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Prevalence of Molar Incisor Hypomineralization: Meta-Analysis Study

Can Özükoç[1]*, Beyza Ballı Akgöl[1], Aslı Patır Münevveroğlu[1]

Abstract

Objective: Molar Incisor Hypomineralization (MIH) is defined as the hypomineralization of one or more first permanent molars, which may often also affect permanent incisors. The prevalence rate of MIH has been reported to vary between 2.5%-40.2% in various populations. This study aimed to reveal the general dimensions of MIH and to determine its prevalence in societies to plan long-term disease control programs.

Material and Methods: The database obtained by reviewing all studies on the relevant subject in English literature was examined and the prevalence was calculated using the random effect model. All studies were assessed in terms of publication bias while examining the heterogeneity and meta-regression by using sensitivity analysis.

Results: A total of 70 studies were included in the study and the prevalence of MIH was calculated to be 11.88% (95% CI 10.2%-12.4%). The sample size explained 99% heterogeneity.

Conclusion: This study has revealed that more strategies are needed for the preservation of dental health in this patient group due to the high prevalence of MIH, and there is a need for further prevalence studies involving isolated populations in different parts of the world.

Keywords: Meta-Analysis, Molar Incisor Hypomineralization, Pediatric Dentistry, Prevalence.

Introduction

Tooth development stages are affected by both genetic factors and environmental factors. Ameloblasts are highly vulnerable in the transition stage and the early maturation stage in particular. Their short-term or long-term exposure to environmental or systemic factors leads to enamel hypoplasia or hypomineralization. Structural deviations caused by an impairment during enamel formation result in permanent damage as there is no reshaping or repairing possibility. Damage to ameloblastic activity during the secretion or maturation phase causes impaired enamel formation (1). However, the sensitivity of ameloblasts to this damage is not the same at all stages of enamel development. All defects caused by damage to ameloblasts during enamel formation are called developmental enamel defects (2).

Enamel hypomineralization, a qualitative defect of enamel, is characterized by the demarcated opacity with normal enamel thickness and with the color varying from white to yellow-brown, soft porous enamel of poor appearance, fractures in the molars after the eruption, and hypomineralized enamel or enamel opacity with asymmetric opacity (2).

Etiological factors that lead to molar-incisor hypomineralization (MIH) by changing the organic or inorganic structure are still unknown. However, many factors are thought to be involved in its etiology and therefore, it is thought to have a multifactorial etiology. In a comprehensive study conducted in Southeast Sweden, 4,000 possibilities were found to potentially cause enamel opacity in six-year molars (3). Although MIH occurs in the third trimester and within the first year after birth, it can be noticed at the age of six, i.e. with the eruption of the first molar teeth, at the earliest. During this period, the medical history of the child may be forgotten and the socioeconomic status of the family may change (3).

To the best of our knowledge, genetic factors include enamelysin, Kallikrein (Klk 4), 22q11 gene deletions, and Runx2 suppression; medical factors include middle ear infection, chickenpox, asthma, pneumonia, prenatal urinary tract infection, infectious diseases, respiratory diseases, high fever, preterm labor, prolonged cyanosis during childbirth, neonatal hypocalcemia, and vitamin D deficiency; and systemic factors include severe malnutrition, bilirubinemia, chronic diseases, thyroid and parathyroid disorders, and maternal diabetes (3).

A study investigating the relationship between preterm labor and MIH has revealed that low birth weight and low gestation period might be effective factors. A 100-g increase in birth weight reduces the development of MIH by 4.5%, while gestation prolonged for one week decreases

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1 Istanbul Medipol University Faculty of Dentistry, Dept of Pediatric Dentistry, Istanbul, TR
*** Corresponding Author:** Can Özükoç **E-mail:** cozukoc@medipol.edu.tr

the development of MIH by 9.6%. Malnutrition, particularly breastfeeding for less than six months, causes the development of demarcated opacities in molars by five times more (4). The use of amoxicillin and erythromycin, vaccines, socioeconomic factors, and dioxins can be regarded as environmental factors (3).

Dioxins, which are known to be the most carcinogenic substances, are found in plastic materials. They accumulate in fatty tissues and pass into milk. According to the results of a study involving mice, bisphenol A (BPA), which the plastic industry cannot avoid using and is used in the production of the water bottles that we use in our homes, has been proven to cause MIH by affecting amelogenesis via the estrogen receptor alpha (ERα). In the same study, white opacity has been found in mandibular incisors in 75% of male mice and 31% of female mice (5).

Recent studies have revealed the correlation between gene expression and MIH. During the process of amelogenesis, the size, shape, shade, and caries susceptibility of teeth, and even enamel microhardness are under genetic control (6). Anomalies in the number of teeth and eruption, as well as enamel hypoplasia and hypomineralization, can be seen in 22q11 deletion syndrome (7).

In the literature, ameloblastin (AMBN), Tuftelin (TUFT1), ENAM gene rs3796704, and tuftelin-interacting protein 11 (TFIP11) rs5997096 have been revealed to correlate with MIH (8).

Molar-incisor hypomineralization is characterized by the morphological enamel defects caused by hypomineralization of systemic origin on the occlusal surfaces of first permanent molars and one third or more of the incisal surface of the incisors (9).

The term MIH refers to that at least one first permanent molar is affected and this is accompanied by incisors frequently (10). It has been reported that permanent canines, permanent second molars, and premolars may accompany this condition rarely. However, opacity seen only in incisors cannot be considered as MIH since it may also occur as a result of local factors (10). Therefore, researchers may have different views while establishing the diagnosis. European Academy of Paediatric Dentistry (EAPD) criteria are considered in recent studies on MIH (9). According to these criteria, the diagnosis of MIH is established on wet teeth after the teeth surfaces are cleaned meticulously. The age of eight is the best age for an accurate diagnosis. Since four first permanent molars and most of the incisors of children have already erupted at this age, four first permanent molars and eight permanent incisors are evaluated when they are wet in terms of the presence of demarcated opacity, fractures occurring after the eruption, atypical restorations, molars extracted due to MIH, and failure of the eruption in molars or incisors (9).

According to the results of the studies, the prevalence of MIH varies between 2.5%- 40.2% all over the world, which has been reported to be between 3.6%–37.5% in Europe, 40.2% in Brazil, and 2.8% in Hong Kong (1). However, different evaluation criteria are used in the diagnosis of MIH in the studies, and therefore, the prevalence of MIH cannot be calculated accurately due to the differences in these criteria.

This study aimed to evaluate the prevalence of MIH reported in epidemiological studies carried out considering the EAPD 2003 criteria, and to provide a more reliable source of the prevalence of MIH by conducting a meta-analysis on the study data obtained.

Material and Methods

Study Selection and Data Collection

Preferred Reporting Items for Systematic Reviews (PRISMA) and Meta-analysis of Observational Studies in Epidemiology (MOOSE) criteria were used in the preparation of systematic review and meta-analysis (11,12). PubMed, Google Scholar, Ovid Medline, and Web of Science Core Collection databases were scanned on 30 September 2020 to identify eligible studies.

The reviews achieved during the scanning of the sources and databases of all the articles were evaluated in terms of whether they were eligible for the study. Studies that included classification according to EAPD criteria and prevalence value, even if their main objective was not to determine MIH prevalence, were evaluated. In the case of missing data, the authors of the relevant study were contacted and missing data were tried to be obtained. The following keyword was scanned in the study: MIH=(molar OR incisor OR hypomineralization AND =(prevalence OR incidence OR incident), Molar incisor hypomineralization=(molar OR incisor OR hypomineralization AND =(prevalence OR incidence OR incident), Enamel Hypomineralization=(enamel OR hypomineralization AND =(prevalence OR incidence OR incident).

Studies obtained through these databases were selected by two researchers (CÖ, BBA) independently by firstly checking the titles and abstracts and then full-text articles. In case of a discrepancy in the selection, or if there were any doubts, the opinion of another researcher (APM) was obtained to decide whether the relevant article should be included in the study. The agreement between the two researchers in the selection of articles was analyzed statistically. The article selection process is summarized in the PRISMA flowchart presented in Figure 1.

Evaluation of the studies in terms of bias

All studies to be included in the analysis were evaluated using a bias score that was developed by the research team and took into account representational power, measurement standards, and missing data. (Table 1.) Studies with a score of 2 and above were regarded to be problematic in terms of representational power. Therefore, these studies were evaluated as high risk of bias, and those with a score of 0–1 as low risk of bias. Statistical analyses were performed after eliminating the studies assessed to have a high risk of bias. In the evaluation of the results, the studies assessed to have a low risk of bias were focused on.

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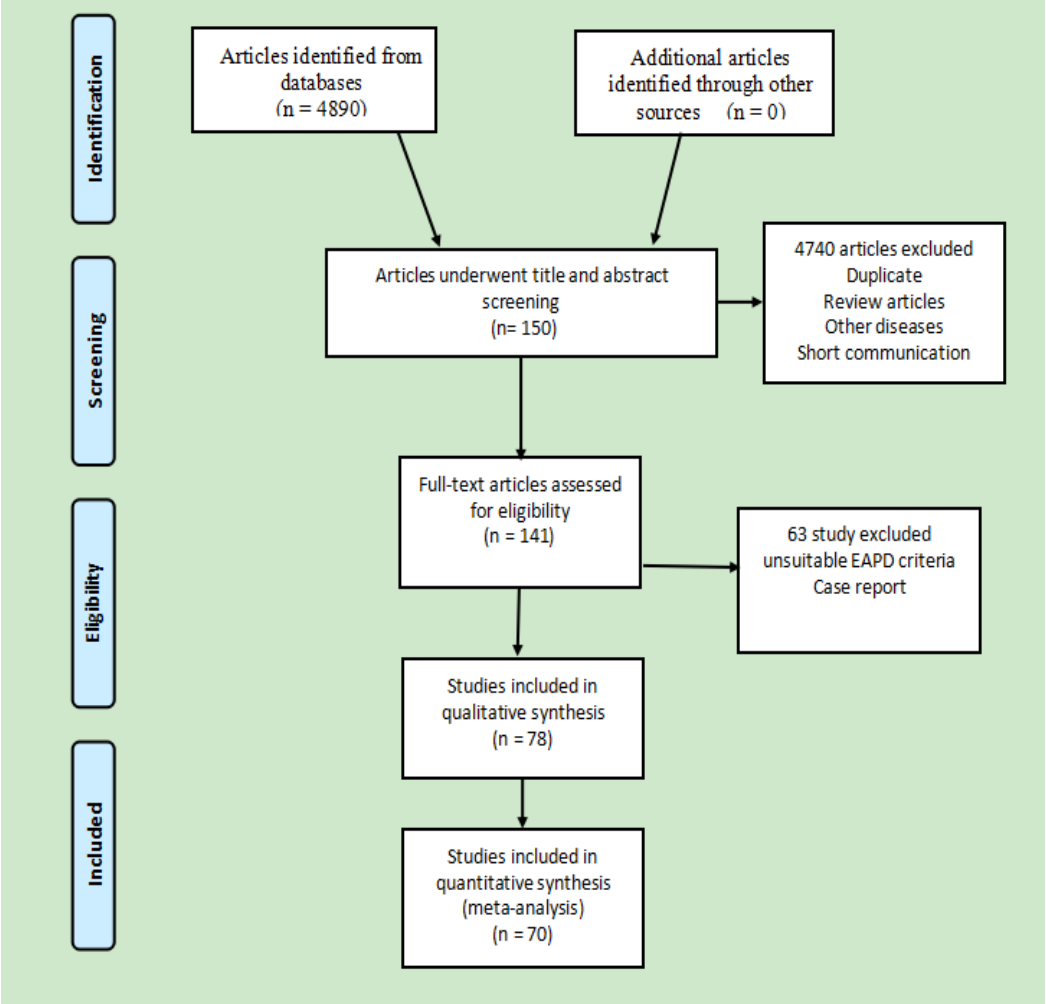

Figure 1. Prisma flowchart

Table 1. Bias score

Criteria	Point
Sampling potential is poor	2
Sampling is not fully representative	2
Probabilistic sampling	2
Selective age (including children less than 6 years old)	2
Missing data (<10%)	1
Missing data (<20%)	2
Small scale work (<100 persons)	1
Small scale work (<10 persons)	2

Calculation of prevalence and obtaining numerical data

Crude prevalence and numerical data that were not standardized by age were used in the calculation of prevalence. The reason for this was that it was not clear which standard population was based on in calculating the standardized values in each article or they were not standardized for the same population. Data obtained from studies in which EAPD criteria were used in the diagnosis of MIH were included in this study.

Statistical analysis

The agreement between the observers was evaluated using Cohen's kappa coefficient for the article selection and bias scores, which were made independently from each other. Kappa values were interpreted as follows: values ranging between 0.41– 0.60 as moderate, 0.61–0.80 as substantial, and above 0.80 as almost perfect agreement (13). Analyses were performed by combining the studies remaining after the exclusion of the articles with a biased score higher than 2. The meta-analysis of the data was calculated using the fixed-effects model and the random-effects model, but the results of the random-effects model were used in the interpretation.

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The heterogeneity between studies was evaluated using Cochran's Q and I2 test statistics. With a conservative approach in the Cochran's Q test statistics, a p-value <0.10 was interpreted as indicating statistically significant heterogeneity. The value of I2>75% was interpreted as high heterogeneity. A funnel plot was drawn to show small-study effects, publication bias, and other possible reasons for heterogeneity. The sensitivity analysis was assessed based on the change occurring in the result following the exclusion of a study at a time.

RevMan 5.4.1 (Cochrane Training, https://www.cochrane.org/) was used as the analysis tool. In the analysis, "psych", "metaphor", and "meta" packages were used. Except for Cochran's Q statistics, other p values <0.05 were considered statistically significant.

Results

A total of 4,890 studies were reached as a result of the database scan. Among them, 968 studies were found to be the same due to the evaluation of different databases. The remaining 3,840 studies were reviewed, and 3,699 studies that were found to be unrelated to the subject were eliminated.

Thirty studies in which EAPD criteria were not used at the time of MIH diagnosis and eight studies that were found to have a high bias score (>2) were excluded from the study.

According to the results of the review of studies on the evaluation of the MIH prevalence, a total of 70 studies (n=93519) meeting the study criteria and 68 articles presenting the results of these studies were reached (Fig 2. Forest plot graphic) The agreement between the raters was found to be perfect both in the selection of articles and bias scoring of selected articles (Cohen's kappa coefficient was 0.95 (95% Confidence Interval [CI] 0.88–1) for article selection, and 0.97 (95% CI 0.92–1) for bias scoring).

The mean prevalence of MIH was found to be 10.1% (95% CI 10.2%-12.4%) in the random-effects meta-analysis of 70 studies involving MIH prevalence data. The heterogeneity between studies was found to be significantly high (i2=99%). The Funnel plot shows an asymmetrical pattern in the whole group (p>0.10). No major problems were detected in the sensitivity analysis. The funnel plot of the study and forest plot are presented in Figure 2 and Figure 3, respectively.

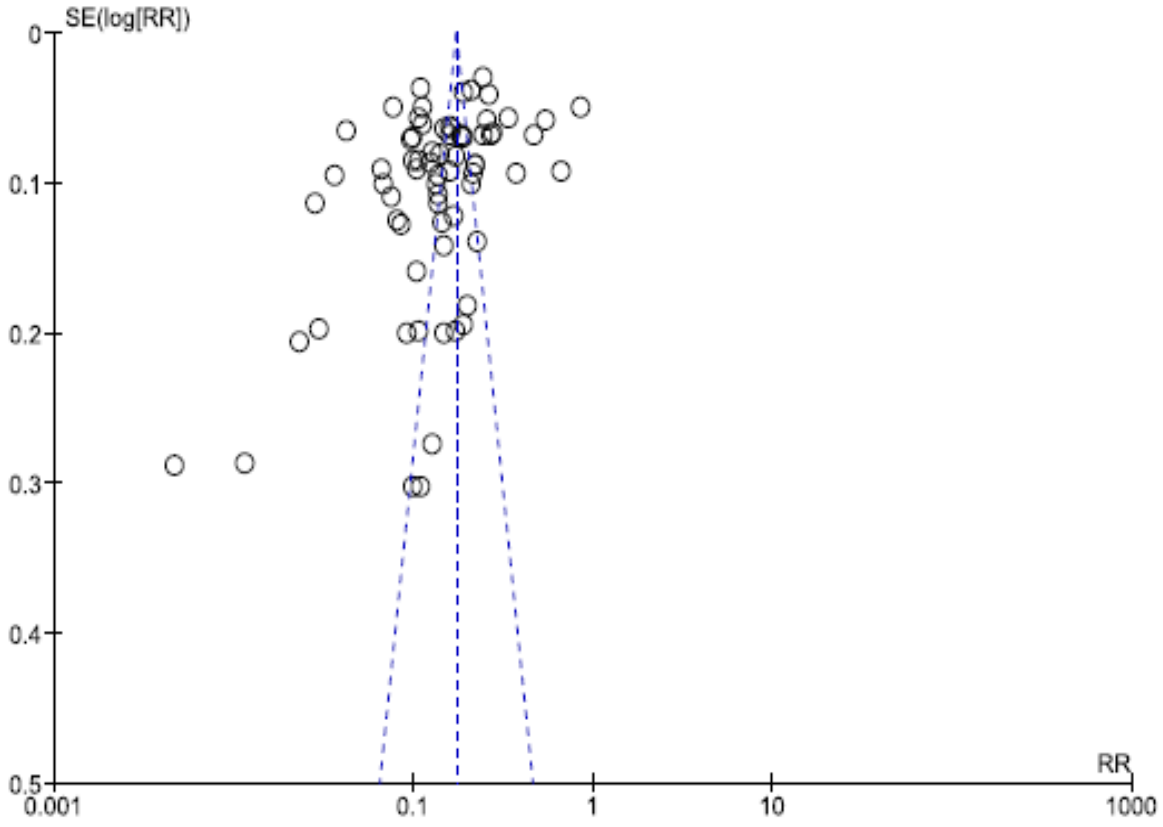

Fig 2. Funnel plot graphic

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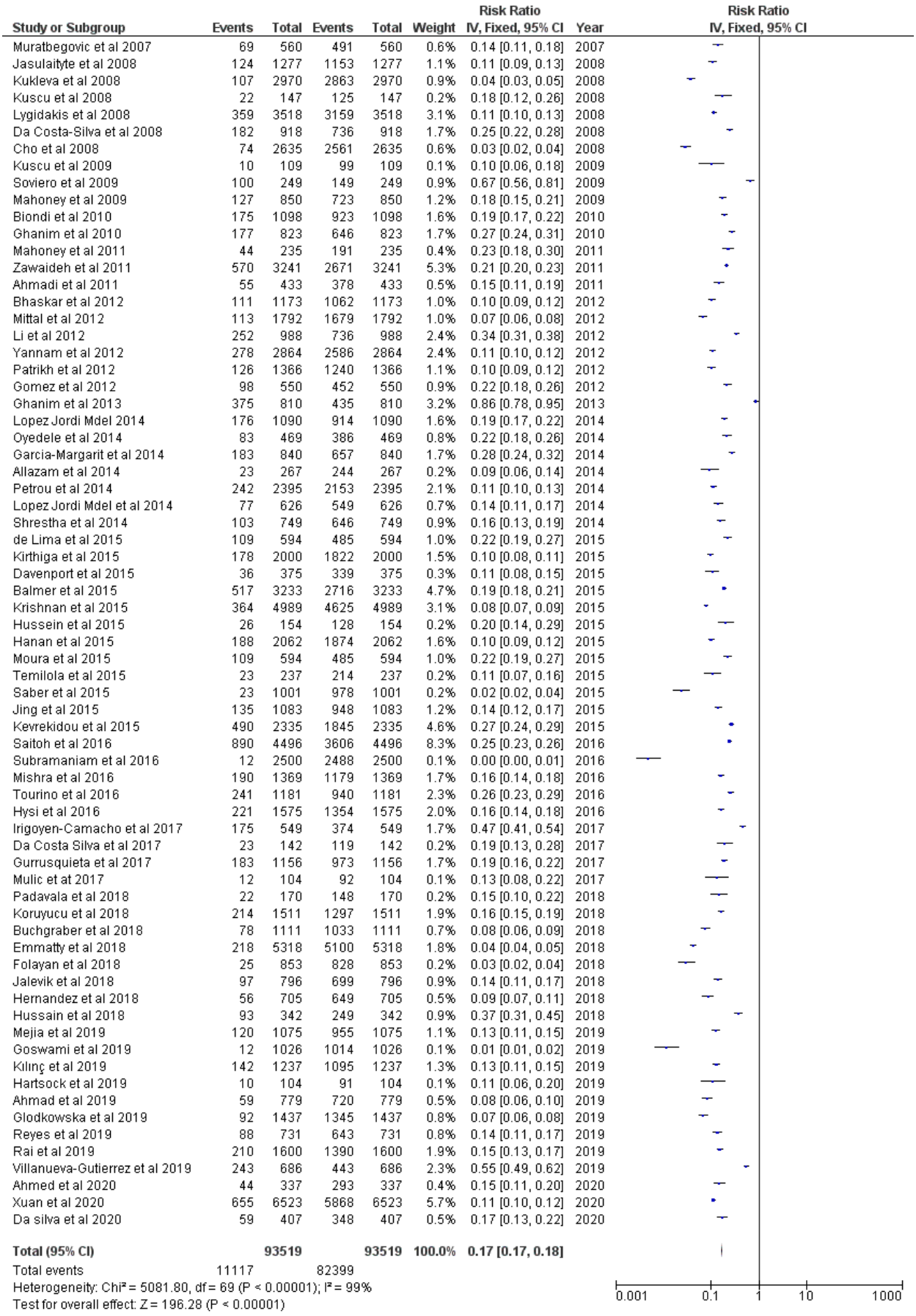

Fig. 3. Forest plot graphic

Discussion

The first epidemiological study of MIH was conducted among Swedish children in the late 1970s. In this study, "cheese" first molars with opacity varying from cream-white to yellow-brown were defined (14). In the first epidemiological studies conducted, there was no consensus among researchers in terms of diagnostic criteria and identification. Various terms have been used in the past to describe this pathology: non-endemic stained enamel (15), idiopathic hypomineralization of the enamel of the first permanent molars (16), hypomineralization of the permanent first molars not caused by fluoride (17), and molar-incisor hypomineralization (10). In 2003, EAPD agreed on the use of the latest terminology and also determined the evaluation criteria (9).

Although its definition was made based on various criteria until 2003, diagnostic criteria determined by the EAPD in that year was started to be used in epidemiological studies. The results of epidemiological studies using EAPD criteria are more reliable since the development and use of common evaluation criteria ensure consensus among researchers. Therefore, the data of studies using the EAPD criteria were analyzed in the present study.

In this meta-analysis, the prevalence of MIH was found to be 11.88% by the assessment of 93519 individuals in 70 studies. The result obtained was compatible with the results of several previous studies (1,10,18,19,20,21). On the other hand, MIH prevalence was reported to be lower in several studies (22,23). The prevalence of MIH could have been found to be lower, as children under six years of age were evaluated in these studies.

Following the analysis, the review of studies reporting low MIH prevalence rates showed that the prevalence was higher in studies involving children under 10 years of age. In studies where the prevalence was reported to be very low, the age group was found to be older (>15 years). Similarly, Yannam et al. (24) found that the prevalence of MIH was lower in children older than 10 years of age and attributed this to the fact that MIH diagnosis cannot be established due to tooth extraction and treatments. Mishra and Pandey (25) reported that the prevalence of MIH increased in children aged eight to nine years due to the increase in the post-eruptive breakdown.

It can be difficult to distinguish between MIH and enamel hypoplasia in cases where decay occurs or losses due to masticatory forces occur in the affected first permanent molars. In children with high caries activity, MIH can be masked by extensive caries or restorations. Enamel hypoplasia and MIH may coexist but they can be distinguished at the histological level. Therefore, it is easier to diagnose MIH when the first permanent molars and permanent incisions have newly erupted. The ideal age at which the incisors and first permanent molars can be seen fully in the mouth and for the diagnosis of MIH is eight years (10). We believe that different results have been obtained in calculating the prevalence of MIH, as the age was not evaluated or it was given as missing information in the studies.

Conclusion

To conclude, the prevalence of MIH has been found to be 10.1% in the present meta-analysis, and it has been revealed that there is a need for further prevalence studies involving isolated populations in different parts of the world. Moreover, more strategies for the preservation of dental health need to be developed in areas with high MIH prevalence.

Author Contributions: CÖ, BBA, APM: Project design, Review of the literature, data collection and analyzes **CÖ;** Writing of the article and Revisions

Ethical issues: All authors declare originality and ethical approval of research. Responsibilities of research, responsibilities against local ethics commission are under the authors responsibilities. The study was conducted under defined rules by the local ethics commission guidelines and audits.

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