplasia, fluorosis and defects related to major disturbances in general health.	NR
Europe	Netherlands	Weerheijm et al	2001	497	11	9.7	mDDE	yes
Europe	UK	Zagdwon et al	2002	307	7	14.6	mDDE	yes
Europe	Germany	Dietrich et al	2003	2408	10-17	5.6	mDDE	yes
Europe	UK	Balmer et al	2005	25	8-16	40	mDDE	yes
Oceania	Australia	Balmer et al	2005	25	8-16	44	mDDE	yes
Europe	Italy	Calderara et al	2005	227	7.3-8.3	13.7	mDDE	yes
Africa	Libya	Fteita et al	2006	378	7-8.9	2.9	mDDE	yes
Europe	Germany	Preusser et al	2006	1022	6-12	5.9	Koch et al 1987	yes
Europe	Lithuania	Jasulaityte et al	2007	1277	7-9	9.7	EAPD 2003	yes
Europe	Netherlands	Jasulaityte et al	2008	442	9	14.3	mDDE	yes
Europe	Bosnia Herzegovina	Muratbegovic et al	2008	560	12	12.3	EAPD 2003	NR
Europe	Greece	Lygidakis et al	2008	3518	5.5-12	10.2	EAPD 2003	yes
Oceanía	Australia	Arrow	2008	511	7.1	22	mDDE	yes
Asia	China	Cho et al	2008	2635	12	2.8	EAPD 2003	yes
Africa	Kenya	Kemoli	2008	3591	6-8	13.71	Demarcated opacities, posteruptive defects, extensive restorations	yes
Europe	Turkey	Kuscu et al	2008	147	7-9	14.9	EAPD 2003	yes
Europe	Denmark	Wogelius et al	2008	647	6-8	37.5	EAPD 2003	yes
Europe	Turkey	Kuscu et al	2009	153	7-10	9.1-9.2	EAPD 2003	yes
South America	Brazil	Soviero et al	2009	292	7-13	40.2	Demarcated opacities, posteruptive defects, extensive restorations	yes
Oceania	N. Zealand	Mahoney et al	2009	522	8.2	14.9	mDDE	NR
South America	Brazil	Da Costa-Silva et al	2010	918	6-12	19.8	Demarcated opacities, posteruptive defects, extensive restorations	yes
Asia	Jordan	Zawaideh et al	2011	3241	8.4± 0.7	17.6	EAPD 2003	yes
Asia	Iraq	Ghanim et al	2011	823	7-9	21.5	EAPD 2003	yes
Oceania	N.Zealand	Mahoney et al	2011	756	8.2	15.7	mDDE	NR
Asia	India	Parikh et al	2012	1366	8-12	9.2	EAPD 2003	yes
Europe	Spain	Martinez et al	2012	550	6-14	17.85	EAPD 2003	yes
Europe	England	Balmer et al	2012	3233	12	15.9	mDDE	yes
Europe	Slovenia	Groselj et al	2013	558	6-11.5	21.4	mDDE	yes

Region	Country	Author	Year	Size	Age in years	Prevalence (%)	Diagnostic criteria	Calibr.
Asia	Iran	Ghanim et al	2014	810	9-11	20.2	EAPD 2003	yes
Europe	Germany	Petrou et al	2014	2395	8-9	10.1	EAPD 2003	yes
Asia	India	Mittal et al	2014	1792	6-9	6.31	EAPD 2003	yes

Table 2. Studies based on EAPD 2003 diagnostic criteria for MIH (NR: not reported).

Region	Country	Author	Year	Size	Age in years	Prevalence (%)	Study group	Calibr.	Wet=W Dry=D	Size
Europe	Lithuania	Jasulaityte et al	2007	1277	7-9	9.7	Random sample	yes	W	NR
Europe	Bosnia Herzegovina	Muratbegovic et al	2008	560	12	12.3	Randomly selected stratified school groups	NR	NR	> 2mm
Europe	Greece	Lygidakis et al	2008	3518	5.5-12	10.2	Two danish communities. Age cohorts	yes	W	Visible
Asia	China	Cho et al	2008	2635	12	2.8	Patients	yes	W	NR
Europe	Turkey	Kuscu et al	2008	147	7-9	14.9	Study of records	yes	W	NR
Europe	Denmark	Wogelius et al	2008	647	6-8	37.5	Consecutive patients in community pediatric dental center	yes	NR	Visible
Europe	Turkey	Kuscu et al	2009	153	7-10	9.1-9.2	Random sample	yes	W	NR
Asia	Jordan	Zawaideh et al	2011	3241	8.4± 0.7	17.6	Nacional cross-sectional study	yes	D	Visible
Asia	Iraq	Ghanim et al	2011	823	7-9	21.5	Cross- cohort study	yes	D	> 2mm
Asia	India	Parikh et al	2012	1366	8-12	9.2	Random sample	yes	W	NR
Europe	Spain	Martinez et al	2012	550	6-14	17.85	Patients from the pediatric dental center	yes	W	NR
Asia	Iran	Ghanim et al	2014	810	9-11	20.2	Random sample	yes	W	NR
Europe	Germany	Petrou et al	2014	2395	8-9	10.1	National cross- sectional study	yes	W	NR
Asia	India	Mittal et al	2014	1792	6-9	6.31	Random sample	yes	W	NR

REFERENCES

- Weerheijm KL, Duggal M, Mejàre I, Papagiannoulis L, Koch G, Martens LC, Hallonsten AL. Judgement criteria for molar incisor hypomineralisation (MIH) in epidemiologic studies: a summary of the European meeting on MIH held in Athens, 2003. Eur J Paediatr Dent 4: 110-3, 2003.
- Van Amerongen W, Kreulen C. Cheese molars: a pilot study of the etiology of hypocalcifications in first permanent molars. ASDC J Dent Child 62: 266-9, 1995.
- Beentjes V, Weerheijm K, Groen H. Factors involved in the aetiology of molar-incisor hypomineralisation (MIH). Eur J Paediatr Dent 3: 9-13, 2002.
- Weerheijm KL, Mejàre I. Molar Incisor hypomineralization: a questionnaire inventory of its occurrence in member countries of the European Academy of Paediatric Dentistry (EAPD). Int J Paediatr Dent 13: 411-6, 2003
- Jälevik B. Prevalence and diagnosis of molar-incisor-hypomineralisation (MIH): A systematic review. Eur Arch Paediatr Dent 11: 59-64, 2010.
- Weerheijm KL. Molar Incisor Hypomineralisation (MIH). Eur J Paediatr Dent 4: 114-20, 2003.
- Rodd H, Boissonade F, Day P. Pulpal status of hypomineralized permanent molars. Pediatr Dent 29: 514-20, 2007.
- Willmott N, Bryan R, Duggal M. Molar-incisor-hypomineralisation: A literature review. Eur Arch Paediatr Dent 9: 172-9, 2008.
- Mathu-Muju K, Wright J. Diagnosis and treatment of molar incisor hypomineralization. Compend Contin Educ Dent 27: 604-10, 2006.
- Fteita D, Ali A, Alaluusua S. Molar-incisor hypomineralization (MIH) in a group of school-aged children in Benghazi, Libya. Eur Arch Paediatr Dent 7: 92-5, 2006.
- Kemoli A. Prevalence of molar incisor hypomineralisation in six to eight year-olds in two rural divisions in Kenya. East Afr Med J 85: 514-9, 2008.
- Cho S, Ki Y, Chu V. Molar incisor hypomineralization in Hong Kong Chinese Children. Int J Paediatr Dent 18: 348-52, 2008.
- Zawaideh F, Al-Jundi S, Al-Jaljoli M. Molar incisor hypomineralisation: prevalence in Jordanian children and clinical characteristics. Eur Arch Paediatr Dent 12: 31-6, 2011.
- Ghanim A, Morgan M, Mariño R, Bailey D, Manton D. Molar-incisor hypomineralisation: prevalence and defect characteristics in Iraqi children. Int J Paediatr Dent 21: 413-21, 2011.
- Parikh D, Ganesh M, Bhaskar V. Prevalence and characteristics of molar incisor hypomineralisation (MIH) in the child population residing in Gandhinagar, Gujarat, India. Eur Arch Paediatr Dent 13: 21-6, 2012.
- Ghanim A, Bagheri R, Golkari A, Manton D. Molar-incisor hypomineralisation: a prevalence study amongst primary schoolchildren of Shiraz, Iran. Eur Arch Paediatr Dent 15: 75-82, 2014.
- 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 15: 11-8, 2014.
- Koch G, Hallonsten A, Ludvigsson N, Hansson B, Holst A, Ullbro C. Epidemiologic study of idiopathic enamel hypomineralization in permanent teeth of Swedish children. Community Dent Oral Epidemiol 15: 279-85, 1987.
- Alaluusua S, Lukinmaa P, Vartiainen T, Partanen M, Torppa J, Tuomisto J. Polychlorinated dibenzo-p-dioxins and dibenzofurans via mother's milk may cause developmental defects in child's teeth. Environ Toxicol Pharmacol 1: 193-7, 1996.
- Alaluusua S, Lukinmaa P, Koskimies M, Pirinen S, Hölttä P, Kallio M, Holttinen T, Salmenperä L. Developmental dental defects associated with long breast feeding. Eur J Oral Sci 104: 493-7, 1996.
- Jälevik B, Klingberg G, Barregård L, Norén J. The prevalence of demarcated opacities in permanent first molars in a group of Swedish children. Acta Odontol Scand 59: 255-60, 2001.
- Leppäniemi A, Lukinmaa P, Alaluusua S. Non fluoride hypomineralizations in the permanent first molars and their impact on the treatment need. Caries Res 35: 36-40, 2001.
- Weerheijm K, Groen H, Beentjes V, Poorterman J. Prevalence of cheese molars in elevenyear- old Dutch children. ASDC J Dent Child 68: 259-62, 2001
- Zagdwon A, Toumba K, Curzon M. The prevalence of developmental enamel defects in permanent molars in a group of English school children. Eur J Paediatr Dent 3: 91-6, 2002.

- Dietrich G, Sperling S, Hetzer G. Molar incisor hypomineralisation in a group of children and adolescents living in Dresden (Germany). Eur J Paediatr Dent 4: 133-7, 2003.
- Balmer R, Laskey D, Mahoney E, Toumba K. Prevalence of enamel defects and MIH in non-fluoridated and fluoridated communities. Eur J Paediatr Dent 6: 209-12, 2005.
- Calderara P, Gerthoux P, Mocarelli P, Lukinmaa P, Tramacere P, Alaluusua S. The prevalence of Molar Incisor Hypomineralisation (MIH) in a group of Italian school children. Eur J Paediatr Dent 6: 79-83, 2005.
- Preusser S, Ferring V, Wleklinski C, Wetzel W. Prevalence and severity of molar incisor hypomineralization in a region of Germany - a brief communication. J Public Health Dent 67: 148-50, 2007.
- Jasulaityte L, Veerkamp J, Weerheijm K. Molar incisor hypomineralization: review and prevalence data from the study of primary school children in Kaunas/Lithuania. Eur Arch Paediatr Dent 8: 87-94, 2007.
- Jasulaityte L, Weerheijm K, Veerkamp J. Prevalence of molar-incisor-hypomineralisation among children participating in the Dutch National Epidemiological Survey (2003). Eur Arch Paediatr Dent 9: 218-23, 2008.
- Muratbegovic A, Zukanovic A, Markovic N. Molar-incisor-hypomineralisation impact on developmental defects of enamel prevalence in a low fluoridated area. Eur Arch Paediatr Dent 9: 228-31, 2008.
- Lygidakis N, Dimou G, Briseniou E. Molar-incisor-hypomineralisation (MIH). Retrospective clinical study in Greek children. I. Prevalence and defect characteristics. Eur Arch Paediatr Dent 9: 200-6, 2008.
- Kuscu O, Caglar E, Aslan S, Durmusoglu E, Karademir A, Sandalli N.
 The prevalence of molar incisor hypomineralization (MIH) in a group of children in a highly polluted urban region and a windfarm-green energy island. Int J Paediatr Dent 19: 176-85, 2009.
- Wogelius P, Haubek D, Poulsen S. Prevalence and distribution of demarcated opacities in permanent 1st molars and incisors in 6 to 8-year-old Danish children. Acta Odontol Scand 66: 58-64, 2008.
- Kuscu O, Caglar E, Sandalli N. The prevalence and aetiology of molar-incisor hypomineralisation in a group of children in Istanbul. Eur J Paediatr Dent 9: 139-44, 2008.
- Martínez T, Guinot F, Bellet L, Giner L. Prevalence of molar-incisor hypomineralisation observed during transillumination in a group of children from Barcelona (Spain). Int J Paediatr Dent 22: 100-9, 2012.
- Groselj M, Jan J. Molar incisor hypomineralisation and dental caries among children in Slovenia. Eur J Paediatr Dent 14: 241-5, 2013.
- Petrou MA, Giraki M, Brissar AK, Basner R, Wempe C, Altarabulsi MB, et al. Prevalence of molar-incisor hypomineralisation among school children in four German cities. Int J Paediatr Dent 24: 434-40, 2014.
- Sönmez H, Yildirim G, Bezgin T. Putative factors associated with molar incisor hypomineralisation: an epidemiological study. Eur Arch Paediatr Dent 14: 375-80, 2013.
- 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 22: 250-7, 2012.
- Arrow P. Prevalence of developmental enamel defects of the first permanent molars among school children in Western Australia. Aust Dent J 53: 250-9. 2008
- Mahoney EK, Morrison DG. The prevalence of MIH in Wainuiomata children. N Z Dent J 105: 121-7, 2009.
- Mahoney EK, Morrison DG. Further examination of the prevalence of MIH in the Wellington region. N Z Dent J 107: 79-84, 2011.
- Soviero V, Haubek D, Trindade C, Da Matta T, Poulsen S. Prevalence and distribution of demarcated opacities and their sequelae in permanent 1st molars and incisors in 7 to 13 year old Brazilian children. Acta Odontol Scand 67: 170-5, 2009.
- Da Costa-Silva C, Jeremias F, De Souza J, Cordeiro R, Santo-Pinto L, Zuanon A. Molar incisor hypomineralization: prevalence, severity and clinical consequences in Brazilian children. Int J Paediatr Dent 20: 426-34, 2010.
- FDI. A review of the development defects of enamel index (DDE Index).
 Commission on Oral Health, Research and Epidemiology. Report of an FDI Working Group. Int Dent J 42: 411-26, 1992.
- 47. Ogden A, Pinhasi R, White W. Nothing new under the heavens: MIH in the past? Eur Arch Paediatr Dent 9: 166-71, 2008.