Resumen: Objetivo: Identificar la prevalencia y los criterios diagnósticos de la hipomineralización de incisivos molares (HIM) en la literatura científica. Materiales y métodos: Investigación bibliográfica realizada a través del análisis de artículos indexados hasta octubre de 2017 en las bases de datos PubMed, Web of Science y Scopus. Los Medical Subject Headings (MESH) utilizados fueron "Dental Enamel Hypoplasia" y "Molar Incisor Hypomineralization". El análisis de los artículos fue llevado a cabo por dos revisores, quienes recolectaron información de manera independientemente. Se recopiló la siguiente información: autor, año de publicación, lugar de trabajo (continente y país), cálculo y número de muestra, edad de los participantes, tipo de estudio, prevalencia de molar-incisor hipomineralization y criterios utilizados para el diagnóstico. Los datos se tabularon con Microsoft Excel para Windows y se presentaron con estadísticas descriptivas. Resultados: Se encontraron un total de 484 artículos y 57 se incluyeron en el estudio. La mayoría de los estudios se llevaron a cabo en Europa (35%), y el 31.6% de los estudios mencionaron utilizar una muestra probabilística. El número de participantes en el estudio varió de 99 para un estudio en Brasil a 3,591 en Kenia. La edad más frecuente fue 8 años, mientras que el tipo de estudio predominante era transversal (91.2%). La prevalencia varió entre 0.4% y 37.3% y la mayoría de los estudios (73.6%) emplearon los criterios de la European Academy of Pediatric Dentistry para el diagnóstico de MIH. Conclusion: Hay gran variabilidad en la prevalencia en diferentes países, probablemente debido al uso de diferentes criterios diagnósticos y a diferentes grupos de edad y geográfica.

Keywords: Dental enamel hypoplasia; molar incisor hypomineralization; child.
INTRODUCTION.

Molar-Incisor Hypomineralization (MIH) is a qualitative defect in tooth enamel development. In general, it affects from one to four first permanent molars, and may also be present in permanent incisors. The etiological factors of MIH remain uncertain, but prenatal, perinatal and postnatal factors, genetic and environmental conditions are related to this condition. Diseases such as acute otitis media, chicken pox and respiratory illnesses during the first year of life, as well as prolonged use of antibiotics and exposure to dioxins due to prolonged breastfeeding are some of the associated factors described in literature.

MIH is a result of an injury to enamel-forming cells during calcification or maturation of the dental organ and is characterized by the opaque appearance of the enamel. It presents as well-delimited spots varying in color from white, yellow to brown. Due to the porous enamel, the affected teeth are more prone to frature and, in more severe cases, may present unusual cavities and extensive disintegration, leading to large bacterial biofilm deposits, responsible for increasing susceptibility of teeth with MIH to dental caries. Hypersensitivity is another characteristic, which makes tooth brushing difficult as well as dental treatment due to the difficulty in achieving local anesthesia of the affected tooth.

Therefore, teeth with MIH require recurrent interventions due to continuous disintegration from masticatory forces and difficulty in the adhesion of restorative materials to the defective enamel. In severe cases with major coronary destruction, extraction of affected teeth is recommended in association with the use of orthodontic devices to manage the edentulous space.

Children who suffer from MIH demonstrate behavior management problems and are at increased risk of developing fear and anxiety. Thus, this condition has a negative impact on the patient’s quality of life and represents a challenge for dentists.

In the dental literature, there is a great variation regarding the occurrence of MIH in different countries. European countries account for the largest number of studies, reporting distinct prevalences such as 7% and 15.4%. This variation also can be found in studies performed in other continents.

The prevalence rate varies widely among populations due to the age of subjects examined (five to six years, seven to nine years, eight to twelve years, and six to thirteen years), due to methods of recording information, methodological differences (transversal versus cohort studies) and the criteria used for the diagnosis (EAPD, Kemoli or another set of criteria developed by some study authors themselves). Therefore, this study aimed to analyze, through a bibliographic review, the prevalence of molar-incisor hypomineralization and the methodological criteria adopted for its diagnosis.

MATERIALS AND METHODS.

Literature Search

This is a bibliographical research conducted through the analysis of articles indexed until October 2017 in the PubMed (US National Library of Medicine National Institutes of Health), Web of Science (Clarivate Analytics) and Scopus (Elsevier) databases. Medical Subject Headings (MESH) used were ”Dental Enamel Hypoplasia” and ”Molar Incisor Hypomineralization”. The PRISMA guidelines were followed (Available at: http://prisma-statement.org/).

The included studies met the following eligibility criteria: observational (cross-sectional, cohort and case-control) and experimental studies (clinical trials); studies that presented data regarding the prevalence or raw data that could be used to calculate the prevalence of MIH, and articles describing criteria used for the diagnosis of the condition. Studies that reported only hypomineralization in deciduous molars were excluded.

The analysis of articles was carried out by two reviewers.
(LF and ICCL), who collected information independently. At the end of the analysis, the collected information was compared and discrepancies were discussed. In cases of disagreements, a third researcher (CRBA) made the final decision to include or exclude the article.

The following information was collected: author, year of publication, workplace location (continent and country), use of probability sampling, sample number, age of participants, type of study, prevalence of molar-incisor hypomineralization and diagnosis criterion. Data were tabulated using Microsoft Excel 2016 for Windows (Microsoft Press, Redmond, WA, USA) and presented using descriptive statistics.

RESULTS.

Overall, 484 articles were found, of which 226 from PubMed, 163 from Web of Science and 95 from Scopus. After duplicate articles were removed, 240 articles remained, of which 61 were selected and carefully examined. Of these, 57 were selected for further analysis and 4 were excluded as they did not meet the eligibility criteria. (Figure 1)

Regarding the geographic distribution, most articles were carried out by researchers in Europe (35.1%) and Asia (29.8%), followed by those in the Americas (26.3%) and in Africa (8.8%). The number of participants ranged from 99 Brazilian children to 3,591 Kenyan individuals. Among the articles, 31.6% mentioned having performed sample calculation in their methodology. The most frequent age was 8 years (77.2%), ranging from 0 to 19 years. Regarding the type of study, the most common was the cross-sectional design (91.2%). The prevalence of MIH ranged from 0.48% in Indian children to 37.3% in Danish children. Most articles (73.6%) used the guidelines proposed by the European Academy of Pediatric Dentistry as a diagnostic criterion for MIH.

Table 1 shows the distribution of articles from the European continent. There was a predominance of cross-sectional studies (85%), involving children and adolescents from 0 to 16 years. The prevalence of MIH ranged from 5.9% to 37.3%. With regard to the Asian continent, almost half of articles were conducted in India (41.1%) and included children and adolescents aged 6-16 years. (Table 2)

The highest prevalence found was 27.7% in a study conducted in Thailand. Similarly, most articles adopted the criteria proposed by the European Academy of Pediatric Dentistry (82.3%). In the Americas, 73.3% of articles were conducted in Brazil (Table 3), involving individuals aged 5-17 years. The prevalence varied from 2.5%, considering the Modified Enamel Developmental Defect Index (DDE) to 33.2%, using the criteria of the European Academy of Pediatric Dentistry.

Only 8.8% of articles found were conducted in Africa and they presented the lowest variation in prevalence, from 2.9% to 13.7%. (Table 4)

Figure 1. Flowchart of selection procedure for the articles included in the review.
Table 1. Distribution of studies conducted in Europe.

| Author          | Year | Country  | Design | Probability Sampling | Sample (n) | Age (Years) | Prevalence | Diagnostic Criteria |
|-----------------|------|----------|--------|----------------------|------------|-------------|------------|---------------------|
| Koch et al.     | 1987 | Sweden   | CS     | No                   | 2,226      | 8-10        | 15.4%      | Author’s Criterion  |
| Jâlevik et al.  | 2001 | Sweden   | CS     | No                   | 516        | 7 to 9      | 18.4%      | DDE Modified       |
| Jasulaityte et al. | 2007 | Lithuania| CS     | No                   | 1,277      | 7 to 9      | 9.7%       | EAPD               |
| Preusser et al. | 2007 | Germany  | CS     | No                   | 1,022      | 6 to 12     | 5.9%       | Other              |
| Wogelius et al. | 2008 | Denmark  | CS     | Yes                  | 745        | 6 to 8      | 37.3%      | EAPD               |
| Laise et al.    | 2009 | Finland  | CT     | No                   | 141        | 10.7*       | 16.3%      | Other              |
| Condó et al.    | 2012 | Italy    | CS     | No                   | 1,500      | 0 to 15     | 7.3%       | Author’s Criterion  |
| Elfrink et al.  | 2012 | Netherlands | CH  | No                   | 2,327      | 5 to 6      | 8.7%       | EAPD               |
| Kühnisch et al. | 2012 | Germany  | CH     | Yes                  | 693        | 10          | 14.7%      | EAPD               |
| Garcia-Margarit et al. | 2014 | Spain    | CS     | Yes                  | 840        | 8           | 21.7%      | EAPD               |
| Janković et al. | 2014 | Serbia   | CS     | No                   | 141        | 8           | 12.7%      | EAPD               |
| Wuollet et al.  | 2014 | Finland  | CS     | No                   | 818        | 7 to 13     | 17.1%      | EAPD               |
| Kevrekidou et al. | 2015 | Greece   | CS     | Yes                  | 2,335      | 8 to 14     | 21.3%      | EAPD               |
| Kühnisch et al. | 2015 | Germany  | CS     | Yes                  | 1,048      | 10          | 13.6%      | EAPD               |
| Opydo-Szymaczek et al. | 2015 | Poland   | CS     | No                   | 470        | 6 to 8      | 8.1%       | DDE Modified       |
| Negre-Barber et al. | 2016 | Spain    | CS     | Yes                  | 414        | 8 to 9      | 24.1%      | EAPD               |
| Schmalfuss et al. | 2016 | Norway   | CS     | No                   | 794        | 16          | 13.9%      | EAPD               |
| Van Der Tas et al. | 2016 | Netherlands | CS  | No                   | 2,370      | 6           | 8.5%       | EAPD               |
| Wuollet et al.  | 2016 | Finland  | CS     | No                   | 287        | 7 to 12     | 11.5%      | EAPD               |
| Buchgraber et al. | 2017 | Austria  | CS     | Yes                  | 1,111      | 6 to 12     | 7%         | EAPD               |

CS: Cross-sectional. CT: Clinical Trial. CH: Cohort. *: Average age. EAPD: European Academy of Paediatric Dentistry. DDE: Enamel Developmental Defect Index.

Table 2. Distribution of studies conducted in Asia.

| Author          | Year | Country  | Design | Probability Sampling | Sample (n) | Age (Years) | Prevalence | Diagnostic Criteria |
|-----------------|------|----------|--------|----------------------|------------|-------------|------------|---------------------|
| Cho et al.      | 2008 | China    | CS     | No                   | 2,635      | 11 to 14    | 2.8%       | Author’s Criterion  |
| Kuscu et al.    | 2009 | Turkey   | CS     | No                   | 153        | 7 to 10     | 9.1%       | EAPD               |
| Ahmadi et al.   | 2012 | Iran     | CS     | No                   | 433        | 7 to 9      | 12.7%      | DDE Modified       |
| Allazzam et al. | 2014 | Saudi Arabia | CS  | No                   | 267        | 8 to 12     | 8.6%       | EAPD               |
| Bhaskar et al.  | 2014 | India    | CS     | Yes                  | 1,173      | 8 to 13     | 9.5%       | EAPD               |
| Pitiphat et al. | 2014 | Thailand | CS     | No                   | 282        | 7 to 8      | 27.7%      | EAPD               |
| Pitiphat et al. | 2014 | Thailand | CS     | No                   | 484        | 6 to 7      | 19.6%      | EAPD               |
| Shrestha et al. | 2014 | Nepal    | CS     | No                   | 747        | 7 to 12     | 13.6%      | EAPD               |
| Hussein et al.  | 2015 | Malaysia | CS     | No                   | 154        | 7 to 12     | 16.9%      | EAPD               |
| Kirthiga et al. | 2015 | India    | CS     | No                   | 2,000      | 11 to 16    | 8.9%       | EAPD               |
| Ng et al.       | 2015 | Singapore| CS     | No                   | 1,083      | 7.7*        | 12.5%      | EAPD               |
| Mishra et al.   | 2016 | India    | CS     | No                   | 1,369      | 8 to 12     | 13.9%      | EAPD               |
| Mittalet et al. | 2016 | India    | CS     | No                   | 1,726      | 12 to 16    | 9.8%       | EAPD               |
| Mittal et al.   | 2016 | India    | CS     | No                   | 886        | 6 to 12     | 7.1%       | EAPD               |
| Salem et al.    | 2016 | Iran     | CS     | No                   | 553        | 6 to 13     | 18.4%      | EAPD               |
| Subramaniam et al. | 2016 | India    | CS     | Yes                  | 2,500      | 7 to 9      | 0.4%       | EAPD               |
| Yannam et al.   | 2016 | India    | CS     | Yes                  | 2,864      | 8 to 12     | 9.6%       | EAPD               |

CS: Cross-sectional. CT: Clinical Trial. CH: Cohort. *: Average age. EAPD: European Academy of Paediatric Dentistry. DDE: Enamel Developmental Defect Index.
DISCUSSION.

In recent years, MIH has become a condition that has attracted the interest of researchers, who have published their findings. This is illustrated by a single study published in 2006 making reference to the prevalence of MIH, and ten years later, this number had increased vertiginously, with a total of 14 publications in 2016. It could be suggested that this growth occurred due to the similarity of MIH with other recurrent oral pathologies, especially dental caries, and to its negative impact on oral health and consequently on the quality of life of children and adolescents.

MIH can be considered a public health problem, due to the prevalence of this disease in the population, the implications of this condition in general health, social relationships and vulnerability. The scientific community is still far from recognizing the real prevalence of MIH due to the great variability among surveys, ranging from low prevalence results to studies that identified that more than one third of the studied population had such condition.

Most studies were conducted in Europe (35%). That the first report of MIH came from Sweden as well as the greater concentration of resources and investments in research in such geographical area can justify this predominance of studies from Europe. The results of studies that are concentrated in specific regions...
cannot be extrapolated to other countries due to regional differences. Among studies conducted in the Americas, 73.3% correspond to Brazilian studies. In Brazil, the highest prevalence of MIH found was 33.2% in São Paulo among 10-year-old students.

The wide variation in prevalence reflects the methodological differences of the studies. Divergences in sample size, diagnostic criteria and age groups may contribute to the lack of an uniform prevalence.

In the selected studies, there are wide-ranging age groups with participants ranging from 1 to 19 years or from 0 to 15 years for example. This factor may underestimate the prevalence, since when older children are evaluated, occlusal wear and restorations may hide developmental defects. In addition, the condition can be masked by the presence of dental caries and this fact is not mentioned by the authors.

With regard to the sample number, there is a variation from 99 to 3,591 individuals; however, few studies have used probability sampling.

To estimate the prevalence of a condition in studies, it is necessary to have a minimum number of children randomly selected. In studies with a smaller number of children, the prevalence may be higher or lower than estimated.

The etiology of MIH is unclear, with several possibilities for etiological factors such as gestation problems, complications during delivery, diseases of early childhood and use of antibiotics. These conditions increase the prevalence of MIH, as can be assessed in studies of HIV patients, monozygotic twins and individuals who have used antibiotics in the first year of life.

Almost all studies have a cross-sectional design. This is a useful tool for the description of population characteristics and the identification of risk groups, but they are methodologically fragile, since they determine the exposure and the disease simultaneously, so that no cause and effect relationships can be established. Thus, this type of studies are useful to suggest the presence of associations, enabling the generation of hypotheses, without, however, testing them.

Regarding the diagnostic criteria, in 2003, the European Academy of Pediatric Dentistry defined the characteristics of MIH and created a method for the examination of the first permanent molars and incisors. This body recommends studying MIH in 8-year-old children because incisors and first molars have already erupted by then, facilitating the detection of the defect before being covered up by physiological wear or other pathologies. However, some studies have chosen other age groups to verify possible signs of MIH in other teeth, including second molars, premolars and canine teeth.

The European Academy of Pediatric Dentistry established five criteria to be considered in epidemiological studies: absence or presence of demarcated opacities; post-eruptive fracture; atypical restoration; extraction due to MIH and failure in the eruption of a molar or incisor.

However, even after establishing guidelines for the diagnosis of this condition, there are still studies adopting old criteria or following their own methods, making it difficult to compare results among surveys.

In view of these findings, with the aim of carrying out studies that allow their replication and the comparison of results, further work should be carried out with representative groups of the population, using a probability sampling method, which allows for the extrapolating of results and guaranteeing the calculation of a reliable prevalence value.

In addition, the standardization of diagnostic criteria is of paramount importance so that conditions may be compared and assessed. The use of the method proposed by the European Academy of Pediatric Dentistry is recommended, as it is the most used among studies and the most consolidated in the relevant literature.

Current studies have important implications for the planning of public policies and aim to draw the attention of pediatric dentists to the identification of MIH, as well as the treatment and control of its etiology. In clinical matters, dentists need to consider the specific condition of each tooth and the needs and expectations of patients when deciding how to manage MIH, prioritizing whenever possible preventive and minimally invasive or conservative treatments.
CONCLUSION.

The prevalence of MIH presents great variability due to the use of different diagnostic criteria, age groups and geographic variation in the analyzed surveys, which makes the comparison results difficult.

Epidemiological studies to assess the prevalence of MIH should be carried out with similar methodological criteria, allowing for the extrapolation of results to other regions.

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