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Prevalence of molar-incisor hypomineralization in Mexican population: A systematic review and meta-analysis

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ABSTRACT

Background: Molar-incisor hypomineralization (MIH) is a qualitative defect in enamel formation with a multi-factorial etiology. Studies indicate a high prevalence of MIH across the Americas, yet the prevalence in Mexico remains uncertain.

Aim: This study aimed to review the literature on the prevalence of MIH in the Mexican population and its associated factors.

Methods: Six electronic databases were searched for relevant studies: PubMed, Scopus, Dentistry & Oral Science, Science Direct, Web of Science, and Google Scholar, covering the period from March 10th, 2024. Cross-sectional studies were assessed for risk of bias using the Joanna Briggs Institute (JBI) tool.

Results: Nine studies met the inclusion criteria, encompassing 5039 children aged 6-12 years, with a mean age of 9.02 ± 1.19 years; 50.1% were boys, and 49.9% were girls. The overall prevalence of MIH was 23%, with a higher prevalence in boys (34.1%) than in girls (30.4%). MIH was more common in molars (30.7%) than in incisors (10.8%), with no cases reported in permanent second molars. Five studies (55.5%) noted dental caries in MIH-affected individuals, with 78.7% showing caries and 21.3% caries-free. The JBI analysis found 33.3% of studies with moderate risk and 66.7% with low risk of bias.

Conclusion: The prevalence of MIH in Mexico aligns with rates reported in Brazil and Venezuela. The evidence indicates no significant gender differences in MIH distribution, with molars being more frequently affected than incisors. A substantial proportion of Mexican children with MIH also present with dental caries.

1. Introduction

Weerheijm et al., in 2001, proposed the term Molar-Incisive Hypomineralization (MIH) to describe the first permanent molars with idiopathic enamel defects, known as "cheese molars" [1]. Subsequently, in

2003, the European Academy of Paediatric Dentistry (EAPD) characterized this condition as a hypomineralization of systemic origin with an unknown cause, affecting one to four first permanent molars and possibly involving the permanent incisors [2].

Clinically, teeth affected by MIH exhibit asymmetrical opacities that

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are white, cream, yellow, or brown on the buccal surface or the incisal/occlusal third of the crown, with varying degrees of extent and severity. Moreover, MIH can result in significant issues, including hypersensitivity, pain, post-eruptive breakdown, difficulties with chewing and eating, as well as aesthetic and treatment challenges [3].

The etiology of MIH is multifactorial, as several genetic and prenatal, perinatal and postnatal factors have been proposed that can affect the maturation of tooth enamel, from the last trimester of pregnancy to the third year of the child's life. Genetic factors are single nucleotide polymorphisms of different genes expressed at the secretory, transitional, or maturation stage of amelogenesis [4]. Prenatal factors include, diseases and/or complications during pregnancy, alcohol, tobacco and antibiotic use. Perinatal factors include type of birth such as preterm birth, hypoxia or respiratory problems and low birth weight [5]. Postnatal factors include long-term breastfeeding, asthma, high fever, infections, varicella, diarrhea, and pneumonia [6].

MIH generally affects children aged 6–17 years, has no gender or racial predilection, and shows a worldwide prevalence of about 2.8%–44% [7]. This depends on the country, region and age group under study. Low and middle-income countries and children with poor general health during the first three years of life are more likely to have MIH [8]. A recent systematic review showed a higher prevalence of MIH in the American Continent (15.3%), followed by Oceania (14.7%), Africa (14.5%), Europe (14.4%) and Asia (10.7%) [9]. The prevalence of MIH in the Mexican population remains to be elucidated about the American continent. For these reasons, a new systematic review on the topic would be convenient and relevant worldwide. Therefore, the overall objective of the present study was to conduct a comprehensive review of the literature on the prevalence of MIH in the Mexican population, as well as its associated factors.

2. Materials and methods

2.1. Protocol and registration

The design of this study was performed following the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) [10] and was registered in Open Science Framework (OSF): 10.17605/OSF.IO/A6ZS4.

2.2. Focused question

Our objective was to answer the PECO question, "What is the prevalence of MIH in the Mexican population?" The respective statements were.

- (P) Population: Human clinical or epidemiological studies.
- (E) Exposure: Children diagnosed with MIH.
- (C) Comparison: Children without MIH.
- (O) Outcome: Prevalence of MIH.

The general objective was to determine the prevalence of MIH in the Mexican population. The secondary objectives were to evaluate the prevalence of MIH by gender (boys and girls), tooth involvement (molars and incisors), and the presence of dental caries. In addition, we carried out a comprehensive review of the literature to compare the prevalence of MIH in the countries that make up the American continent.

2.3. Eligibility criteria

Studies that were eligible for inclusion had to meet the following criteria: Cross-sectional clinical studies reporting the prevalence of MIH in the Mexican population, studies written in English and Spanish language, studies published after 2003, studies clearly reporting the diagnosis of MIH, children of both genders and without systemic alterations.

Studies with incomplete data, without the possibility of access by the authors, narrative, comprehensive, systematic reviews, meta-analyses, and book chapters were excluded.

2.4. Search strategy

Six electronic databases were used for study identification for this systematic review: PubMed, Scopus, Dentistry & Oral Science, Science Direct, Web of Science, and Google Scholar, from March 10th, 2024. For PubMed, our search strategy was based on the following algorithm: ("Molar Hypomineralization" [Mesh]) AND ("Prevalence" [Mesh]). For the rest, the following keywords were used: Molar-incisor AND Hypomineralization AND Prevalence AND Mexican. Also, to further enrich our search strategy, a comprehensive hand search was conducted in the following journals: Community Dentistry and Oral Epidemiology, Journal of Public Health Dentistry, Operative Dentistry, Oral Health & Preventive Dentistry, Pediatric Dentistry and American Journal of Dentistry.

2.5. Study selection

Study selection was independently evaluated by two investigators (M.A.A.S and J.S.B.R), who performed the evaluation of the titles and/or abstracts of the retrieved studies. Any disagreement was resolved by discussion in consultation with a third expert reviewer (C.C.A.S).

2.6. Data extraction process

Data extraction was performed by two investigators (C.C.A.S and S.I. V.J) independently. The following information was collected: author, year, type of work funding, inclusion and exclusion criteria, age, gender, sample size, classification of MIH, total prevalence of MIH, prevalence of MIH by gender, description of severity of MIH, percentage of affected molars and incisors, description of other symptoms and the percentage of children with MIH affected by dental caries or free of caries.

2.7. Summary measures and synthesis of results

Data analysis was performed using descriptive statistics. Predefined tables were prepared in Microsoft Excel to collect continuous data, mean age \pm standard deviation (SD), minimum-maximum range and frequency distribution (%). The data were analyzed in STATA V18 software (Stata Corp, College Station, TX, USA). The graphs were made in Graphpad Prism 8 software.

2.8. Risk of bias

Two reviewers (M.A.A.S and A.H) independently assessed the risk of bias of the included studies. The Joanna Briggs Institute (JBI) tool was used to assess cross-sectional studies [11]. Eight items were assessed, and the final score was obtained. If the score was between 1 and 3 there was a high risk of bias; between 4 and 6 there was a moderate risk and $\geq \! 7$ a low risk of bias assessment. A third investigator (J.S.B.R) verified the ratings obtained, and the group discussion resolved any discrepancies.

2.9. Statistically analysis

Forest plots were utilized to display odds ratios (OR) and 95% confidence intervals (CI). The $\rm I^2$ statistic assessed the heterogeneity among the studies included. A random-effects model was employed to aggregate the primary outcomes when heterogeneity exceeded 50% and was statistically significant. Furthermore, a funnel plot and Egger's regression analysis were performed to evaluate potential publication bias.

3. Results

3.1. Study selection

In the identification phase, 531 articles were found from the six databases included (PubMed 43 records; Scopus 6 records; Dentistry & Oral Science 5 records; ScienceDirect 24 records; Web of Science 6 records; and Google Scholar 447 records). The manual search identified no records relevant to this study. Duplicates (31 records) were then removed giving a total of 500 articles. Then, in the screening phase, based on title and abstract, 491 records were excluded because they did not focus on the research topic. After analyzing the full text of the remaining articles, no articles were excluded. Thus, a total of 9 articles were assessed for eligibility and included in systematic review and meta-analysis. Details of study selection are shown in Fig. 1.

3.2. Sociodemographic and clinical characteristics of the studies

In this study, 9 articles with a cross-sectional design were reviewed [12–20]. The total number of children studied in the included investigations was 5039. The ages of the children ranged from 6 to 12 years; the mean \pm SD age of the patients studied was 9.02 \pm 1.19 years, of whom 50.1% were boys and 49.9% were girls. Most of the articles

were published after 2019 (7:77.7%) [12–18]. The oldest study was from 2016 [20], whereas, the most recent was from 2022 [12] (Table 1).

The 77.7% of the included studies used the MIH classification proposed by the EAPD [12,15–21], the remaining 11.15% used the system proposed by Ghanim et al. [13,22] and Mathu-Muju and Wright [14,23]. With respect to the classification proposed by the EAPD, it was found that 19.45% of the affected teeth had mild MIH [12,15–20], 28.5% had moderate MIH [12,16–20] and 12.53% had severe MIH [12,15–20].

The prevalence of MIH in boys was 34.1% and in girls was 30.4% [12,14–18,20]. The prevalence of MIH was higher in molars (30.7%) than in incisors (10.8%). No study reported involvement in permanent second molars [12–20].

Only one (11.11%) study [16] reported that children had symptoms such as sensitivity and pain. Five (55.5%) studies reported the prevalence of dental caries in children affected by MIH [12,15–18]. A total of 78.7% had dental caries, while 21.3% had no caries (Table 2, Fig. 2, panel A–C).

3.3. Meta-analysis

The prevalence of MIH in the Mexican population ranged from a minimum of 12%, reported by Sosa-Soto et al. [13] to a maximum of 42%, reported by Villanueva-Gutiérrez et al. [16]. The mean prevalence

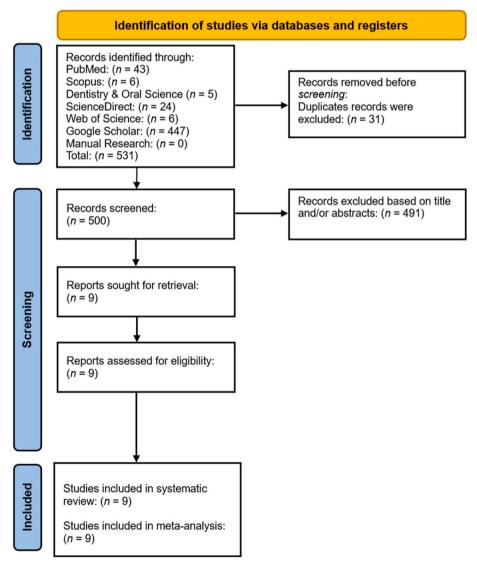


Fig. 1. PRISMA flow diagram. PRISMA: Preferred Reporting Items for Systematic and Meta-Analyses.

 Table 1

 Sociodemographic characteristics of the included studies.

Author/Year	Ethical	Funding	Inclusion criteria Exclusion criteria		Age (years)	Gender B ^o /G ⁱ	Sample size
García-Pérez et al., 2022 [12]	Yes	None	Schoolchildren of either gender aged 8–10 years; written parental authorization to participate; the four upper and lower incisors and the first four permanent molars fully erupted; the parents/guardians of the participant residing at the same address	Declining to cooperate with OHRQoL questionnaire; the presence of a craniofacial deformity; a history of dental trauma; current orthodontic treatment; not cooperating during the oral examination	9.2 8–10	318/ 315	633
Sosa-Soto et al., 2021 [13]	Yes	NR	Children aged 8 years who exhibited the first four permanent molars and the eight lower and upper permanent incisors	Wearing fixed orthodontic appliances; or a chronic systemic disease	8.6	327/ 303	630
García-Vázquez et al., 2020 [14]	NR	NR	Children 10 and 11 years of both gender; whose parents authorize participation in the study	Children with orthodontic or maxillary orthopedic appliances; with unerupted first molars and permanent incisors and with molars affected by other enamel defects	11.3 10–11	21/14	35
Irogoyen- Camacho et al., 2019 [15]	Yes	None	Children has at least one erupted or partially erupted first permanent molar	Children with fixed orthodontic appliances; or children who were absent during the days of oral evaluation	7.1 6–8	262/ 287	549
Villanueva- Gutiérrez et al., 2019 [16]	Yes	Self- funded	Schoolchildren aged 8–12 years presenting the eruption of at least one first permanent molar	Children with orthodontic attachments that prevented the examination of tooth surface	9.7 8–12	250/ 256	506
Villanueva- Gutiérrez et al., 2019 [17]	Yes	NR	Schoolchildren aged 8 to 10 presenting the eruption of at least one first permanent molar	Children with orthodontic attachments that prevented the examination of the tooth surface	8.9 8–10	217/ 194	411
Villanueva- Gutiérrez et al., 2019 [18]	Yes	CONACYT	The parents signed a consent form for the participation of their children in the study and that the child assented to an oral examination; the children were also required to be present during the days of the oral examination	Children in whom the first permanent molars had not erupted or who had no more than one- third of the anatomical crown visible on any first permanent molar; children who had not attended school during the days of the study	9	321/ 365	686
Gurrusquieta et al., 2017 [19]	Yes	NR	Children with first four erupted permanent molars; whose parents had provided written consent and completed the medical history questionnaire	NR	8.4	574/ 582	1156
Murrieta-Pruneda et al., 2016 [20]	Yes	FES Zaragoza	Schoolchildren aged 8 to 12 presenting the eruption of at least one first permanent molar	Children whose parents did not authorize their inclusion in the study had premature loss of the teeth of interest to the study for reasons other than those caused by the presence of MIH of any of the teeth of interest to the study; were undergoing orthodontic treatment; were uncooperative at the time of the examination; or had a physical disability	9.8 8–12	235/ 198	433

Abbreviations: NR Not Reported; B^o Boys; Gⁱ Girls; OHRQoL Oral Health Related Quality of Life; CONACYT Consejo Nacional de Ciencia y Tecnología; FES Zaragoza Facultad de Estudios Superiores Zaragoza.

of all studies combined was 23% (Fig. 3, panel A).

Statistically significant high heterogeneity was found. Funnel plot and Egger's test indicated publication bias (p = 0.003) (Fig. 3, panel B).

3.4. Risk of bias in the evaluation of included studies

The JBI analysis showed that 33.3% of the studies had a moderate risk of bias [13,14,20], while the remainder (66.7%) had a low risk of bias [12,15-19]. One hundred percent of the studies complied with items 1, 2, 4, 7, and 8 [12-20]. Eighty-eight percent complied with item 3 [12-18,20]. While 66.6% complied with items 5 and 6 [12,15-19]. (Fig. 4).

4. Discussion

This systematic review and meta-analysis investigated the prevalence of MIH in the Mexican population. A total of nine articles with a cross-sectional design published in the six different databases were analyzed. Overall, the most important findings showed a 23% prevalence of MIH in Mexican boys and girls aged 6–12 years and no gender differences were observed.

Recent studies have determined a prevalence of MIH of 13.1%–14.2% worldwide [24,25]. Particularly, the prevalence of MIH in the Americas (15,3%) was higher than in Oceania (14.7%), Africa (14.5%), Europe (14.4%) and Asia (10.7%) [9]. In relation to the American continent and according to recently published scientific evidence, of the

thirty-five countries that comprise it, studies have only been conducted in nine countries, which are Mexico, USA, Argentina, Brazil, Chile, Colombia, Peru, Uruguay and Venezuela [26-38] (Table 3). It was observed that the prevalence of MIH was higher in Brazil, Mexico and Venezuela. A study published by Dourado et al. who evaluated a total of 251 Brazilian children and adolescents aged 8-14 years, found the highest prevalence of MIH (46.6%). In addition, they demonstrated that MIH was associated with gestational diabetes and acute fetal distress [33]. On the other hand, in the study published by Reis et al. they evaluated a total of 450 Brazilian children aged 8 years and applied a survey to parents to assess socioeconomic factors possibly associated with MIH. The authors found a prevalence of MIH of 28.7%, moreover, the upper molars were the most affected, however the lower molars showed a higher severity. It was observed that the number of incisors with MIH increased with increasing number of affected molars. Clinically, most of the children with MIH showed creamy-white opacities and no association was found between MIH and socioeconomic factors. Interestingly in this study, MIH was more prevalent in boys than in girls [32]. In the study published by Rodriguez-Rodriguez et al. they evaluated a total of 121 Venezuelan children aged 6-12 years and found a prevalence of MIH of 25.6% and contrary to what was observed previously, MIH was more common in the female sex. The mean number of teeth affected was 4.6 \pm 2.19 and the most frequent involvement was in the upper molars [38].

It was observed that the prevalence of MIH was lower in the USA, Uruguay and Argentina. A study published by Davenport et al. who

 Table 2

 Clinical characteristics of the included studies.

Author/Year	MIH classification	Total (%) MIH Y/N	MIH Boys (%)	MIH Girls (%)	MIH Severity (%)	Molars affected (%)	Incisors affected (%)	Other symptoms	Dental Caries (%)
García-Pérez et al., 2022 [12]	EAPD [21]	38.6/61.4	37.3	39.9	Mild: 6.6 Moderate: 25.7 Severe: 6.3	NR	NR	NR	85
Sosa-Soto et al., 2021 [13]	Ghanim et al. [22]	12.4/87.6	NR	NR	Code 2: 76.4 Code 3: 5 Code 4: 2.7 Code 5: 15.9	74.5	25.5	NR	NR
García-Vázquez et al., 2020 [14]	Mathu-Muju and Wright [23]	28.5/71.4	21	14	Mild: 28.57	17	8	NR	NR
Irogoyen-Camacho et al., 2019 [15]	EAPD [21]	26.1/73.9	29.3	24.7	Mild:19.05 Severe: 7.05	NR	NR	NR	22.4
Villanueva-Gutiérrez et al., 2019 [16]	EAPD [21]	42.4/57.6	51.6	48.4	Mild: 21.7 Moderate: 7.7 Severe: 13	NR	NR	Sensitivity Pain	96
Villanueva-Gutiérrez et al., 2019 [17]	EAPD [21]	40.4/59.6	52.8	47.2	Mild: 6.8 Moderate/ Severe: 33.6	NR	NR	NR	100
Villanueva-Gutiérrez et al., 2019 [18]	EAPD [21]	35.4/64.6	38.3	32.9	Mild: 18.5 Moderate: 67.1 Severe: 14.4	17.4	3.7	NR	90.1
Gurrusquieta et al., 2017 [19]	EAPD [21]	15.8/84.2	NR	NR	Mild: 56.6 Moderate: 31.7 Severe: 12	NR	NR	NR	NR
Murrieta-Pruneda et al., 2016 [20]	EAPD [21]	14/86	8.1	5.8	Mild: 6.9 Moderate: 5.5 Severe: 1.4	13,9	6	NR	NR

Abbreviations: NR Not reported; EAPD European Academy of Pediatric Dentistry; MIH Molar-incisor hypomineralization; Y Yes; N No.

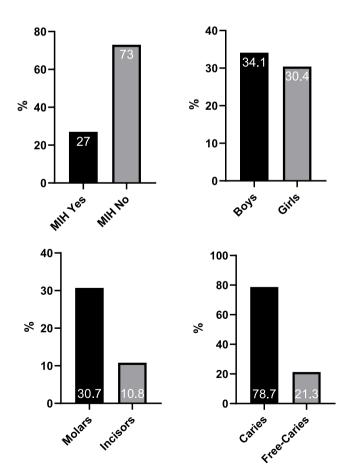


Fig. 2. Prevalence of MIH in Mexican population. A) General, B) By Gender, C) By teeth and D) By the presence or absence of dental caries.

examined a total of 375 US children, found a prevalence of 9.6%, and among teeth with MIH defects, severe defects were higher in lower molars than in upper molars. In addition, the authors found no significant differences between children with and without MIH by gender, race, and socioeconomic status [28]. Another study, published by the research group of Biondi et al. found a similar prevalence of MIH in children attending a public school in Uruguay (7.12%) compared to those children attending a public school in Argentina (6.4%). In this study, no significant differences were found comparing the distribution by gender, affected teeth or severity of each tooth. However, the authors found a positive correlation with respect to year of birth [29].

With all of the above, it should be taken into account that the high variability of the results depends largely on the diagnostic criteria used to evaluate MIH, the lack of calibration or standardization among clinicians, environmental conditions, clinical examination, age, social characteristics and idiosyncrasies of the study subjects [39].

The present study also found a high prevalence of children with MIH affected with dental caries. These results are in agreement with what has been published in the literature, a recent systematic review based on a sample size of 17,717 children with a mean age of 8.6 years, showed that MIH correlates significantly with an increased risk of caries in both primary and permanent dentition [40]. Another study, confirmed these findings and showed that the scores of different caries indices increase proportionally to the severity of MIH [41]. This is partly explained by the fact that enamel affected by MIH shows a higher protein content (3-21 times more) and a lower concentration of calcium and phosphorus compared to normal enamel, which reduces its hardness, elasticity, and makes it more porous. This structural modification of the enamel surface creates different niches that favor bacterial colonization, which increases the overall risk of other oral diseases [42]. In this regard, a study described for the first time the composition of the supragingival microbiota in teeth affected by MIH using 16S rRNA gene sequencing. In this work, the authors found a higher bacterial diversity in samples with MIH compared to healthy controls, suggesting better bacterial adhesion or a higher number of niches on those surfaces. In addition, a higher prevalence of the genera Catonella, Fusobacterium, Campylobacter,

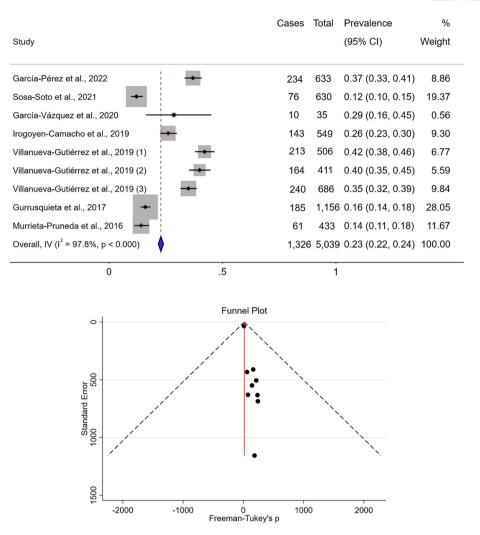


Fig. 3. (A) Prevalence of MIH in Mexican population (mean values) and (B) Funnel plot of included studies showed asymmetrical pattern.

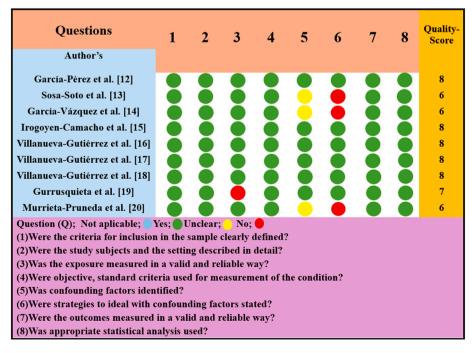


Fig. 4. Quality assessment according to the JBI for clinical cross-sectional studies.

Table 3Prevalence of MIH in American continent countries.

Country	Prevalence reported
Mexico	23% → this study
USA	14% [26]/9.6% [27,28]
Antigua and Barbuda	Unknown
Argentina	6.4% [29]/15,9% [30]
Bahamas	Unknown
Barbados	Unknown
Belize	Unknown
Bolivia	Unknown
Brazil	14.3% [31]/28.7% [32]/46.6% [33]/9.8% [34]
Canada	Unknown
Chile	12.8% [35]
Colombia	11.2% [36]
Costa Rica	Unknown
Cuba	Unknown
Dominica	Unknown
Ecuador	Unknown
El Salvador	Unknown
Granada	Unknown
Guatemala	Unknown
Guyana	Unknown
Haiti	Unknown
Honduras	Unknown
Jamaica	Unknown
Nicaragua	Unknown
Panama	Unknown
Paraguay	Unknown
Peru	19.8% [37]
Dominican Republic	Unknown
Santa Lucia	Unknown
Saint Kitts and Nevis	Unknown
San Vicente and the Granadinas	Unknown
Suriname	Unknown
Trinidad and Tobago	Unknown
Uruguay	7.12% [29]
Venezuela	25.6% [38]

Tannerella, Centipeda, Streptobacillus, Alloprevotella and Selenomonas was found associated with hypomineralized teeth, while Rothia and Lautropia were associated with healthy sites. The bacteria found associated with MIH were highly proteolytic, i.e., they could degrade the high protein content of MIH-affected teeth, facilitating microbial invasion of dentinal tubules and contributing to cavitations and hypersensitivity [43]. However, at the species level the composition of the supragingival microbiota in teeth with MIH has not yet been characterized, therefore, it would be interesting to explore which bacterial species might increase the risk of other diseases such as dental caries, periodontal disease and endodontic infections.

This study has some limitations that should be pointed out, such as the cross-sectional design of the investigations, the lack of sufficient articles included in the review, the publication bias (p=0.003), which can be explained due to methodological deficiencies (unfavorable response in 33.3% of the studies in relation to items 5 and 6/JBI), as well as a high variability regarding some specific aspects of the studies such as, the differences presented in the genetic profile, age, gender, environmental and sociocultural conditions of the study subjects, so the results should be interpreted with caution, as it could influence the certainty of the evidence. In addition, it is important to generate future epidemiological studies that show the prevalence of MIH in the rest of the countries that make up the American continent, particularly in Mexico; this will be of utmost importance for health personnel since it will be possible to develop and implement oral health programs focused on MIH.

5. Conclusion

Based on the present qualitative analysis, it can be concluded that.

- To the authors' knowledge, this is the first systematic review that evaluates the prevalence of studies published to date on MIH in the Mexican population.
- 2. There were no differences in gender distribution; that is, both boys and girls have a similar distribution of MIH lesions.
- Molar teeth are affected more frequently compared to permanent incisors.
- There is a high prevalence of boys and girls with MIH affected with dental caries.
- 5. The prevalence of MIH in the Mexican population was 23%.
- 6. Regarding methodological design, future studies should take into account a clear description of the exposure measurement method, highlighting two important aspects: validity and reliability (concordance). On the other hand, it would also be important to identify confounding factors that could be influencing the direction of the results, as well as to implement strategies to address their produced effects (regression analysis).

Informed consent statement

Not applicable.

Ethical approval

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The data supporting this study's findings are available from the corresponding author upon reasonable request.

Author contributions

Conceptualization, M.A.A.-S, and J.S.B.-R.; methodology, M.A.A.-S.; software, M.A.A.-S.; validation, M.A.A.-S, J.S.B.-R., C.C.A.S, and S.I.V.J.; formal analysis, M.A.A.-S, J.S.B.-R., C.C.A.S, and S.I.V.J.; investigation, M.A.A.-S, and J.S.B.-R.; resources, M.A.A.-S, J.S.B.-R., C.C.A.S, and S.I.V.J.; data curation, M.A.A.-S.; writing—original draft preparation, M.A.A.-S, and J.S.B.-R.; writing—review and editing, M.A.A.-S, J.S.B.-R, C.C.A.S, S.I.V.J, L.S.E.V, A.H, and S.A.M; visualization, M.A.A.-S, J.S.B.-R, C.C.A.S, S.I.V.J, L.S.E.V, and A.H; supervision, M.A.A.-S, J.S.B.-R., C.C.A.S, S.I.V.J, L.S.E.V, and A.H; project administration, M.A.A.-S. All authors have read and agreed to the published version of the manuscript.

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Competing interests

The authors declare no conflict of interest.

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