Universidad Europea

GRADUATION PROJECT

Degree in Dentistry

MOLAR INCISOR HYPOMINERALIZATION (MIH). HISTORICAL EVOLUTION AND CURRENT PREVALENCE IN SPAIN. ETIOLOGY, PREVENTION, AND MANAGEMENT.

Madrid, academic year 2022/2023

Identification number: **197**

SUMMARY AND KEYWORDS

Introduction: Molar Incisor Hypomineralization (MIH) is a qualitative developmental disorder affecting the enamel of first permanent molars and incisors. In recent years, MIH has become a significant public health concern that can lead to rapid enamel breakdown and sensitivity, causing pain and functional impairment, constituting a major challenge for dentists; **Objectives**: the primary objective was to evaluate the current knowledge on MIH, including its diagnosis, prevalence, etiology, prevention, and management. The specific objectives were to provide a detailed overview of the epidemiology and etiology, describe the clinical aspects and diagnostic guidelines, know the importance of early diagnosis, and analyze the strategies of prevention and clinical management; **Materials and Methods**: a systematic literature review was conducted via databases such as Medline, PubMed, and Google Scholar. Using keywords and MESH terms, a research question has been yielded. According to inclusion and exclusion criteria, a total of 75 articles, published between 1987 and 2023, were obtained; **Results**: 33 articles were revised, reporting on the prevalence and the possible etiologies of MIH. MIH is a prevalent dental condition affecting up to 13,5% of people globally with significant variation across geographic regions. The etiology of MIH has been identified to be multifactorial and several factors was implicated, including prenatal and perinatal factors, childhood illnesses, environmental factors, and genetic factors; **Conclusion**: the review underlines the need for uniform diagnostic criteria and treatment guidelines. While many risk factors have been discovered, the cause of MIH is still unknown. To better understand the genesis, diagnosis, and treatment of MIH, additional studies are required.

KEYWORDS: Dentistry; molar incisor hypomineralization; qualitative defect of the enamel; etiology; management.

RESUMEN Y PALABRAS CLAVES

Introducción: La Hipomineralización Molar Incisivo (MIH) es un trastorno cualitativo del desarrollo que afecta el esmalte de los primeros molares permanentes e incisivos. En los últimos años, MIH se ha convertido en un importante problema de salud pública que puede provocar una rápida degradación y sensibilidad del esmalte, causando dolor y deterioro funcional, lo que constituye un gran desafío para los dentistas; **Objetivos**: el objetivo principal fue evaluar el conocimiento actual sobre MIH, incluido su diagnóstico, prevalencia, etiología, prevención y manejo. Los objetivos específicos fueron brindar un panorama detallado de la epidemiología y etiología, describir los aspectos clínicos y las pautas diagnósticas, entender la importancia del diagnóstico precoz y analizar las estrategias de prevención y manejo clínico; **Materiales y Métodos**: se realizó una revisión sistemática de la literatura a través de bases de datos como Medline, PubMed y Google Scholar. Usando palabras clave y términos MESH, se ha generado una pregunta de investigación. Según criterios de inclusión y exclusión se obtuvieron un total de 75 artículos, publicados entre 1987 y 2023; **Resultados**: se revisaron 33 artículos, informando sobre la prevalencia y las posibles etiologías de MIH. MIH es una condición dental frecuente que afecta hasta el 13,5% de las personas a nivel mundial con una variación significativa entre las regiones geográficas. Se ha identificado que la etiología de MIH es multifactorial y varios factores están implicados, incluidos factores prenatales y perinatales, enfermedades infantiles, factores ambientales y factores genéticos; **Conclusión**: la revisión subraya la necesidad de criterios de diagnóstico y pautas de tratamiento uniformes. Si bien se han descubierto muchos factores de riesgo, aún se desconoce la causa de MIH. Para comprender mejor la génesis, el diagnóstico y el tratamiento de MIH, se requieren estudios adicionales.

PALABRAS CLAVES: Odontología; hipomineralización molar incisivo; defecto cualitativo del esmalte; etiología; manejo.

1. INTRODUCTION

Molar Incisor Hypomineralization (MIH) is a developmental qualitative enamel defect of systemic origin, typically affecting first permanent molars (FPMs) and permanent incisors (1). This syndrome is a growing dental condition and constitutes one of the most urgent problems in pediatric dentistry nowadays, mostly impacting children between the ages of 6 and 12 years old (2). MIH is characterized by abnormalities of the enamel, such as white, yellow, or brown discoloration, as well as porous and fragile enamel that is vulnerable to injury and decay and may cause pain and sensitivity in the afflicted teeth (3). MIH can range in severity, with some cases just affecting a single tooth and others potentially impacting multiple teeth in various mouth regions. This condition may affect the patient's quality of life due to multiple impairment caused to the tooth, and so create difficulties for dentists offering adequate care (4). Although the exact origin of MIH is unknown, it is thought to be connected to disturbances in early childhood tooth development, such as infections or exposure to toxins from the environment, or others prenatal and perinatal conditions. In light of this ongoing burden, early detection, prevention and management are key to refrain this condition and MIH should receive more global attention as it is a challenging dental public health issue (3).

1.1. Historical evolution: "The Beginning"

100 years ago, in dental literature, a variety of nomenclature and descriptions for enamel defects in hypomineralized molars were used (5). Teeth with "chalky enamel" and "chalky spots" that "crumble" easily is how scientist Bernhard Gottlieb describe them (6). In the late 1970s, the Public Dental Service (PDS) in Sweden have reported a disproportionately high proportion of children with widespread and clearly defined severe enamel hypomineralization in their first molars and incisors of unidentified cause. The PDS was asked by the Swedish National Board of Health and Welfare in 1978 to report instances exhibiting these distinct and particular enamel defects to the board. These studies revealed that the majority of the kid groups with high rate of enamel abnormalities were born around 1970 (3).

In the literature, the first article talking about an idiopathic enamel hypomineralization in children was described by Koch et al in 1987 (7). Throughout many years, more and more investigations have followed to raise relevant information to settle a significant knowledge regarding this new condition they were facing more and more frequently.

In 2001, During the Congress of the European Academy of Pediatric Dentistry (EAPD), the theme of developmental enamel defects (DDE) affecting FPMs has been discussed. From this, four different designations have been proposed to describe this recent dental condition: “hypomineralized FPMs”, “idiopathic enamel hypomineralization in the FPMs”, “non-fluoride hypomineralization in FPMs” and “cheese molars” (1).

First proposed by *Weerheijm et al.* in 2001 (1,8), the term of MIH was finally accepted by the assembly of the 6th congress of EAPD Congress in March of 2003 in Athens, to characterize the clinical picture encountered in one or more of the FPMs (9).

And it is finally in 2010, thanks to the cooperation of *Lygidakis et al.,* that the first clinical Guide regarding “Best Clinical Practice Guidance for clinicians dealing with children presenting with MIH: An EAPD Policy Document” has been published for the benefit of all clinicians (10). A new update is now available since February of 2022 (11).

1.2. Pathogenesis of MIH

1.2.1 Developmental Defects of Enamel

The term DDE refers to changes in the quantity and/or quality of enamel that may impact the size, toughness, and color of teeth because of problems during the amelogenesis. Depending on the stage of enamel production where the ameloblast has been harmed, several types of enamel defects may manifest (12).

Regarding the defects caused by MIH to the tooth, the loss of enamel may occur soon after eruption, known as post-eruptive breakdown, or because of masticatory pressures. This is due to softer and less mineralized enamel, with a decreased hardness and not due to a deficit of enamel thickness. In fact, the hypomineralized condition of MIH, which is a qualitative deficit of enamel mineralization, must be differentiated from hypoplasia, which is a quantitative defect of the enamel that do not affect the degree of mineralization of enamel (1).

1.2.2 Relevant facts about the enamel and its formation

Dental enamel is a highly mineralized content, similar to bone. 87% of its volume and 95% of its weight is given by the highly organized framework of crystallites which therefore makes it the hardest and most mineralized material of the human body. Enamel crystallites have a volume that is 1,000 times more than that of other mineralized structures including dentin, cementum and bone (3). Mature enamel has less than 1% of organic material, compared to other mineralized tissues that contain roughly 20% of organic material (13).

During the amelogenesis, enamel formation takes place. The ameloblasts are the enamel-forming cells and originate from the inner enamel epithelium. When teeth enter the bell stage of growth, enamel production begins along the eventual dentin-enamel junction (DEJ), where the dentin starts its formation simultaneously. Enamel is formed at the cusp tips or in the central part of the incisal edge and is then deposited layer by layer in the cervical region (3,13). During the different stages of maturation of the ameloblast, enamel protein-rich matrix are formed that will subsequently develop into enamel rods or enamel prisms (3).

Mineralization of the enamel takes places at the interface of tooth surface and oral environment where oppositely charged ions inter-exchange and are joined by strong covalent bonds, to form a mineral structure called Calcium Hydroxyapatite [Ca10(PO4)6(OH)2] (13). These crystals will be deposited in a matrix forming a well-

structured network. Then, the matrix will be reabsorbed to make room for the hydroxyapatite, which will be arranged in a perpendicular manner (3).

1.2.3 Enamel Hypoplasia vs MIH

Hypoplasic enamel must be understood as a direct consequence of disturbance during the secretory stage of amelogenesis (process of formation of the enamel), affecting the normal function of ameloblast in the secretion of enamel protein matrix (14). This will result in a pathological enamel reduced in thickness, but with a normal hardness and mineralization (13). An example of this condition would be the hypoplastic type of Amelogenesis Imperfecta (Figure 1).

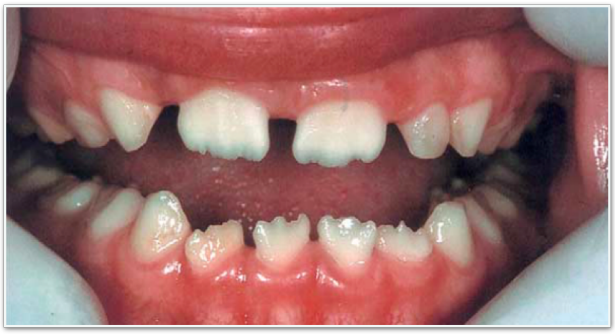


Figure 1. Hypoplastic type of Amelogenesis Imperfecta. Primary and permanent teeth present a thin enamel with normal contour and thickness. (15)

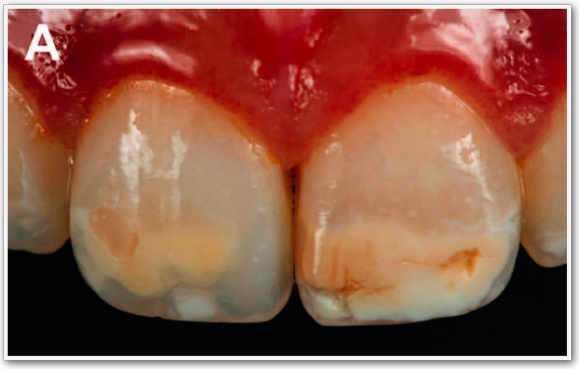


Figure 2. Maxillary central Incisors affected by MIH showing white/yellow/brown stains. (16)

On the contrary, a disturbance during the maturation stage of amelogenesis will result in a hypomineralized enamel (12)(Figure 2). During this stage, the mineral crystal grows in width and thickness which will determine and give the final hardness to the enamel.

A disruption during the first three years of the child's life, which corresponds to the time needed for the maturation process to be completed, will result in a pathologically soft, fragile and porous enamel of normal thickness (13). The formation process of the crowns of first permanents molars and incisors will be then compromised as they are formed during this period of time (1).

In fact, it is really important to distinguish between these two developmental enamel anomalies, as MIH will only affect the quality of the enamel, that is, the hardness and the translucency of the enamel. The tooth will then appear soft and more fragile, increasing the risk of post-eruptive breakdown and will absorb stains from the oral environment due to the greater porosity.

However, a recent study published in The Journal of Clinical Pediatric Dentistry in March of 2022, has shown an association between MIH and enamel hypoplasia. Patients with MIH had a considerably greater frequency of enamel hypoplasia (5.5%) than the control group (0.49%), a difference that was statistically significant. Their conclusion was that these defects appear to be the result of the same hazardous factor operating at various amelogenesis phases (12).

1.2.4 Histological evidence and mineral density

Histologically, a tooth affected by this hypomineralization pattern will present some characteristics. The inorganic content will be slightly lower, so the solubility by acids will increase and less calcium and phosphorus will be found. Focusing on the affected areas (Figure 3), crystals are disorganized and the "hypomineralized enamel has less distinct prisms edges and crystals, and the interprismatic space is more

marked”(2,17) (Figure 4). As a consequence, the organic content will be higher with a larger concentration of carbon (1), and a considerably higher protein content (3).

Regarding the mineral density of the MIH enamel, it has been found that the crystal concentration shows a decreased pattern from the cement-enamel junction (CEJ) towards the occlusal surface with an inverse tendency to increase again in the cusp tip area ; near the dentin-enamel junction (DEJ), the highest mineral density values were recorded (3).

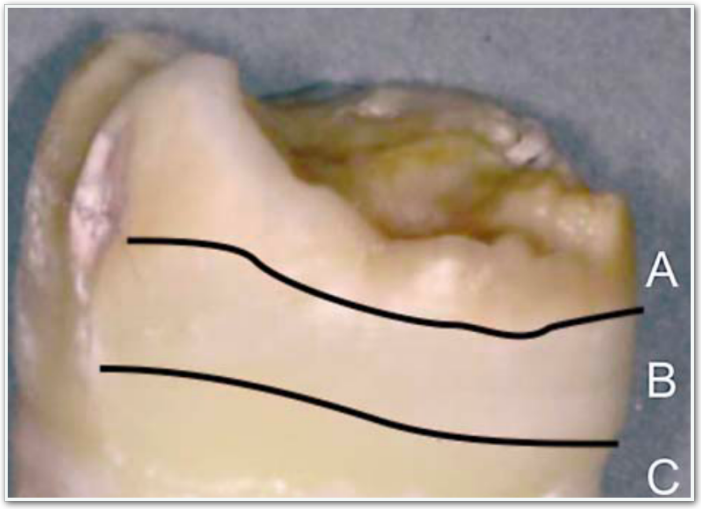


Figure 3. Affected permanent molar which enamel defects caused by MIH have been marked: A) Moderate lesion with ochre-brown stains, B) Mild lesion with cream-white stains, C) Clinically sound enamel. (17)

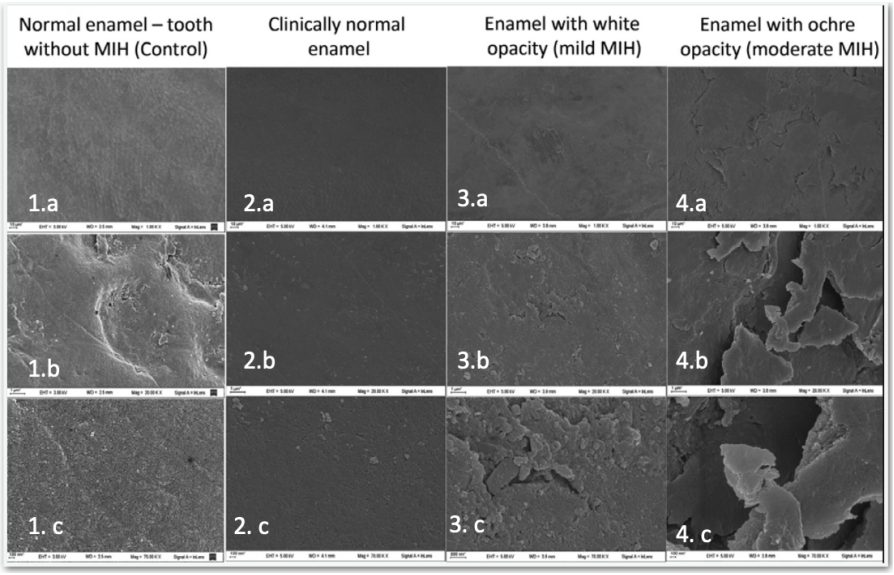


Figure 4. SEM microphotographs of the adamantine. (17)

Comparison between normal and affected enamel (Figure 4):

1. Normal enamel on tooth without MIH (control):
   a) Surface of prismatic enamel without structural changes (magnification 10Kv);
   b) The head of an enamel prism (20Kv);
   c) Surface of the crystals that make up the prism (70Kv).
2. Clinically normal enamel on tooth with MIH:
   a) Prism-like enamel surface without structural changes;
   b) Loss of prismatic pattern image without structural changes;
   c) Prism-like crystals with more rounded ends than the control.

3. Enamel with cream-white opacity (mild MIH):
   a) Surface with minor structural differences from the control;
   b) Presence of cracks and various surface planes (“staggering”);
   c) Globulous surface with tiny fractures.

4. Enamel with ochre-brown opacity (moderate MIH):
   a) Irregular surface with erosions, round hollows with visible bottoms, and scale-like enamel plaques;
   b) Adamantine surface scaling;
   c) Very large, deeply recessed “Y”-shaped crack with an invisible bottom.

1.2.5 Mechanical alterations

Mechanical properties of the enamel could be measured according to different factors such as flexural stress, compressive strength, hardness… An easy way to approximate the harness of the enamel, is by using a probe or a Black spoon and feeling the consistency of the underneath enamel.

Studies that have investigated mechanical alterations of MIH enamel compared to sound enamel, have shown significant lower value in the affected enamel such as the hardness and modulus of elasticity. Therefore, comparing to sound enamel, which has

an elevated degree of hardness, MIH enamel is unlikely to support restorations placed above it which constitutes a real challenge for dentist nowadays (3).

1.2.6 Genetically encoded Enamel

Besides the unknown etiology of MIH, another hypothesis has been raised up. According to James P. Simmer et al, the formation of dental enamel is genetically controlled and apparently encoded in our DNA. As a matter of fact, dental enamel can be inherited from parents and be transmitted across generations in terms of size, shape, color, and even caries susceptibility (13,18,19).

However, DNA can only encode RNA, and the majority of the RNA is used to synthesize proteins. Consequently, according to Bittencourt y Simmer, a gene mutation that code for enamel proteins will not affect the enamel mineral, nevertheless the proteins that will be synthesized from this RNA would be defective and will be the origin of enamel malformations (12,13). Agenesis, microdontia, and tooth transposition are three other examples of several genetically based dental malformations that tend to be in association (12).

1.3. Prevalence / Epidemiology

MIH is considered a worldwide dental concern with an estimated global prevalence of 13,5 % (20) in 2021, affecting 878 million individuals (21). The prevalence of MIH varies by continent, with America exhibiting the highest prevalence (15,3%), Asia showing the lowest prevalence (10,7%), and Europe (14,4%), Africa (14,5%), and Oceania (14,7%) showing nearly identical frequency (Figure 5).

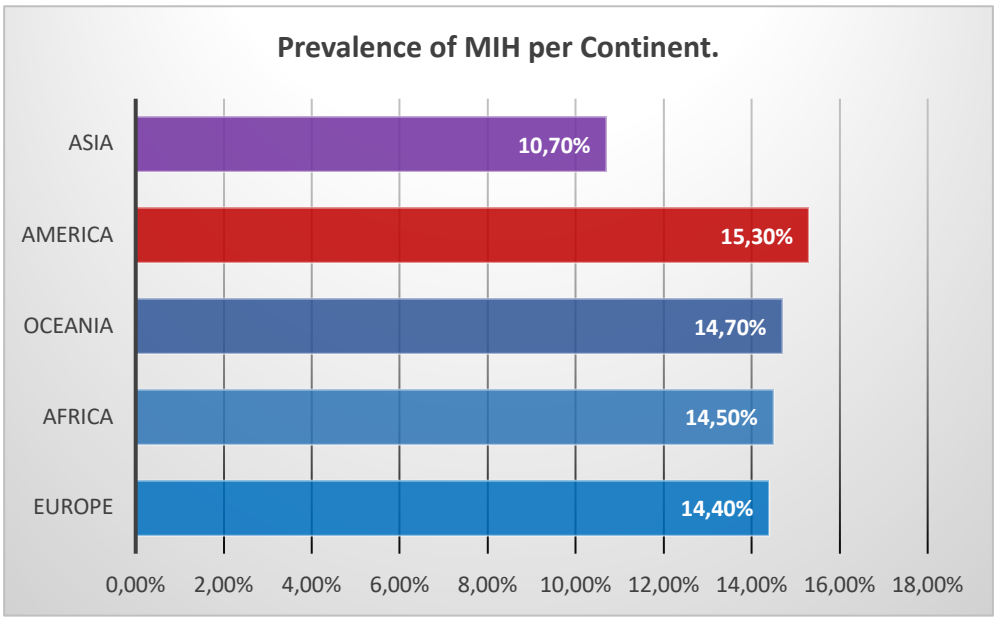


Figure 5. Diagram representing the prevalence of MIH per continent. (20)

Focusing in the south of Europe, only a few research have been done on the incidence of MIH in Spain, where it ranges from 7.94% (22) to 12,4% (23), 17.8% (24) to 21.8% (25).

As a critical issue for oral public health, it became crucial to establish the prevalence of MIH as a measure of interest in oral health programs. Each year, 17.5 million people are affected by this condition and 27.4% of them require special therapy because of pain or discomfort, high susceptibility to caries, hypersensitivity or post-eruptive enamel deterioration (21,26). It is essential to remember that MIH is often ignored or misdiagnosed, especially in the early stages, therefore the prevalence of the condition may be underestimated.

Although prevalence rates can vary significantly, these figures offer insightful information on the global impact of MIH and emphasize the significance of early diagnosis and care to stop further dental issues.

In agreement with the European meeting on MIH held in Athens in 2003, in conjunction with the 6th Congress of the European Academy of Pediatrics Dentistry (EAPD), dentists scientists have agreed on the fact that this new dental condition is

increasing in frequency among children, and that the need of collecting data and knowledge is increasingly needed as “In Denmark, at the present time, for example, hypomineralized defects are found more frequently in FPMs than occlusal caries”(9).

1.4. Possible etiological factors of MIH

Despite several publications on its genesis, MIH’s causative causes are still unknown, but all agreed that it has a multifactorial systemic origin (5).
Several studies have tried to establish a relationship between different causes and the appearance of MIH. Despite their good will, only hypothesis have been raised. Until today, it is not possible to affirm that one cause or another is 100% responsible for the development of this enamel hypomineralization. However, some factors seem to be more relevant and could potentially participate in the origin of MIH or could increase the risk of suffering from it in the future.

Researchers have found several etiological factors that may be involved with MIH. Among these factors, antibiotics, early childhood illnesses, fever, pregnancy and perinatal complications, such as cesarean section, prematurity or low birth weight have established a possible relationship with the development of MIH in children (27,28). A correlation between genetic involvement and environmental issues as well as prenatal and perinatal health issues have been demonstrated (29).

There is an evidence that the causative factors need to be present in the last time of prenatal period and/or during the first three year of life in order for MIH to develop (10).
To truly understand the root causes of MIH and create efficient prevention and treatment plans, more research is required. The eventual etiologies of MIH will be more developed in the bibliographic review section, where we will see different studies discussing its etiology.

1.5. Consideration in clinical practice: Diagnosis and Clinical Criteria

MIH is described as characteristic well delimited opaque stains on the tooth surface, ranging from creamy-white, yellow to brown color (25), and distinct from healthy enamel (29). Due to its impaired mineralization, the tooth will be more easily dissolved by the acids and will present a much higher porosity than sound enamel and will be therefore significantly more fragile. Occasionally, the tooth could suffers or not post-eruptive breakdown (16) and is subjected to a higher risk of caries, as well as higher sensitivity that could provokes stimulated pain when exposed to cold, air and even to mechanical stimuli as toothbrushing (1). A rapid attrition of the enamel is also observed that could provokes mastication impairment (3).

Clinically, this condition will affect at least one FPM and may include upper incisors, more frequently, or lower incisors, more rarely, that could lead to aesthetic problem. The maxillary FPMs are generally more affected by this condition compared to mandibular lower FPMs (30,31). Concomitantly, the more severely affected the FPMs, the greater the risk for the incisors to be affected as well (1).
More recent study conducted in 2021, shows the possible involvement of the 2nd primary molar with a prevalence of affectation estimated at 3,6% (20).

According to an investigation realized in Barcelona between 2008 and 2009, among 550 children evaluated, 90 of them presented MIH and were analyzed to determine the distribution of the numbers of affected teeth in different individuals (24)(Figure 6).

This pattern of affectation suggests that the best time to diagnose MIH in 2nd primary molar is at age 3, and for permanent dentition is around 8 years old (5,32). Most children's four permanent molars and most of their incisors will have erupted by this age. The four FPMs and the 8 permanent incisors are the teeth that should be inspected the most (9).

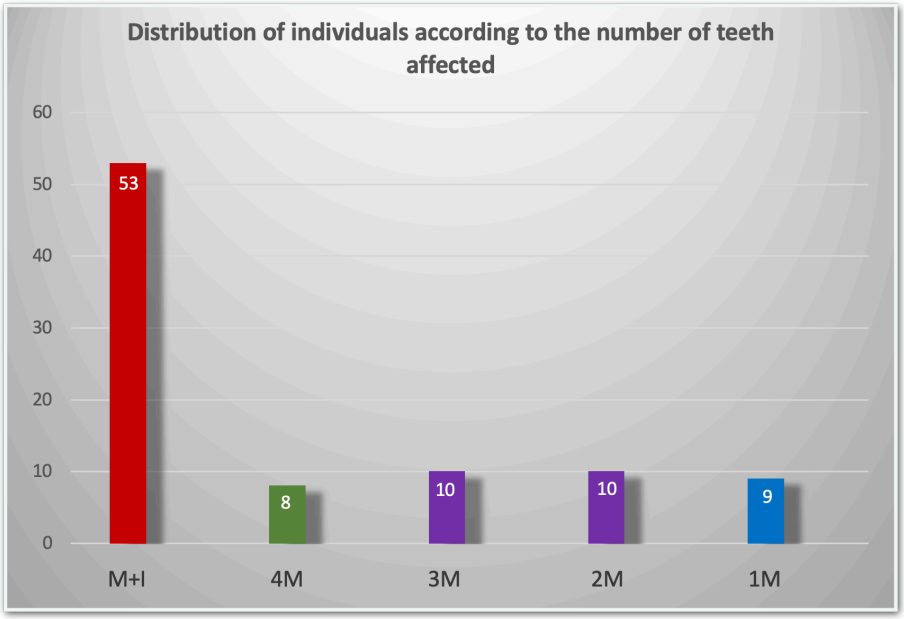


Figure 6. Distribution of individuals according to the number of affected teeth. 53 were truly MIH as both, incisors and molars were affected, 8 had all four FPMs affected, 10 had 3 FPMs affected, 10 had 2 FPMs affected and 9 had only one molar affected. (24)

Regarding the severity levels of affectation, MIH is usually classified according to 3 grades:

- Mild MIH: Delimitated opaque patches in non-stress areas, with no caries associated to the affected enamel, with no structural loss and no or low hypersensitivity. Incisors could be mildly affected (4,16) (Figure 7).

- Moderate MIH: Demarcated opacities on molars and incisors, with normal or increased sensitivity, with post-eruptive breakdown (PED) limited to one or two surface excepting the cusps (4).

- Severe MIH: More severe PED and structural loss with crown destruction, caries associated to the affected enamel and increased hypersensitivity (10,18)(Figure 8). Enamel that has been severely damaged and is being exposed to masticatory forces quickly breaks down, exposing unprotected dentine and accelerating the development of caries due to more accumulation of biofilm in porous areas (10).

This lesions may lead to aesthetics and functional problems and have a negative impact on socio-psychological state of the patient (3).

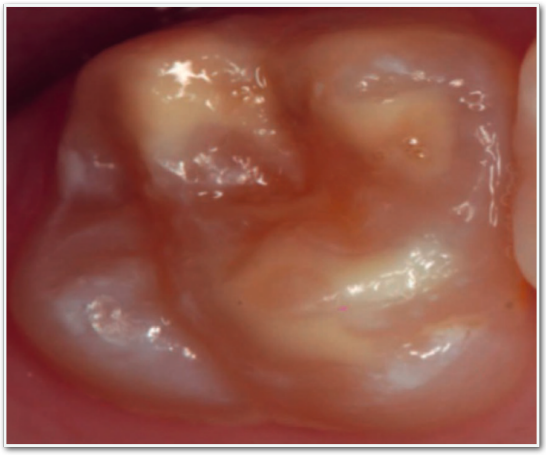


Figure 7. FPM affected by mild MIH. (4)

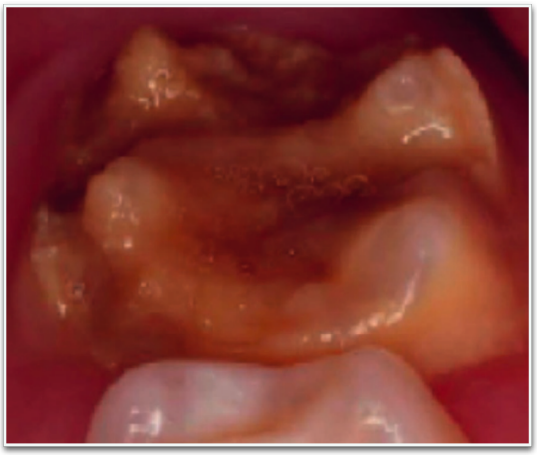


Figure 8. FPM affected by severe MIH, with Post-eruptive breakdown. (4)

1.6. Differential diagnosis of MIH

As mentioned above, before that time, defects due to enamel hypomineralization was referred as many possible lesions still difficult to differentiate between each other. MIH was mismatched and confused with other DDE as fluorosis, enamel hypoplasia, amelogenesis imperfecta, white spot lesions…

A patient's history is necessary to look for acquired, environmental, or genetic etiologies, in addition to knowing the main characteristics of MIH that are necessary for an effective diagnosis (3).

Differential diagnosis:

- Fluorosis: Dental enamel defect of different severity that appears to be the cause of a systemically high ingestion of fluoride during a precise period. Compared to MIH, that presents clearly delimitated opaque lesions separated from healthy non-affected enamel, the pattern of fluorosis slightly

differs and appears to be more diffused with lineal patches without clear boundary (Figure 9). Another significant difference will be that fluorosis affects teeth in a bilateral and symmetrical pattern, distinct from MIH that follow an asymmetrical pattern (3,33).

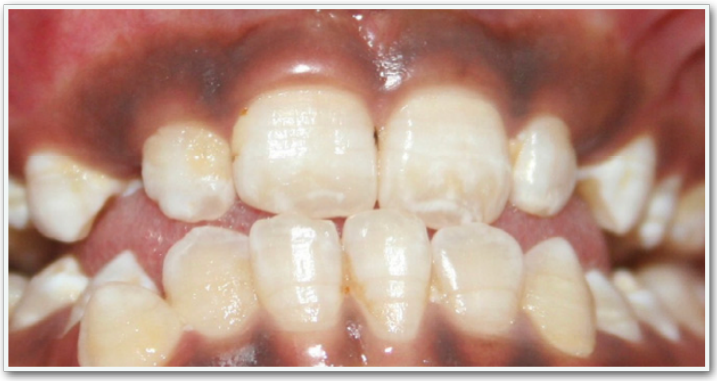


Figure 9. Moderate Fluorosis. Notice the diffuse white opacities. (34)

- Amelogenesis Imperfecta: It corresponds to a genetic condition that generally affects all teeth of both primary and permanent dentition (Figure 10). Different subtypes exist: hypoplasic type, hypocalcified type (the most common) and hypomineralized type. A similarity with MIH would be the possible existence of a family history (3,15,35).

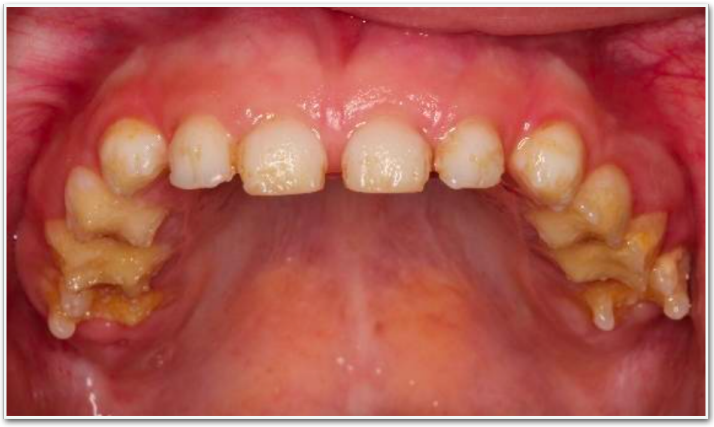


Figure 10. Amelogenesis imperfecta affecting enamel of upper teeth. (35)

- Enamel Hypoplasia: As mentioned before, it describes a quantitative defect of the enamel that take place during the matrix secretion stage of amelogenesis. The enamel will be reduced in thickness but the mineralization of the enamel will be intact (3,36).

- White spot lesion: This is the initial stage of enamel caries, corresponding to Code 1 or 2 according to ICDAS classification. The lesion will appear white and opaque and will be localized in area where caries are more susceptible to developed (plaque accumulation forming biofilm) (3,37)(Figure 11).

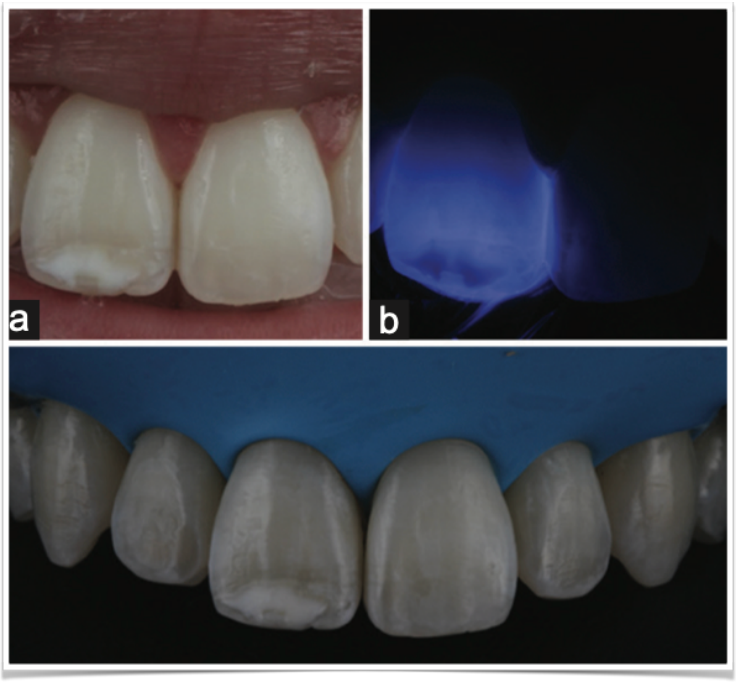


Figure 11. (a) Clinical appearance of the white spot lesion. (b) Transillumination of the white spot using a photopolymerizer device, demonstrating that the darker the stain appears when transilluminated, the deeper it is. (38)

- Traumatic Hypomineralization: Lack of enamel mineralization appears to be a consequence of a dental trauma. Different causes could be at the origin of this lesion, for example a periapical infection of a primary tooth could disrupts the mineralization of the crown enamel of the subjacent permanent tooth. The pattern will therefore be asymmetrical and limited to one tooth (3).

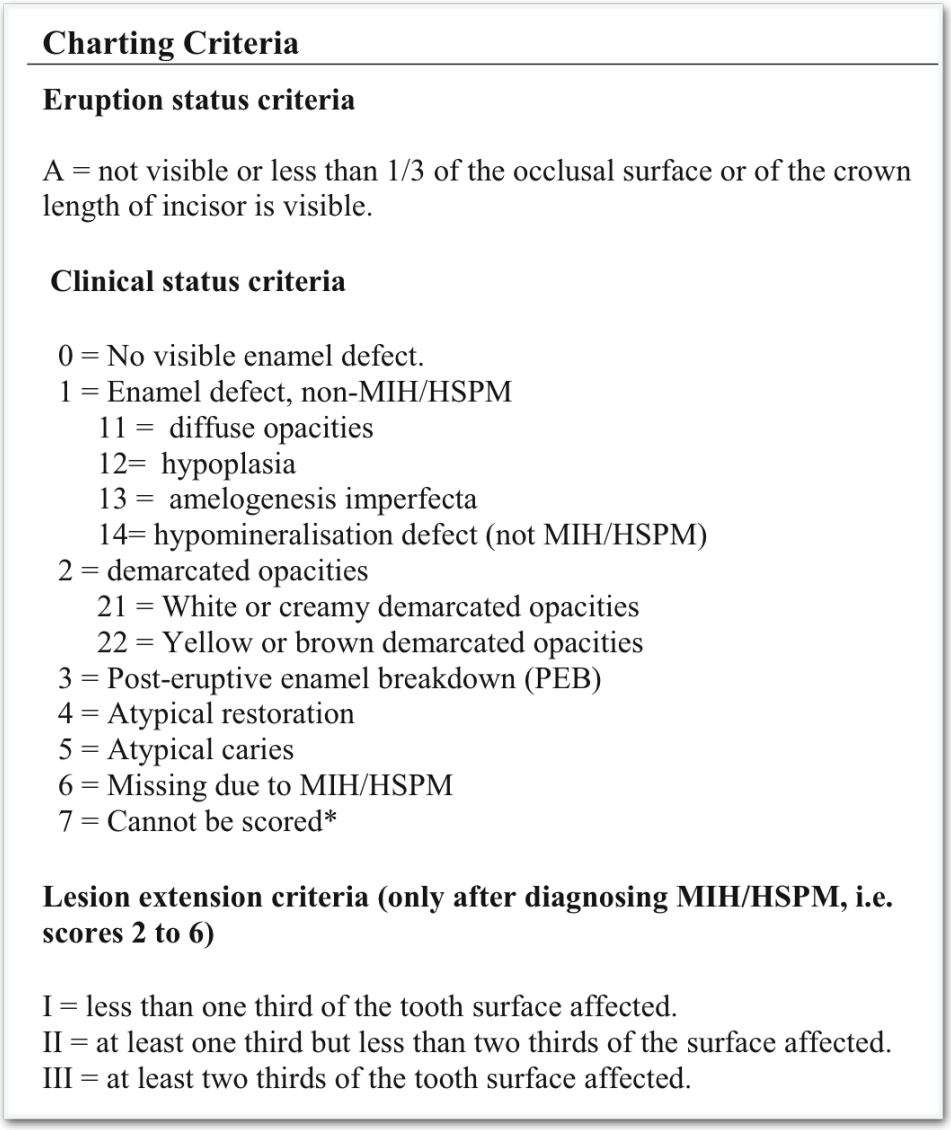
1.7. MIH Index and MHI-TNI: an aid for diagnosis and treatment

Early diagnosis and treatment are crucial when facing MIH in order to reduce the risk of future complications. A correct diagnosis is therefore fundamental to select the best treatment possible in each case.

Weerheijm et al. suggested that the optimal period for clinical evaluation would be 8 years old, when all FPMs and the majority of permanent incisors might have emerged. Examination of teeth should be done while still wet, but if necessary, the tooth's surface can be cleaned with cotton rollers to improve visibility (4,9,32).

Regarding clinical diagnosis, the European meeting on MIH in Athens in 2003 has established some diagnostic criteria to be evaluated in each teeth previously cited (9). They have been updated in 2010, by *Lygidakis et al.* (10) and are the follow : demarcated opacities, enamel disintegration or porosity, hypersensitivity, atypical extended restorations, premature extraction of a molar with opacities in others (10) and unerupted incisor or molar (9).

A MIH Index has been then created to facilitate and increase the chance to have the correct definitive diagnosis (Figure 10). This index has been based, according to *A. Ghanim* et al in 2015 and updated in 2018, on 3 criteria, which are eruption status, clinical status (defined opacities, post-eruptive enamel breakdown, unusual restoration, abnormal caries, missing due to MIH/HSPM), and lesion extension (39,40)(Figure 12).



Charting Criteria

Eruption status criteria

A = not visible or less than 1/3 of the occlusal surface or of the crown length of incisor is visible.

Clinical status criteria

0 = No visible enamel defect.
1 = Enamel defect, non-MIH/HSPM
11 = diffuse opacities
12= hypoplasia
13 = amelogenesis imperfecta
14= hypomineralisation defect (not MIH/HSPM)
2 = demarcated opacities
21 = White or creamy demarcated opacities
22 = Yellow or brown demarcated opacities
3 = Post-eruptive enamel breakdown (PEB)
4 = Atypical restoration
5 = Atypical caries
6 = Missing due to MIH/HSPM
7 = Cannot be scored*

Lesion extension criteria (only after diagnosing MIH/HSPM, i.e. scores 2 to 6)

I = less than one third of the tooth surface affected.
II = at least one third but less than two thirds of the surface affected.
III = at least two thirds of the tooth surface affected.

Figure 12. Description criteria of MIH Index. (40)

Based on the number of afflicted teeth, the type, and the degree of the enamel defect, *Ghanim et al.*, in 2017, created a rigorous scoring system to determine the severity of MIH, described as MIH-Treatment Needed Index (MIH-TNI) (3,41,42)(Figure 13,14). Then, once the severity of the lesion has been scored, different treatment options for each index would be eligible according to the risk of caries ; low or high (3)(Figure 15, 16).

Index	Definition
Index 0	No MIH, clinically free of MIH
Index 1	MIH without hypersensitivity, without defect
Index 2	MIH without hypersensitivity, with defect
2a	<1/3 defect extension
2b	>1/3 < 2/3 defect extension
2c	>2/3 defect extension or/and defect close to the pulp or extraction or atypical restoration
Index 3	MIH with hypersensitivity, without defect
Index 4	MIH with hypersensitivity, with defect
4a	<1/3 defect extension
4b	>1/3 < 2/3 defect extension
4c	>2/3 defect extension or/and defect close to the pulp or extraction or atypical restoration

Figure 13. The MHI-TNI. (42)

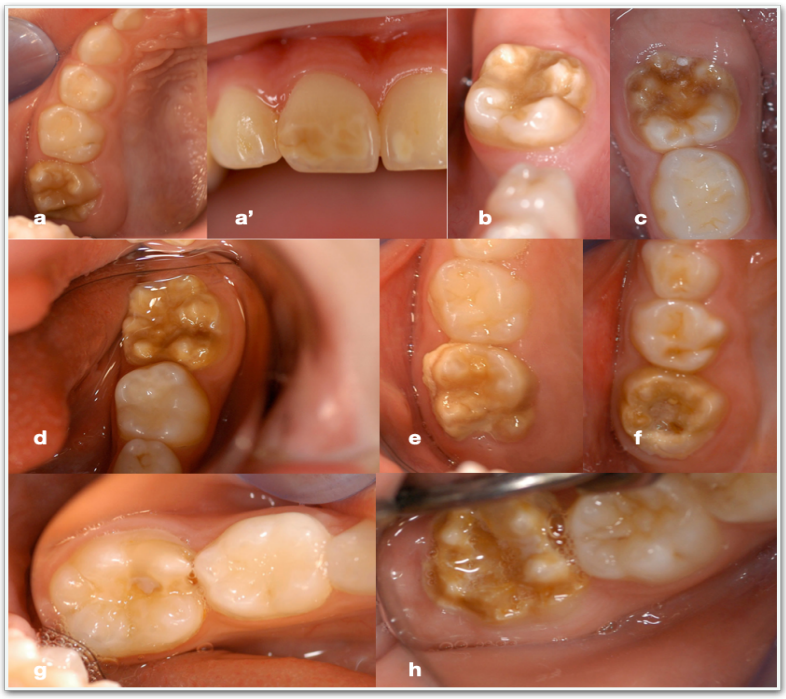


Figure 14. MIH-TNI: Index 1 (a, a'). Index 2a (b), 2b (c), 2c (d). Index 3 (e). Index 4a (f), 4b (g), 4c (h). (42)

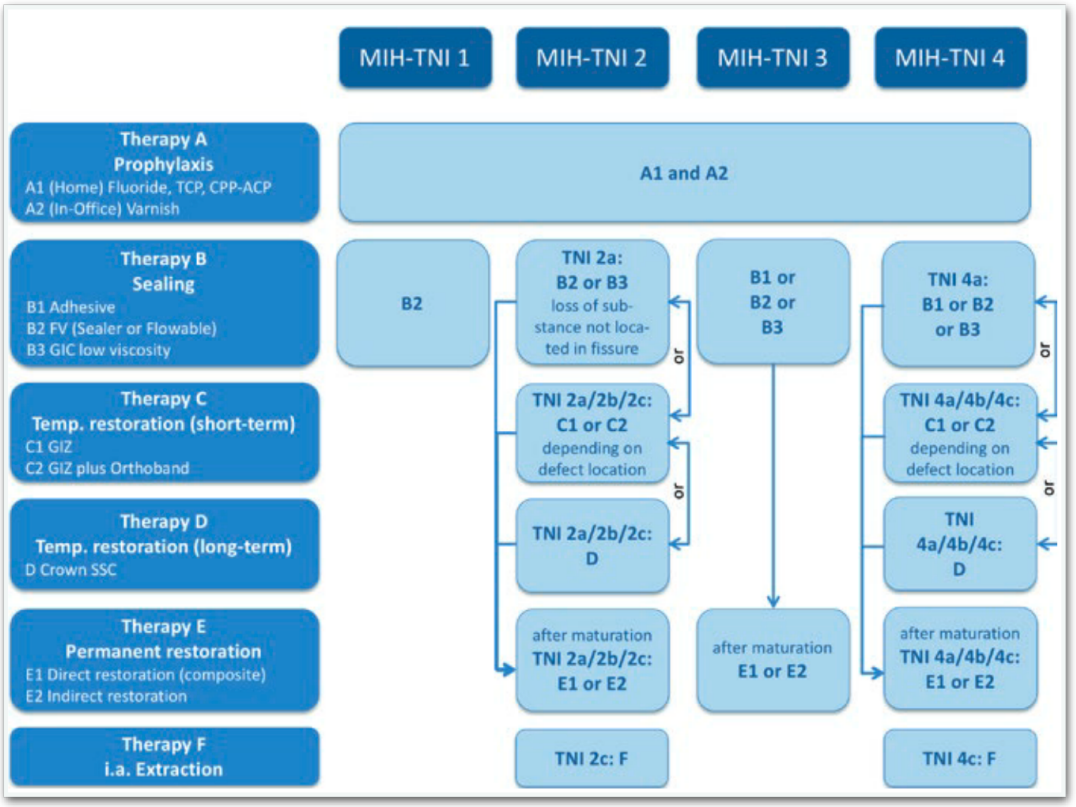


Figure 15. MIH-TNI therapeutic strategy in patients with low risk of decay. (Original figure in German). (43)

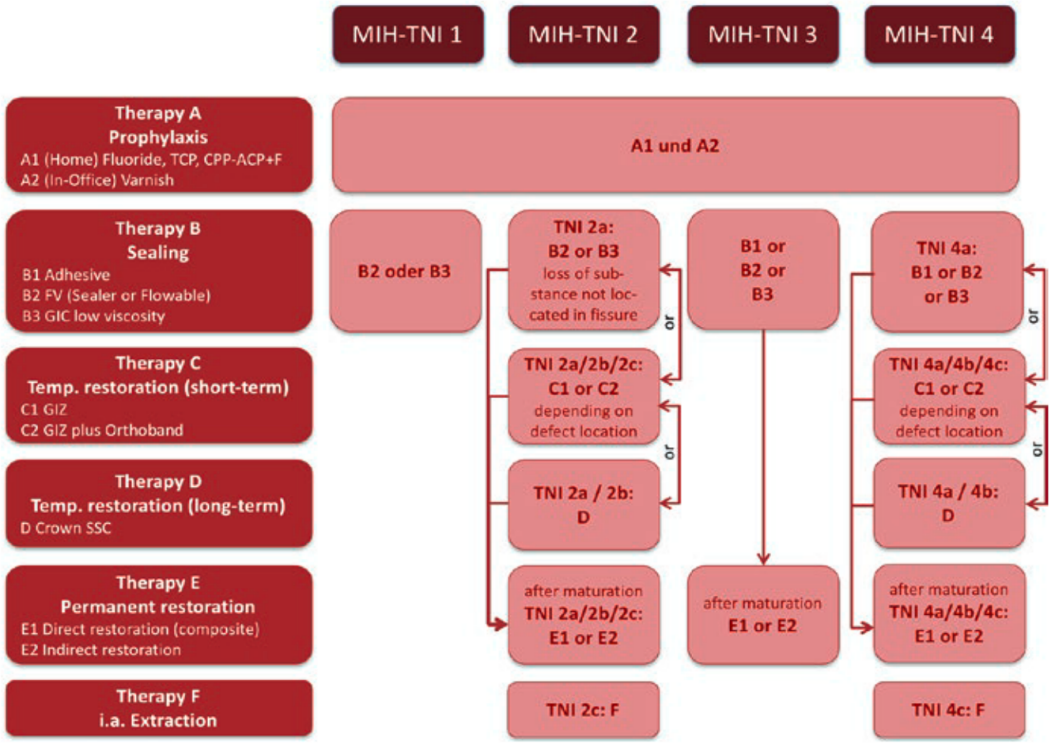


Figure 16. MIH-TNI therapeutic strategy in patients with high risk of decay. (Original figure in German). (43)

1.8. Treatment approaches of MIH

When it comes to treating MIH affected teeth, there are a number of various methods available, and the best course of action will depend on the severity of the condition, the patient's age and general health, as well as the impacted teeth (29).
If left untreated, MIH can result in severe discomfort, sensitivity, and chewing difficulties as well as tooth decay, infection, and tooth loss. Early diagnosis of the afflicted individuals and rapid, suitable intervention, can make the condition be simpler to cure and prevent potential severe outcomes with a significant health-cost benefit (25).
On another hand, early identification is crucial due in part to tissue fragility, to prevent or interrupt the spiral of decay in hypomineralized teeth. It will allow the rapid establishment of appropriate therapy as soon as the tooth partially appears through the mucosa (44).

The range of treatment options for teeth with MIH includes from non- or minimally invasive prevention and restoration, to extraction (3).
One common treatment for MIH is placing dental fillings or crowns to replace broken or weak teeth. To prevent additional damage to the tooth, it may be necessary to remove any decayed, weak and porous or damaged areas of the tooth and replace the space with a filling substance or the tooth may need to have a crown placed over it, as preformed stainless-steel crowns or partial indirect restoration. Resin composite (RC) or Glass ionomer cements (GIC) could be used as restorative materials. Even though RC has better mechanical and physical properties than GIC, the latter could be used as a temporary restoration thanks to its easy application, release of fluoride and chemically bonding to the tooth surface, or when the absolute isolation of the tooth is not possible. RC still remains the main effective restorative material when treating MIH tooth (45).

Regarding the different enamel characteristics of theses teeth, it is even more challenging for dentist to deal with it during treatment, and even more regarding the longevity of it (3). “Children with MIH undergo dental treatment nearly 10 times more than unaffected children”(2). This is mainly due to a lower adhesion capacity of restorative material or cements to the damaged hypomineralized enamel surface.

In fact, the hypomineralized enamel impedes the correct etching and bonding of restorative material, due to its lower mineral concentration and higher protein content (45). According to some studies, the pre-treatment of enamel with sodium hypochlorite 5% after acid-etching is recommended as a deproteinizing agent to expose the hydroxyapatite crystals (46).

An additional therapeutic option is remineralizing therapy that can aid to strengthen weak enamel, lower the risk of tooth decay and reduce the hypersensitivity. The most common component is fluoride, which can be used topically as a gel or varnish or can be incorporated with toothpaste or mouthwash (45). Casein phosphopeptide-amorphous calcium phosphate (CPP-ACP), casein phosphopeptide-amorphous calcium fluoride phosphate (CPP-ACFP), sodium fluoride varnish (5–6%) with and without tricalcium phosphate, ozone therapy, low-level laser therapy, calcium carbonate paste and 8% arginine are some of the management options that are available (11). The CPP-ACP component has been shown to promote the remineralization and desensitization of damaged teeth, especially at the beginning when the enamel has not fully developed and has not matured yet (4,45).

When treating anterior teeth with MIH, several treatment options are proposed as micro-abrasion, resin infiltration, composite restoration, and external bleaching.
The latter will be used in adolescents to cover up white opacities by making the rest of the teeth whiter. To protect the tooth and remineralize the MIH stains without influencing the bleaching process, the CPP-ACP Tooth Mousse paste will be applied simultaneously (10,45). As a preventive measure, even for young patients who are not undergoing the bleaching process, the Tooth Mousse paste or Recaldent may be applied topically to the damaged teeth by applying it on with a finger or cotton swab.

Teeth with a poor prognosis that have been severely impacted by MIH may need to be extracted to stop additional infection or destruction. This is often only advised as the last option because missing teeth can worsen chewing and speaking issues and may necessitate additional treatments like orthodontic space closure or even implant placement or bridges to replace the lost teeth (10,45).

Finally, it is crucial to remember that MIH prevention is key. MIH and other dental diseases can be avoided by maintaining proper dental hygiene habits including brushing at least two times per day, daily floss and scheduling routine dental checkups (45). In addition, protecting teeth and promoting overall oral health can be accomplished by avoiding sugary or acidic meals and beverages and drinking lots of water.

Ultimately, the most effective course of treatment for MIH will depend on the subject in question and how serious their condition is. A dentist can collaborate with the patient to create a treatment strategy that corresponds to their individual requirements and objectives and aids in regaining their teeth's health and function. A multidisciplinary strategy is necessary for the management of MIH, comprising pediatric dentists, orthodontists, and restorative experts.

1.9. Justification

MIH is a relatively common dental disorder that affects the enamel of FPMs and incisors. This disorder has the potential to cause rather severe incapacitating abnormal functions that can significantly affect a person's oral health and quality of life. Because of its high frequency and influence on dental health, MIH has grown in importance as a research topic in recent years.

Due to the serious potential effects of MIH on oral health, it is imperative to have sufficient knowledge to understand this condition and be capable of employing the appropriates prevention and treatment techniques, as well as the potential causes to prevent them.

The goal of this project will be to evaluate the existing literature on MIH to give a thorough summary of the current understanding on MIH, including its epidemiology, etiology, diagnosis, and management. The results of this study can be used to improve our understanding of the genesis, prevention, and management of this growing worldwide condition.

2. OBJECTIVES

2.1. Main Objective

- Analyze the actual knowledge about the diagnosis, etiology, prevention, and management of MIH.

2.2. Specific Objectives

- Provide a detailed overview of the epidemiology and etiology of MIH.
- Describe the clinical aspects and diagnostic guidelines of MIH.
- Know the importance of early diagnosis and prevention.
- Analyze the strategies of prevention and clinical management of MIH.

3. MATHERIALS AND METHODS

Starting by establishing and defining the eligibility criteria which includes inclusion and exclusion criteria, the research for this review was guided through different steps.

The following inclusion criteria was used to guide the research and to select articles: studies documenting on the prevalence, diagnosis, etiology, and management of MIH in children, dated from less than 12 years, available in PDF, published in English or Spanish, in relation to the field of Dentistry, with relevant information related to the main subject, keywords contained in the abstract.

On the contrary, articles that did not meet these inclusion criteria or did not complete relevant information were excluded from the selection. The exclusion criteria were as follow: articles dated from more than 12 years (exceptions were made for some relevant articles), not available in PDF, not in English, Spanish (with the exception of two articles in German and in French), not related to the field of Dentistry, with no relation to the main subject, no relevant information, information found on website and not from articles.
As cited above, some exceptions were made regarding the date of publications; 6 articles were dated from more than 12 years but were chosen due to their importance in this review.

To realize this review, the research was conducted through a bibliographic search thanks to different databases as Medline complete, PubMed, and Google scholar. The study has started in October of 2022 and has finished in March of 2023.
Most of the articles were encountered using Medline complete as it gathers many scientific databases selected in order to conduct this review as Academic Complete, Dentistry and Oral Sciences Source, Academic Search Ultimate…

The first step while entering in those databases, were to conduct a basic search. It was a good way to start finding some articles regarding more general information

about the topic. For example, searching “Molar Incisor Hypomineralization” or “Clinical guide for Molar Incisor Hypomineralization”, or “Management protocol of MIH for dentist”, or “Molar Incisor Hypomineralization: an overview” in the research bar of Medline complete, as a basic research. Once the selection of more general articles was done following the inclusion criteria, a comprehensive analysis of the title was performed to enhance the effectiveness of searching databases for relevant articles. Boolean operators were utilized to refine the search criteria and achieve more precise and targeted search results.

More advanced research has been conducted and a research question has been yielded that was: ((((patients) AND (MIH OR Molar Incisor Hypomineralization)) AND (prevalence) AND (etiology)) AND ((prevention) AND (treatment))) that has given rise to a list of 648 articles on Medline and 10 articles on PubMed.

Other examples of search equation used in order to conduct the review was:

(“MIH OR Molar incisor hypomineralization” AND “prevalence” AND “evolution”),

(“MIH” AND “prevention” AND “treatment” OR “management”),

(“MIH” AND “Index” OR “Code”, “Restorative” OR “Adhesive techniques” AND “MIH”),

(“Remineralizing agents” AND “MIH”),

(“MIH” AND “possible etiological factors” OR “causes” OR “predictive factors”).

The result of the research has conducted to 75 articles selected.

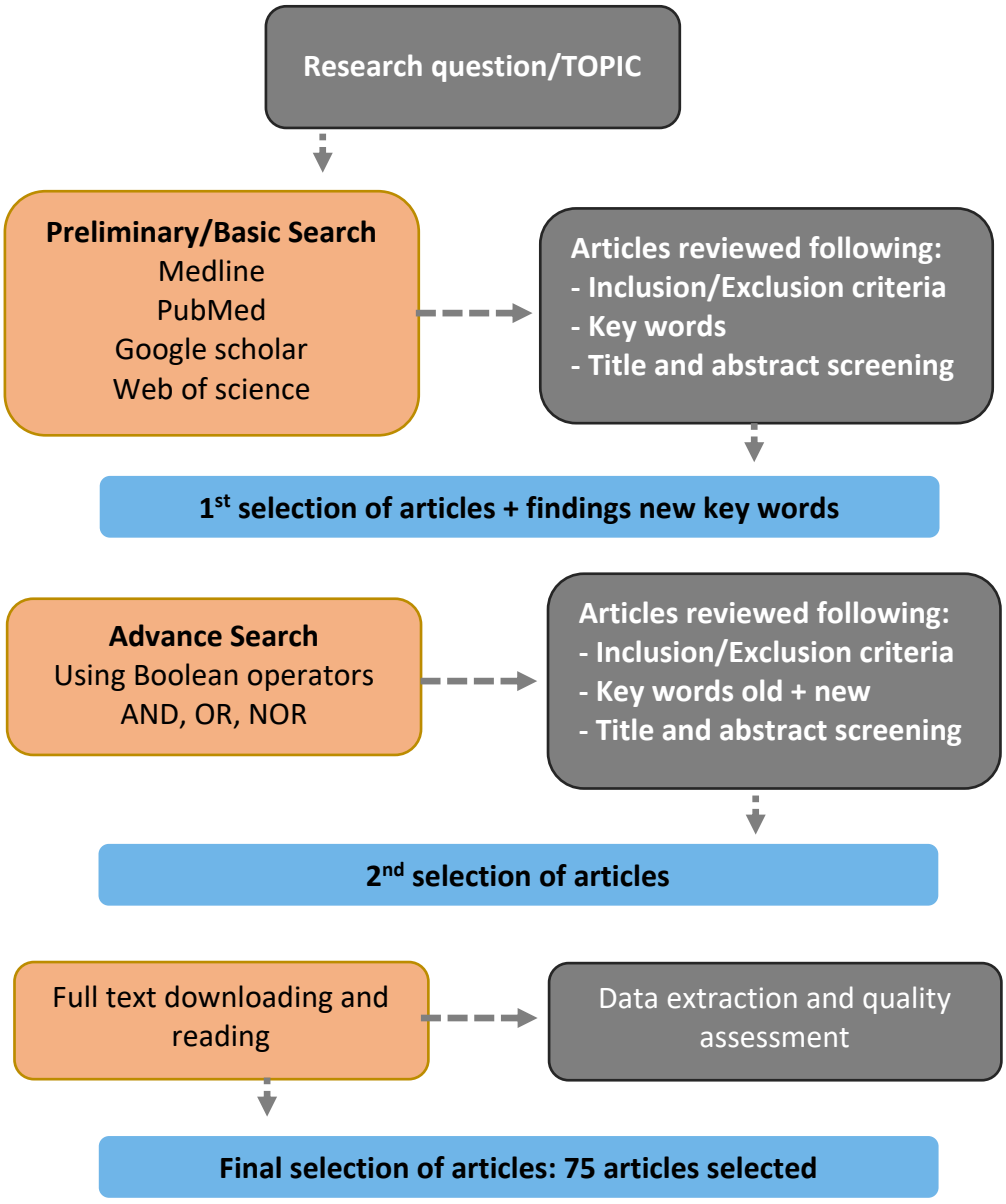


Figure 17. Bibliographic research cascade.

4. RESULTS

According to PICO question methodology, a research question has been established, with the aim of drawing up the flow chart (Figure 18), which makes it possible to select articles to conduct and guide the results of this review. The search equation was as follows: ((((patients) AND (MIH OR Molar Incisor Hypomineralization)) AND (prevalence) AND (etiology)) AND ((prevention) AND (treatment))).

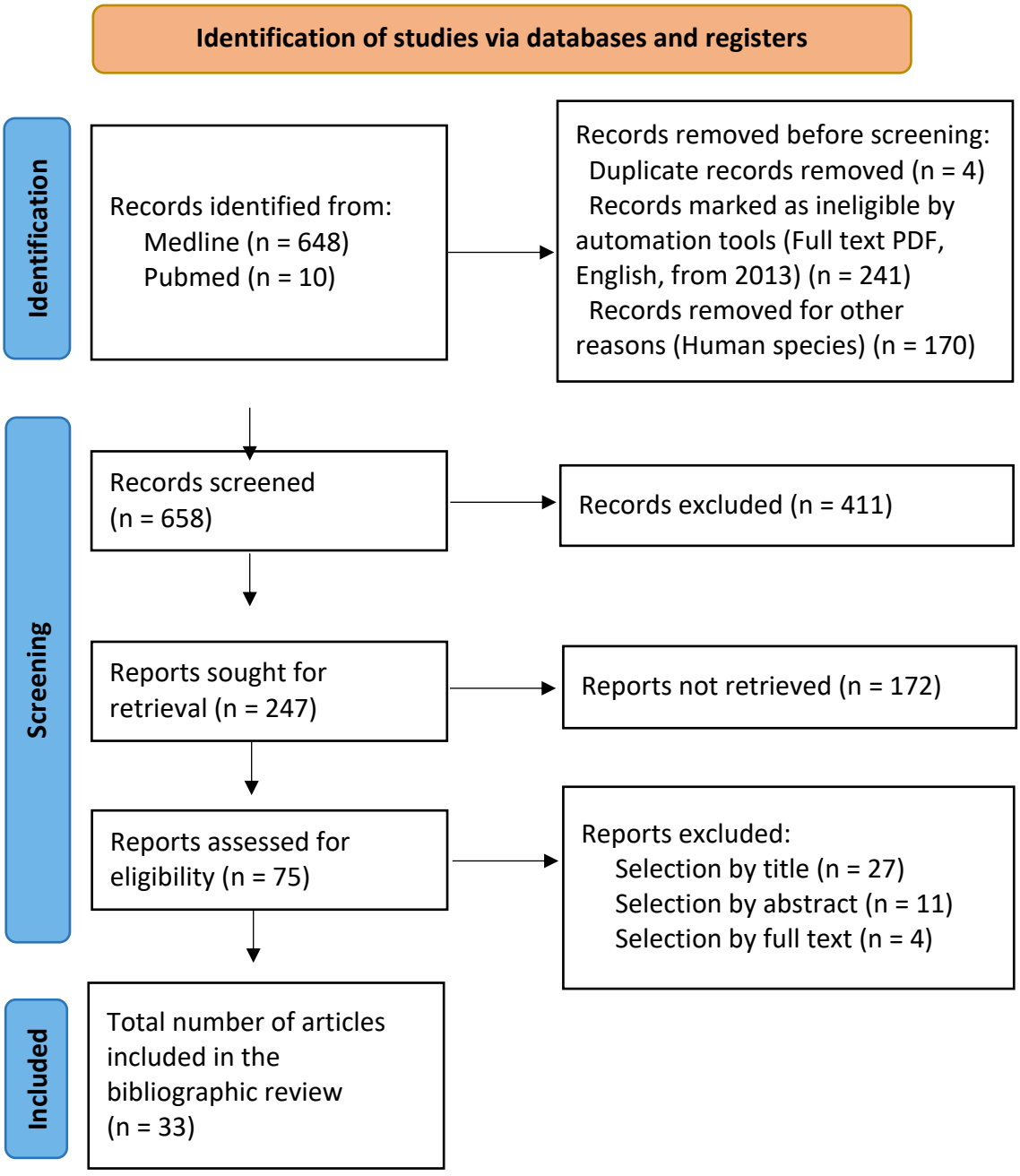


Figure 18. PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only. (47)

The data extracted from the articles included in the review are going to be presented in the form of two tables discussing about the prevalence and etiology of MIH.

4.1. Worldwide distribution of MIH

MIH is a growing worldwide condition and constitutes one of the most common oral health problems among children. MIH affects 1 in 5 five children worldwide and is well-documented but yet underappreciated, whereas it constitutes a principal risk factor for childhood dental decay and other dental pathologies (6). This constitutes one of the reasons why the need to be well documented about its prevalence is important.

Table 1: Epidemiological studies on MIH's prevalence.

Study	Date	Country	Age of the population	Prevalence
Koch et al. (32)	1987	Sweden	6 age cohorts, 8-13yr	3.6%- 15.4%
Alaluusua et al. (32)	1996	Finland	6-7 yr.	17%
Alaluusua et al.. (32)	1996	Finland	12 yr.	25%
Zagdwon et al. (32)	2002	UK	7 yr.	14,6%
Dietrich et al. (32)	2003	Germany	8yr / 10-17 yr.	2.4-11%, mean 5.6%
Balmer et al. (32)	2005	UK / Australia	8-16 yr.	**40% - 44%**
Calderara et al. (32)	2005	Italy	7-8 yr.	13,7%
Jasulaitte et al.. (32)	2007	Netherlands	9 yr.	14,3%
Preusser et al.. (32)	2007	Germany	6-12 yr.	5,9%
Cho et al. (32)	2008	Hong Kong	11-14 yr.	**2,8%**
Kemoli. (32)	2008	Kenya	6-8 yr.	13,7%
Kuscu et al. (32)	2008	Turkey	7-9 yr.	14,9%
Soviero et al. (32)	2009	Brazil	7-13 yr.	40,2%

Martínez Gómez TP et al. (24)	2012	Spain	6-14 yr.	17,8%
Oyedele TA et al. (48)	2015	Nigeria	8-10 yr.	17,7%
Hussain G et al. (49)	2018	Dubai	8-12 yr.	27,2%
Glodkowska N et al. (50)	2019	Poland	6-12 yr.	6,43%
Abdelaziz M et al. (51)	2022	Switzerland	4-12 yr.	6,6%
Grieshaber A et al. (52)	2023	Switzerland	7-16 yr.	14,8%
Lim C et al. (53)	2023	Australia	13 yr. (mean age)	19,2%

In this table, the prevalence of MIH across the world has been investigated. The several researches have revealed distinct prevalence rates for age groups ranging from 6 to 17 years old. The studies listed above covered practically every continent, including South America, Europe, Africa, and Oceania, between 1987 and 2023, giving us a comprehensive picture of the prevalence of MIH worldwide over the years. The prevalence ranges from 2,8% to 44%. This first part of this table displays the findings of a study that conducted a systematic review of epidemiological studies done in multiple countries between 1987 and 2009 (32). More recent research from 2012 to 2023 have been added to it, indicating incidence ranging from 6,6% to 27,2% in the latest years. The diverse characteristics and diagnostic criteria that the authors used to pilot their study, such as the sample size, the age and gender of the participants, the year of publication, and the geographic region, may have contributed to this heterogeneity between authors.

4.2. Results regarding different etiology of MIH

Table 2: Results from different articles regrouping the possible etiological factors of MIH.

Article Title	Author	Date/ Country	Conclusion summary
Association Study on Nutrition in the First Year of Life and MIH (MIH)-Results from the GINIplus and LISA Birth Cohort Studies. (54)	Khazaei Y et al.	2021, Germany	No correlation between MIH in the permanent dentition and early nutrition during the first year of life.
Background factors of MIH in a group of Finnish children. (55)	Wuollet E et al.	2014, Finland	Correlation between urban residency and the prevalence of MIH, that could not be explained by any other research factor.
Best clinical practice guidance for clinicians dealing with children presenting with MIH: an updated European Academy of Paediatric Dentistry policy document. (11)	Lygidakis NA et al.	2022	Several baby and childhood disorders are connected to MIH (perinatal hypoxia, preterm, and other hypoxia-related perinatal issues, including caesarean section). There may be a genetic predisposition and epigenetic impacts function.
Elevated serum 25(OH)-vitamin D levels are negatively correlated with MIH. (56)	Kühnisch J et al.	2015, Germany	Higher serum 25(OH)D concentrations were linked to better oral health indicators and fewer permanently carious teeth.
Etiology of MIH - A systematic review. (57)	Silva MJ et al.	2016	Significant relationships between MIH and pre- and perinatal variables like maternal sickness,

			preterm birth, and difficulties during childbirth. A link was found between maternal alcohol use, infantile fever, and ethnicity. It may be linked to other childhood illnesses (fever, asthma, and pneumonia).
Exploring the association between genetic and environmental factors and MIH: evidence from a twin study. (58)	Teixeira RJPB et al.	2018, Brazil	The better concordance in the diagnosis of MIH among monozygotic twins suggests a genetic contribution.
Factors associated with MIH in schoolchildren aged 8-10 years: a case-control study. (59)	Dantas-Neta NB et al.	2018, Brazil	Link between MIH and having a fever while pregnant and needing medical attention.
Fetal, neonatal and child vitamin D status and enamel hypomineralization. (60)	Van der Tas JT et al.	2018, Nether-lands	The presence of hypomineralization of the second primary molars (HPSMs) or MIH at the age of six are not related to 25(OH)D concentrations in the prenatal, early postnatal, or later postnatal period.
Frequency of MIH and associated factors among children with special health care needs. (61)	Mohamed RN et al.	2021, Saudi Arabia	Among children with special health care requirements (CSHCN), MIH should be acknowledged as one of the common oral health issues to reduce tooth mortality.
Gene-environment interaction in molar-	Bezamat et al.	2021	All markers examined in the Turkish cohort had a potential interaction

incisor hypomineralization. (18)			with TGFA rs930655. There were additional associations (p0.05) between MIH and medication use beyond the age of three.
Inheritance pattern of MIH. (62)	Jeremias F et al.	2021, Brazil	Evidence that hereditary variables, such as the multifactorial complex deficiency, influence MIH is strengthened by this outcome.
Is There an Association between Asthma and Dental Caries and MIH ? (63)	Flexeder C et al.	2020, Germany	A strong correlation between the number of MIH-affected teeth and asthmatic teenage patients who did not take MDI medication was discovered.
Molar incisor hypomineralisation. (64)	Taylor GD.	2017, Australia	Prenatal and perinatal variables rarely cause MIH, according to the research. MIH seems to be linked to early childhood illness (fever).
MIH in Lebanon: association with prenatal, natal and postnatal factors. (65)	Elzein R et al.	2021, Lebanon	To reduce the incidence it is advised to control high fevers carefully, raise public awareness about antibiotic abuse, and educate people about bisphenol A and how to prevent it during pregnancy and lactation.
MIH: Positive Correlation with Atopic Dermatitis and Food Allergies. (66)	Hernandez M et al.	2018, Spain	Link between atopic dermatitis and food allergies.
Perinatal hypoxia and the risk of severe MIH (MIH): a retrospective	Hoberg C et al.	2022, Germany	No significant correlation between MIH and the pH level of the

analysis of the pH value of umbilical arterial blood after birth. (67)			umbilical cord blood or birth via c-section could be detected.
Peripartum events and MIH (MIH) amongst young patients in southwest France. (68)	Garot E et al.	2016, France	Peripartum occurrences like hypoxia during birth or caesarean delivery are proposed as risk factors. No link between MIH and premature birth.
Pre- and postnatal determinants of deciduous molar hypomineralisation (DMH) in 6-year-old children. The generation R study. (69)	Elfrink ME et al.	2014, Nether-lands	Correlation between DMH and Dutch ancestry, low birth weight, maternal alcohol use during pregnancy, and any fever during the first year of life.
Predisposing factors involved in the aetiology of MIH: a case-control study. (70)	Bagattoni S et al.	2022, Italy	Multifactorial origin.
Prevalence and Possible Etiological Factors of MIH (MIH) in Population of Silesian Children in Poland: A Pilot Retrospective Cohort Study. (27)	Ilczuk-Rypuła D et al.	2022	Link between MIH and environmental risk factors (otitis, atopic dermatitis, and premature delivery).
Prevalence, aetiology, and treatment of MIH in children living in Izmir City. (71)	Kılınç G et al.	2019, Turkey	It was found that patients with asthma/bronchitis, high fever, low birthweight, premature delivery, and MIH were more adversely affected.

Relation between MIH (MIH) occurrence and war pollutants in bombarded regions: Epidemiological pilot study in Lebanon. (72)	Elzein R et al.	2021, Lebanon	The hypothesis of a connection between MIH vulnerability and war pollutants in bombarded regions must be clarified by more in vitro and in vivo investigations.
Second primary molar hypomineralisation (HSPM) and drugs used during pregnancy and infancy. A systematic review. (73)	Serna Muñoz C et al.	2020	There is no conclusive evidence linking drug use during pregnancy and the first year of life to HSPM. The use of preventative protocols would prevent difficulties in both the primary and permanent dentition because HSPM is a predictor of MIH.
Standardised studies on MIH (MIH) and Hypomineralised Second Primary Molars (HSPM): a need. (74)	Elfrink ME et al.	2015	Standardization of the study procedure should involve the use of the same calibration sets and methodologies.
The impact of environmental air pollution on the prevalence of MIH in schoolchildren: A cross-sectional study. (75)	Głódkowska N et al.	2020, Poland	Link between enamel developmental disorder in the form of MIH and air pollution levels that are greater.

The potential causes of MIH have been listed in this table in accordance with various authors and studies carried out between 2015 and 2022. These investigations were conducted across a variety of nations, including Germany, Sicily, and Lebanon, and each one provides information regarding one or more potential causes based on their research. Several factors have been under study, and some of them have shown a

positive correlation with the appearance of MIH such as: genetic factors, prenatal or perinatal traumas (low birth weight or preterm birth, delivery by caesarean) environmental factors, administration of bisphenol A in pregnant women, maternal consumption of alcohol, illness during childhood (asthma, hypoxia, baby fever, pneumonia). Most of these studies have reached the conclusion that additional research is needed to gain a better understanding of the origin of MIH.

5. DISCUSSION

5.1. Epidemiology and worldwide prevalence

MIH is a growing dental condition that causes damages to the enamel of the FPMs and incisors and constitutes one of the most urgent problems in pediatric dentistry nowadays. Many epidemiological studies have recently focused on the prevalence of MIH. It is generally recognized that the disorder is relatively frequent even if the reported rates of MIH vary greatly.

The global prevalence of MIH is significant to be evaluated for various reasons:

- Planning public health initiatives can be aided by understanding the incidence of MIH. This can involve raising awareness among patients, healthcare providers, and the general public, creating guidelines for diagnosis and treatment, and providing funds to manage the condition.

- Early detection and treatment: Treating MIH at an early stage can save the teeth from additional harm and enhance the affected people's oral health over the long term. If MIH is prevalent, efforts can be made to advance the condition's detection and diagnosis so that those who are afflicted can get immediate medical attention.

- Research: Understanding the causes and risk factors related to MIH can be aided by knowing how common the disorder is around the world. New treatments and preventative measures may be created as a result.

- Patient education: Making patients and their families more aware of MIH is possible with knowledge of the condition's prevalence. It can also urge them to seek treatment if they think they or their child may have MIH. This can help them to realize the importance how crucial it is to practice proper dental hygiene and scheduling routine checkups.

According to studies conducted in Northern European nations, the prevalence of MIH ranges from 3.6% to 37.3% (32). The largest numbers were reported in Denmark and Finland, while research in England, Sweden and Germany indicated prevalence rates of 10–18% (25). However, as this condition appears in different clinical forms, this may point to a prevalence that is far higher than what has been reported (45).

Bandeira Lopez L. et al, in a metanalysis conducted in December of 2021, with the aim to estimate the global prevalence of MIH, have established the different prevalence according to each 5 continents, and showed similar prevalence in 3 of them ranging from 14,4% to 14,7%, except in Asia with 10.7% being the continent where less cases of MIH has been revealed, and 15,3% in America being the geographic zone where most cases were evaluated (20)(Figure 5).

According to different authors, the prevalence of MIH ranges from 2.8% in Hong Kong to 44% in United Kingdom and Australia (4,25) (Table 1).

Two studies have conducted their research in Finland and have found different results ranging from 17% to 25%. Both were conducted in 1996 by the same author, Alaluusua et al., and the results were different due to non-similar age group studied. The highest prevalence was found in the group aged 12 years old with 25% compared to 17% in the group aged from 6 to 7 years old (32)(Table 1).

Regarding the prevalence of MIH in United Kingdom, 2 studies were done, and the outcomes were extremely dissimilar. According to Zagdwon et al in 2001, the prevalence of MIH in UK among children aged 7 years old was 14.6% compared to Balmer et al. in 2005, where the highest frequency of MIH was found in young of 8 to 16 years old ranging from 40 to 44% (32)(Table1).

On other example concerns two epidemiological studies carried out in Germany, by Dietrich et al. in 2003 and Preusser et al. in 2007, where similar outcomes with respective prevalence of 5.6% and 5.9% were discovered (32)(Table1).

In several nations, nearly equal frequencies were discovered. In Italy, Kenya, the Netherlands, the United Kingdom, and Turkey, children between the ages of 6 and 9 showed percentages of 13.7%, 13.7%, 14.3%, 14.6% and 14.9% correspondingly (32)(Table 1).

According to more recent studies conducted between 2014 and 2023, the incidence of MIH seems to show lower values in general but is still high in some countries such as in Spain (17,8%), Australia (19,2%) and Dubai (27,2%) (24)(53)(49). In 2015, a in Nigeria (17,7%) (48), and nowadays, in 2023 the incidence found in Australia (19,2%) and Switzerland (14,8%) approximate more or less the worldwide mean value (13,5%) (53)(52)(Table 1).

Regarding prevalence in Spain, it is true that, insufficient information has been collected to far on the prevalence of permanent molar and incisor hypomineralization (25). Relaying on a randomized clinical trial, performed among 840 children aged between 8-9 years old from Valencia in Spain, the results show a prevalence of 21,8% with no significant difference between gender, 22.5% for boys and 21.1% for girls. As a conclusion of this study, gender does not appear to be a dependent variable of MIH (25). In comparison with two previous studies conducted in Spain, the prevalence found was lower compared to the previous one: 12,4% in Madrid (2003) and 17,8% in Barcelona (2012) respectively (23,24) (Table 1).

This heterogeneity between authors could results from the different variables and diagnostic criteria employed to pilot their study as the sample size, the age and gender of individuals, the year of publication and the geographic zone, as seen above (20). All of them constitute an important source of variation in their results and therefore those in charge of oral health programs need to be aware of these differences and take into account these variations when establishing preventive programs according to the type of population they are facing, their needs and the diagnostic criteria used.

As a consequence, the European Academy of Pediatrics Dentistry (EAPD) meeting in 2003, came to a consensus on MIH diagnosis criteria for epidemiological studies in order to help increase the reliability and reproducibility of investigations (25).

5.2. Possible etiological factors

Concerning the etiology of MIH, most of the studies confirm that this condition has a multifactorial etiology, but it is still not possible to firmly confirm the different positive association between each determinant that have been studied and the appearance of MIH. In fact, at present, the specific cause of MIH is still unclear.

However, some studies were able to establish some correlation between possible etiological factors and the development of MIH. Most of them have studied prenatal, perinatal, and postnatal factors, others have tried to demonstrate a positive association with genetic inheritance and environmental influence.

Several studies have suggested that factors affecting prenatal or early childhood health, including maternal disease, pregnancy drug usage, prematurity, caesarean sections, and delivery difficulties, may exist. In multiple investigations, early childhood illness—particularly fever, asthma, hypoxia, and pneumonia—was implicated as an etiological component in MIH (11,57–59,63,68,69). In one investigation, associations with numerous variables were reported as being plausible; the most frequent variables were perinatal variables and neonatal illnesses, followed by prenatal variables (64).

According to Hoberg C et al., there was no conclusive evidence linking MIH to either cesarean birth, hypoxia or the pH level of the umbilical cord blood in the patient group under study (67).

Dentas-Netal et al. found that pregnant women who had a fever during pregnancy had a 2.54 times higher likelihood of having children with severe MIH than mothers who did not ($P = 0.045$) (59). Moreover, newborns that experience fever throughout the first year of life have a higher risk of developing MIH (69).

With the presence of MIH, a study indicates for the first time a statistically significant association between atopic dermatitis and food allergies (66).

According to one study, maternal alcohol consumption during pregnancy may be connected with HSPM, although maternal antibiotic use during pregnancy is unlikely to be (64). Therefore, the implementation of preventive measures will avoid issues in both the primary and permanent dentition because HSPM is a predictor of MIH (73).

Nonetheless, different research suggests raising public awareness of antibiotic abuse and educating people on how to prevent bisphenol A during pregnancy in order to reduce the incidence of MIH. Furthermore, breastfeeding would also be recommended to reduce the risk of MIH in childhood (65).

Considering the genetic contribution to the genesis of MIH, a twin study was conducted and found out that genetic component involving genetic variation in genes expressed during dental enamel formation could be linked with the appearance of MIH (18,58,62).
However, because there is still some ambiguity around this correlation, more research regarding potential determining variables has to be done, specifically to explain its relationship to genetic factors and the impact of environmental factors (11,64).

The fact that the criteria used to conduct the studies were not always comparable was one of the limitations discovered in many investigations. As an example, the age investigated, and the sample used were different. Among several of the investigations, there were notable differences in the calibration techniques, participant and examiner counts, and study approaches, as well as the countries where the studies were conducted. Another issue is that a lot of research on MIH are cross-sectional, which means they can only provide data for a specific point in time and cannot prove a cause-and-effect relationship. For figuring out the origin and development of MIH, longitudinal research would be more beneficial. Also, most of the research have used small sample sizes, which restricts the generalizability of the results. Moreover, there is a lack of consistency in the diagnosis and evaluation of MIH, which can cause results to vary.

Several factors, including genetic factors, prenatal or perinatal traumas, and environmental factors, have been suggested as possible contributors of MIH.

Exposure to certain toxins or chemicals, like as bisphenol A (BPA), may interfere with the process of enamel formation and cause MIH. A higher risk of MIH may be linked to genetic variables that are involved in the formation and mineralization of enamel. Prenatal or perinatal insults like low birth weight or preterm birth, fever during pregnancy, and difficult deliveries have also been linked to MIH.

Additional variables that have been suggested as potential causes of MIH include issues with the body's mineral balance, poor maternal nutrition, alcohol consumption during pregnancy, and specific illnesses that occur during early childhood, such as fever, asthma, hypoxia, and pneumonia. Although these factors have been related to the onset of MIH, it is still unknown exactly how they affect the formation and mineralization of enamel. In fact, additional research is needed to confirm the real impact of each of these variables in the development of MIH.

6. CONCLUSIONS

In conclusion, MIH is a frequent dental disorder affecting children's permanent molars and incisors. It is characterized by a reduction of mineral density in the teeth that is associated with sensitivity, pain, and an elevated risk of decay. This current review has offered a thorough examination of the actual knowledge and the most recent information regarding MIH's genesis, diagnosis, treatment, and prevention.

- After a detailed analysis of MIH prevalence around the world, it was shown that 13,5% of people are affected globally, making it a prevalent dental condition that impacts a significant portion of the population.
- Although the exact cause of MIH is still unknown, it has been found that environmental variables, genetic predisposition, and systemic disorders may contribute to the development of MIH. It is believed to be influenced by several prenatal and perinatal variables, such as infections, fever and drug use.
- The diagnostic clinical criteria and guideline for MIH have been updated, and the significance of early detection and prevention has been highlighted since this can help to prevent the progression of the disorder and the requirement for more invasive therapies. The diagnosis of MIH requires a comprehensive clinical examination and radiographic evaluation. To help dentists with diagnosis, MIH indices have been created.
- Depending on the severity of the condition and the patient's age, different therapeutic modalities, including remineralization therapy, restoration and extractions have yielded encouraging outcomes. A variety of preventive therapies, such fluoride therapy, CCP-ACP components and restoration treatments, like resin-based composites, have been found to be successful in managing MIH. The effectiveness of these procedures also depend on a number of other variables, such as the size and severity of the enamel defects.

Which is why, it is crucial for dental practitioners to be aware of this condition and its potential repercussions to give prompt and appropriate management, thereby enhancing the quality of life for those who are impacted. Lastly, it is obvious that MIH is

an important dental issue that demands greater attention and research to adequately address its impact on individuals and communities worldwide.

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