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HIPOMINERALIZAÇÃO MOLAR INCISIVO: ASSOCIAÇÃO COM CÁRIE DENTÁRIA E O IMPACTO NA QUALIDADE DE VIDA

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Dissertação apresentada ao Programa de Pós-graduação em Odontologia da Universidade Federal do Rio Grande do Sul como requisito parcial para a obtenção do título de Mestre em Odontologia, Área de Concentração em Clínica Odontológica/Odontopediatria.

Orientador: Prof. Dr. Luciano Casagrande

Porto Alegre

2020

"Só é verdadeiramente digno
da liberdade, bem como da vida, aquele
que se empenha em conquistá-la."
Johann Goethe

RESUMO

A presente dissertação de mestrado é composta por dois artigos científicos. O primeiro deles, "*Molar-incisor hypomineralization and dental caries: A hierarchical approach in a populational-based study*" avaliou a associação da hipomineralização molar incisivo (HMI) com cárie dentária. Para investigar essa associação, realizou-se um levantamento epidemiológico em um município do sul do Brasil, entre os meses de abril e dezembro de 2019. Foi feita amostragem por conglomerado, por meio do sorteio das turmas das escolas públicas do município. Como critério de inclusão, foram consideradas potencialmente elegíveis todas as crianças que tinham os quatro primeiros molares permanentes erupcionados. As variáveis HMI (conforme os critérios propostos pela Academia Europeia de Odontopediatria), cárie dentária (de acordo com o índice CPOD) e gengivite foram coletadas. Além das variáveis clínicas, foi enviado aos pais um questionário autoaplicável com perguntas sobre fatores socioeconômicos. Para análise dos dados, utilizou-se Regressão de Poisson com abordagem hierárquica. Ao total, 513 crianças foram incluídas no presente estudo. A prevalência de HMI foi de 19%. A média de idade foi de 11 anos. A HMI esteve associada à cárie dentária. Crianças cujos pais tinham mais anos de estudo e renda familiar mensal maior apresentaram menores índices CPOD. A variável chefe da família também apresentou associação significativa com cárie. Considerando os fatores distais e proximais, a HMI, juntamente com os fatores socioeconômicos, esteve associada à cárie dentária. O segundo artigo, intitulado "*Molar incisor hypomineralization and oral health-related quality of life: A systematic review and meta-analysis*", avaliou a influência da HMI na qualidade de vida associada à saúde bucal. Foi definida uma questão de pesquisa e realizada a busca nas bases de dados PubMed/MEDLINE, Scopus, Trip, Web of Sciense, Embase e Lilacs, sem restrição de ano de publicação e idioma. A presente revisão foi conduzida de acordo com as diretrizes propostas pelo PRISMA e registrada no Prospero. Em relação aos critérios de elegibilidade, incluíram-se estudos observacionais que avaliaram a associação entre HMI e qualidade de vida, e excluídos os estudos que não utilizaram ferramentas validadas ou estudos que não possuíam grupo controle. Dois revisores selecionaram independentemente os estudos e extraíram os dados. O risco de viés dos estudos incluídos foi avaliado por meio da ferramenta Newcastle-Ottawa adaptada para estudos observacionais. Realizaram-se 2 meta-análises usando modelo de efeitos aleatórios, uma considerando o escore global e outra considerando domínios específicos. De um total de 1.771 estudos potencialmente elegíveis, 11 foram selecionados para leitura na íntegra, 5 foram incluídos na revisão sistemática e 3 estudos foram incluídos na meta-análise. O risco de viés variou de moderado a baixo. Crianças com HMI tiveram uma prevalência 27% maior de impacto negativo sobre qualidade de vida associada à saúde bucal; no entanto, não houve diferença significativa (RP 1.27; IC 95% 0.68 – 2.36) no escore global, nem nos domínios específicos. Dessa forma, a qualidade de vida parece não ser afetada pela HMI.

ABSTRACT

The present master dissertation is composed by two scientific articles. The first of them, "Molar-incisor hypomineralization and dental caries: A hierarchical approach in a populational-based study" evaluated the association of molar incisor hypomineralization (MIH) with dental caries. To investigate this association, an epidemiological survey was carried out in a city in the south of Brazil, between April and December 2019. Sampling was carried out by conglomerate, through the drawing of classes from public schools. As an inclusion criterion, all children who had erupted four first permanent molars were considered potentially eligible. The variables MIH (according to the criteria proposed by the European Academy of Pediatric Dentistry), dental caries, (according to the DMFT index) and gingivitis were collected. In addition to the clinical variables, a self-administered questionnaire with questions related to socioeconomic factors was sent to the parents. For data analysis, was used Poisson regression with a hierarchical approach. In total, 513 children were included in the present study. The prevalence of MIH was 19%. The average age was 11 years. MIH was associated with dental caries. Children whose parents had more years of schooling and higher monthly family income had lower DMFT rates. The householder variable also showed a significant association with dental caries. Considering the distal and proximal factors, MIH, together with socioeconomic factors, was associated with dental caries. The second article entitled "Molar incisor hypomineralization and oral health-related quality of life: A systematic review and meta-analysis" assessed the influence of MIH on the quality of life associated with oral health. A research question was defined and the search was performed in the PubMed / MEDLINE, Scopus, Trip, Web of Sciense, Embase and Lilacs databases, with no restriction on year of publication and language. This review was conducted in accordance with the guidelines proposed by PRISMA and registered with Prospero. Regarding the eligibility criteria, observational studies that evaluated the association between MIH and quality of life were included, and studies that did not use validated tools or studies that did not have a control group were excluded. Two reviewers independently selected the studies and extracted the data. The risk of bias of the included studies was assessed using the Newcastle-Ottawa tool adapted for observational studies. Two meta-analysis were performed using a random effects model, one considering the global score and the other considering specific domains. Of a total of 1.771 potentially eligible studies, 11 were selected for full reading, 5 were included in the systematic review and 3 studies were included in the meta-analysis. The risk of bias varied from moderate to low. Children with MIH had a 27% higher prevalence of negative impact on quality of life associated with oral health; however, there was no significant difference (PR 1.27; 95% CI 0.68 – 2.36) in the global score, nor in the specific domains. Thus, the quality of life does not seem to be affected by MIH.

SUMÁRIO

1. INTRODUÇÃO

A Hipomineralização Molar Incisivo (HMI) é definida como um defeito qualitativo de desenvolvimento do esmalte dentário, de origem sistêmica, que afeta os primeiros molares permanentes, podendo também, afetar os incisivos permantes. Esse defeito de esmalte está associado a uma desordem que ocorre durante a fase de mineralização da amelogênese (WEERHEIJM; JÄLEVIK; ALALUUSUA, 2001). A HMI se apresenta, clinicamente, como uma opacidade demarcada com bordas distintas do esmalte normal adjancente, com coloração que varia do branco-creme ao amarelo-acastanhado, geralmente com manifestação assimétrica. Essas opacidades no esmalte afetado, em casos mais severos, podem romper em razão das forças mastigatórias, gerando fraturas pós-irruptivas (WEERHEIJM, 2003).

A Academia Europeia de Odontopediatria (EAPD) padronizou, em 2003, os critérios para diagnóstico da HMI, considerando a presença de opacidade demarcada, quebra de esmalte pós-eruptiva, presença de restauração atípica e extração de molar devido a HMI (WEERHEIJM, 2003). Mesmo após a definição destes critérios, as taxas de prevalência têm apresentado uma variação significativa. Os estudos variam entre 2.9% a 40.2%, de acordo com cada região (DE DEUS MOURA DE LIMA *et al.*, 2015; GARCIA-MARGARIT *et al.*, 2014; JURLINA *et al.*, 2020; SOVIERO *et al.*, 2009; THAKUR *et al.*, 2020; TOURINO *et al.*, 2016; YI *et al.*, 2020). A prevalência mundial reportada é de 14.2% (ZHAO *et al.*, 2018).

Incialmente, a HMI foi definida para molares e incisivos permanentes. Em 2008, o mesmo defeito foi descrito para dentes decíduos (ELFRINK *et al.*, 2008), sendo considerado presente quando afeta pelo menos um dos segundos molares decíduos, podendo também, afetar caninos decíduos. Estudos têm mostrado que a presença de opacidades demarcadas na dentição decídua pode ser preditora para HMI na dentição permanente (DA SILVA FIGUEIREDO SÉ *et al.*, 2017; GAROT *et al.*, 2018). A fase de mineralização do esmalte dos segundos molares decíduos e primeiros molares permanentes se sobropõe, sendo que se um fator de risco ocorreu durante este período de sobreposição, a hipomineralização pode ocorrer simultaneamente na dentição primária e permanente (ELFRINK *et al.*, 2012).

A etiologia da hipomineralização ainda não está completamente elucidada. A maioria dos estudos reportam fatores de risco que ocorrem desde o perído gestacional até os primeiros anos de vida (FATTURI *et al.*, 2019), considerando como uma alteração de origem multifatorial. Uma revisão sistemática investigou fatores pré-natais, peri-natais e pós-natais, encontrando como fatores de risco stress e doença materna durante a gestação, tipo e complicações no parto e febre e doenças respiratórias durante a primeira infância (FATTURI *et al.*, 2019). Como muitos fatores de exposição não acontecem de forma única, é difícil isolar um fator específico e determinar se está diretamente associado com HMI. Além disso, os estudos sobre a etiologia são observacionais retrospectivos, sujeitos ao viés recordatório, portanto, os achados devem ser interpretados com cautela. Outros trabalhos exploram a associação com fatores epigenéticos (TEIXEIRA *et al.*, 2018). Autores também demonstraram que polimorfismos em genes relacionados à resposta imune podem interferir na amelogênese por meio da modulação dos genes envolvidos na maturação do esmalte (BUSSANELI *et al.*, 2019).

A maioria dos estudos têm utilizado o critério da EAPD para reportar HMI. Apesar deste critério estar definido, os estudos diferem quanto à classificação da severidade das lesões. Alguns estudos reportam as lesões como leve (opacidades sem necessidade de tratamento), moderada (lesões em esmalte) ou severa (lesões que afetam esmalte e dentina, restauração atípica, e extração por HMI) (DANTAS-NETA *et al.*, 2018). Outros autores classificam em leve (opacidades demarcadas) e severa (fraturas pós-eruptivas, restauração atípica e e extração atribuída à HMI) (PORTELLA *et al.*, 2019). A heterogeneidade na classificação da severidade das lesões dificulta comparações diretas entre os estudos, além de impedir análises globais em estudos de revisão.

A HMI tem sido associada como fator de risco para cárie (GROSSI; CABRAL; LEAL, 2017). Uma revisão sistemática avaliou essa relação e embora tenha encontrado associação entre HMI e cárie, os estudos incluídos apresentaram limitações metodológicas. Os autores também reportam a necessidade de estudos robustos que investiguem essa associação (AMERICANO *et al.*, 2017). Além disso, pacientes com HMI apresentam diversas limitaçoes envolvidas na terapêutica devido à hipersensibilidade, ansiedade, dificuldades com anestesia e falha das restaurações (GHANIM *et al.*, 2017), o que pode afetar a saúde oral e qualidade de vida dos pacientes (PORTELLA *et al.*, 2019).

Adicionalmente, a qualidade de vida associada à saúde bucal (QVRSB) tem sido investigada em pacientes com HMI (DANTAS-NETA *et al.*, 2016; PORTELLA *et al.*, 2019). A QVRSB é um constructo multidimensional, que reflete o conforto das pessoas ao comer e se envolver em interações sociais, sua autoestima e satisfação com a saúde bucal (LOCKER; ALLEN, 2007). A maioria dos estudos, embora tenha achado resultados conflitantes, encontra impacto no domínio específico saúde oral (GUTIÉRREZ *et al.*, 2019; PORTELLA *et al.*, 2019). Em função da falta de consenso, a compilação de resultados poderia mensurar a associação entre HMI e QVRSB, a fim de compreender como a qualidade de vida é afetada pela HMI.

Nesse contexto, no presente estudo, serão apresentados dois artigos relacionados a temática da HMI. O primeiro, intitulado "*Molar-incisor hypomineralization and dental caries: A hierarchical approach in a populational-based study*" que buscou identificar a associação entre HMI e cárie dentária por meio de uma abordagem hierárquica. E por fim, o segundo artigo "*Molar incisor hypomineralization and oral health-related quality of life: A systematic review and meta-analysis*" que avaliou a relação da HMI e a qualidade de vida associada a saúde bucal, por meio de uma revisão sistemática.

2. ARTIGO 1

Molar-incisor hypomineralization and dental caries: A hierarchical approach in a populational-based study

Este artigo será submetido ao periódico *Caries Research* (ISSN 1421-976X) – Fator de Impacto: 2.186 (2019); Qualis CAPES A1. As normas para publicação estão descritas no ANEXO B.

Original Research Report

Caries Research

Molar-incisor hypomineralization and dental caries: A hierarchical approach in a populational-based study

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Abstract

The last couple of decades has seen an increasing interest in molar-incisor hypomineralization (MIH) studies. Hypomineralized defects can have several consequences such as hypersensitivity, increased plaque accumulation, and consequently higher caries risk. This cross-sectional study aimed to investigate the MIH prevalence and the association with dental caries in schoolchildren from a city in southern Brazil. A random cluster sample of 513 schoolchildren enrolled in public schools was selected. Clinical examinations were performed considering MIH (according to the European Academy of Pediatric Dentistry criteria), dental caries (DMF-S) and gingivitis. Socioeconomic, demographic and behavior variables were accessed by a specific questionnaire which was sent to the child's caregiver. Prevalence ratios (PR) were estimated using Poisson regression analysis with robust variance through a hierarchical approach ($p<0.05$). MIH and caries prevalence was 19.7% and 31.6%, respectively. The mean schoolchildren age was 11.6 (±1.9) years. The caries prevalence was higher for children with MIH (PR 1.39; 95% CI 1.05 – 1.85). Children of more than 12 years of age, whose families received funds from social programs (PR 1.97 95% CI 1.47 – 2.64), and children who did not have their mother or father as the head of the family (PR 1.56 95% CI 1.06 – 2.30) presented a higher prevalence of dental caries. Our findings suggest that schoolchildren with MIH are more likely to develop dental caries.

Key words: molar-incisor hypomineralization, dental caries, dental enamel hypoplasia.

Introduction

Molar-incisor hypomineralization (MIH) is defined as a qualitative defect in the enamel development which affects the first permanent molars, and can also affect permanent incisors[1]. Several studies have evaluated the predictive factors of hypomineralization as a multifactorial defect associated with gestational factors, diseases in early childhood[2] and genetic factors[3].

A systematic review found that the global prevalence of MIH is 14.2%, and ranged from 0.5% to 40.2% between countries[4]. Different diagnostic criteria and the heterogeneity of children's age contribute to this difference. The MIH prevalence in Brazil, in the same way as the global prevalence, also presents significant variability[5–7].

Hypomineralization is clinically characterized by demarcated opacities which vary in color from white to brown, showing clear and distinct borders with the sound enamel[1]. Hypomineralized enamel is more porous than normal enamel[8]. Lower enamel strength can lead to post-eruptive fractures which predispose to plaque accumulation and caries. Plaque accumulation is also favored by lack of proper biofilm control due to hypersensitivity of the affected teeth[9]. It has been evidenced that there is a significant association between MIH and caries. Both the DMF index and caries prevalence were higher in children with MIH than in children without MIH[10]. However, due the low quality of the included studies, the literature still lacks well-designed studies which robustly investigate this association[10].

Considering the relevance to increase the knowledge on the clinical impact of MIH defects on oral health, the aim of the present study was to investigate the MIH prevalence and the association between MIH and dental caries in schoolchildren of a city in southern Brazil. The conceptual hypothesis is that children with MIH were more likely to develop dental caries.

Material and Methods

This study was reported according to the "Strengthening the Reporting of Observational Studies in Epidemiology" (STROBE) guidelines.

Ethical Considerations

The study was conducted in accordance with the Ethical Standards of the Resolution on the National Council on Ethics in Research (no. 466/2012 and no. 510/2016) and the Helsinki Declaration (2008). The local Research Ethics Committee approved the research protocol (no. 2.632.694). Parents or guardians signed a written informed consent form and schoolchildren signed the assent form.

Study design, sample size, and participants

A cross-sectional study was conducted with schoolchildren from the 1st to the 9th year enrolled in public elementary schools in the city of Estância Velha. The city is located in the South region of Brazil (Rio Grande do Sul state), and has a population of 42,574 inhabitants (IBGE, 2010), presenting a human development index of 0.808[11]. The city has 19 elementary schools with 6,467 children aged between 5 and 14 years (IBGE, 2010).

The sample size was calculated using Power and Sample Size Software, considering the difference between the dental caries and MIH averages of a previous study[12]. A significance level of 5% and power of 80% were used, requiring at least 472 participants. Considering eventual losses or incomplete data, 10% was added to the sample size, resulting in 519 participants.

The sampling process used a cluster randomization; first, the schools were selected, followed by the class, while the classes were randomly selected by respecting the proportion of students who were enrolled in each school (www.randomizer.org). Schoolchildren had to present all permanent incisors and erupted first permanent molars to be included in study, and to not be using any fixed orthodontic appliances at the evaluation time.

Data Collection

Data collection occurred in the period from April 2019 to December 2019. All exams were performed at schools and followed the international criteria standardized by the World Health Organization for oral health surveys (WHO, 2013)[13]. The schoolchildren received toothbrushing instructions by a dental undergraduate student before the clinical examinations. Then, the schoolchildren sat on a chair and leaned back, resting the back of their heads on the examiner's lap. The dental examination was realized by two previously-trained and calibrated operators (A.S.A. and L.I.L.B.) assisted by

dental undergraduate students. A flat dental mirror (Duflex, SS White, Brazil), a ball-point probe (WHO-621, Trinity, Brazil), and gauze swab were used under artificial lighting (desk lamp model Pelican, Startec127V, Brazil) for the dental examination. All the teeth were examined after being dried by a gauze swab.

The clinical examination registered dental caries according to the decayed, missing, and filled teeth index (DMF-T)[13]. In addition, the schoolchildren were diagnosed with MIH (categorized as present or absent) when at least one first permanent molar was affected (presented a marked opacity, post-eruptive fracture, the presence of atypical restoration, or exodontia which was attributable to MIH), with or without the involvement of the permanent incisors, according to the EAPD criteria[9]. Gingivitis was also assessed and considered as present when there was 10% or more bleeding sites[14].

Demographic, socioeconomic and behavior data were collected by a self-administered questionnaire specifically developed for this study containing the following information: caregiver education, receipt of social program (family allowance), family structure, the degree of kinship to the child, date of birth and age of the child, and number of dental visits in the last semester. The questionnaire was answered by the child's caregiver. Age was dichotomized by the median. The caregiver's education level was collected in years and categorized in < 8 and ≥ 8 years of formal education. The Family Allowance program was used as a family monthly income proxy.

Calibration exercise

The researchers (A.S.A., L.I.L.B.) were trained and calibrated prior to starting the study. In the first moment, a 2-hour lecture and theoretical discussion about data collection for caries diagnosis, criteria and MIH diagnosis was performed. The possible differential diagnoses for MIH, such as amelogenesis, fluorosis and enamel hypoplasia were discussed. In the second moment, the researchers were tested for diagnosis using clinical images. Lastly (for calibration purpose), 10 patients under treatment at the University Dental Clinic (Children and Youth Dental Clinic - Federal University of Rio Grande do Sul, Porto Alegre – Brazil) were examined (under the same conditions as mentioned above) by the researchers and compared with the exams performed by an experienced specialist in Pediatric Dentistry (Professor of Pediatric Dentistry). Cohen's kappa coefficient inter-examiner calibration was 0.90 (A.S.A.) and 0.86 (L.I.L.B.) for

MIH, 0.89 (A.S.A.) and 0.91 (L.I.L.B.) for dental caries. The researchers were calibrated again when 50% of the sample was reached, and reproducibility was considered adequate.

Pilot Study

A total of 30 schoolchildren from the largest school who did not participate in the study were selected by convenience sampling to participate in the pilot study. The pilot study confirmed the original design, with it not being necessary to make any modifications to the study.

Data Analysis

Data analysis was performed using the Stata 14.0 program (Stata Corp., College Station, TX, USA). The presence of dental caries was set as the main outcome of this study. Descriptive statistics were used to describe the demographic, socioeconomic and clinical characteristics of the sample. Multivariate Poisson regression analysis with robust variance were performed to evaluate the association among predictor variables in the presence of dental caries, considering a fixed effect and random intercept. An adjusted analysis following a hierarchical approach was performed[15], considering model 1 ("empty model"); model 2 included demographic and socioeconomic characteristics; model 3 was composed of model 2 plus clinical variables. Model fit was assessed according to deviance (-2loglikelihood). Variables with $p<0.20$ in the unadjusted analyses were included in the adjusted model. Age and gender variables were included by theoretical criteria[15]. The results are presented in prevalence ratios (PR) and a respective 95% confidence interval (95% CI).

Results

A total of 560 schoolchildren were invited to participate in the study and 513 agreed to participate (91.6%). No participants were excluded. The average age of the students was 11.6 (±1.9) years. Table 1 shows the sample characteristics. The prevalence of MIH and dental caries was 19.7% and 31.6%, respectively. Based on clinical signs of MIH, the most frequent were demarcated opacities (71.3%), following by post-eruptive fractures (14.8%) and atypical restorations (13.9%).

The unadjusted Poisson regression analysis is shown in Table 2. Schoolchildren of more than 12 years of age, children whose families received funds from social

programs and children who did not have their mother or father as head of the family (the family nucleus is not formed by the main guardian – father or mother) were associated to dental caries. Children with MIH presented more prevalence of dental caries (PR: 1.42 95% CI: 1.08 – 1.88).

Table 3 presents the adjusted regression models. After the adjustments, the variables which remained significantly associated with the outcome were age, social program, main head of the family, and MIH. In model 2, schoolchildren whose family received social program and children who did not have their mother or father as head of the family presented more prevalence of dental caries. In model 3, presence of MIH was associated with dental caries (PR: 1.39 95% CI: 1.05 – 1.85).

Discussion

The presented study investigated the association between MIH and dental caries in schoolchildren. The hypothesis that schoolchildren with MIH were more likely to develop dental caries was confirmed. A hierarchical approach for modeling the variables was used in the adjusted analysis, as it was possible to avoid underestimating a distal factor on the outcome using this analysis[16]. To the best of our knowledge, this is the first study which investigated this association as well as MIH prevalence in a region in the South of Brazil. Beyond being associated with MIH, dental caries also influenced by demographic and socioeconomic factors.

The association between MIH and dental caries has been studied recently [Americano et al., 2017; Grossi et al., 2017]. The hypomineralized enamel surface is more porous compared to sound enamel [18], which contributes to greater biofilm accumulation, thus allowing demineralization[19]. In addition, teeth with MIH may present hypersensitivity[20]. It has been speculated that the porosity in the enamel enables bacteria entrance into the dentinal tubules, which can cause pulp inflammation[21]. The consequence of hypersensitivity leads to important aspects such as difficulty in effective local anesthesia and the lack of brushing, with the latter being capable of increasing caries risk[20], which in turn can result in development and rapid caries progression.

The longer exposure time of the affected tooth to the oral environment, the greater the chance of post-eruptive fractures, favoring caries risk[10]. This factor may have contributed to the association found in the present study, since most children evaluated were 10 years old or older. Another case-control study demonstrated that children whose

molars were affected by MIH had greater caries incidence when compared to molars without MIH[12]. These data corroborate our findings which indicate that MIH is associated with higher caries prevalence.

It has been shown that teeth with MIH presented a higher frequency of restorative procedures than teeth without MIH[22]. The difficulty in adhesion is probably due to the affected enamel having lower mineral concentration, disorganized crystalline structure, higher carbonate content and lower calcium-phosphate ratio[23]. The mechanical properties, hardness and elasticity modulus of hypomineralized enamel also appear to be lower than those of sound enamel. Another study reported that the failure of phosphoric acid to create etching patterns in MIH teeth can break the bond compared with sound enamel[24].

The MIH prevalence found in the present study is similar to the overall prevalence found in South America (18%) in a recent systematic review[4]. This prevalence is close to studies which used the same criteria (18.4%; 16.2%; 19.7%)[6,25,26]. In addition, the MIH prevalence found can be associated to a higher prevalence of respiratory disease due to humid subtropical climate of the South region of Brazil[27–29].

Recent studies suggested that distal determinants, and not only biological risk factors, influence the outcome and should also be considered in the analysis[30] in order to obtain more robust and complete results. Socioeconomic factors, such as social program receipt, were also associated with dental caries in the present study. We considered the social program receipt (family allowance) as family monthly income proxy, since this Program is a Conditional Cash Transfer Program intended to help emancipate socioeconomically vulnerable families[31], considering that these families present low monthly income. Some authors found a difference in the caries prevalence in relation to socioeconomic factors, where adolescents from a lower socioeconomic background and poor school context had higher means of dental caries over time[32], corroborating the present findings. Thus, strategies aimed at minimizing economic disparities are indispensable for improving oral health.

Children in which the family nucleus or the head of the family is not formed by the main guardian (father or mother) had a higher prevalence of dental caries in the present study. Although there is no solid evidence to thoroughly investigate the relationship between dental caries and the head of the family, the fact that children cared

for by another person other than a mother may indirectly reflect a family breakdown, or less social support. This factor can contribute to worse oral health outcomes[33], in addition to a lower frequency of toothbrushing[34], which explains the significant association in the present study.

This study has some limitations, such as only considering public schools. The cross-sectional design also prevents establishing a causal relationship between predictor and outcome, therefore longitudinal studies are recommended. However, the present study presents strengths such as considering demographic, socioeconomic, behavioral and biological variables, considering that investigations encompassing these factors are important in schoolchildren, thus enabling to guide future strategies which promote improved oral healthcare in order minimize the impacts of diseases.

Conclusion

Children with MIH have are more likely to present dental caries. Age, receipt of a social program and the main head of the family were also associated with dental caries experience in schoolchildren.

Bullet Points:

- The importance to early diagnosis and follow-up children with molar-incisor hypomineralization.
- Factors associated with dental caries such as, age, receipt of a social program, and the main head of the family, should be considered in the dental caries risk analysis in schoolchildren.

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Table 1. Sample distribution of overall dental caries scores according to socioeconomic, demographic, and clinical characteristics of the sample.

Variables	**n (%)**	**Dental Caries mean (SD)**
Demographic and socioeconomic		
Sex		
Female	281 (54.8)	0.7 (1.3)
Male	232 (45.2)	0.6 (1.1)
Age		
≤ 12 years	259 (50.5)	0.4 (0.9)
> 12 years	254 (49.5)	0.8 (1.4)
Social Program		
No	440 (89.9)	0.6 (1.2)
Yes	49 (10.1)	1.1 (1.4)
Caregiver education		
< 8 years	260 (54.39)	0.6 (1.3)
≥ 8 years	218 (45.61)	0.7 (1.1)
Head of the family		
Wife	179 (37.4)	0.6 (1.1)
Husband	246 (51.5)	0.7 (1.3)
Other	53 (11.1)	0.6 (0.9)
Behavioral variable		
Dental visit in the last 6 months		
Yes	298 (89.0)	0.7 (1.3)
No	37 (11.0)	0.4 (0.9)
Clinical variables		
MIH		
No	412 (80.3)	0.6 (1.2)
Yes	101 (19.7)	0.7 (1.0)
Gingivitis		
No	160 (31.2)	0.6 (1.1)
Yes	353 (68.8)	0.6 (1.2)

Values lower than 513 due to missing data.
SD, standard deviation.

Table 2. Unadjusted assessment of socioeconomic, demographic, clinical variables associated with presence of dental caries (Poisson regression with robust variance).

Variables	**PR (95% CI)**	**P-value**
Demographic and socioeconomic		
Sex		
Female	1	
Male	0.94 (0.73 – 1.22)	0.667
Age		
≤ 12 years	1	
> 12 years	1.44 (1.11 – 1.87)	0.006
Social Program		
No	1	
Yes	1.80 (1.33 – 2.44)	<0.001
Caregiver education		
< 8 years	1	
≥ 8 years	1.13 (0.86 – 1.47)	0.364
Head of the family		
Wife	1	
Husband	1.21 (0.90 – 1.63)	0.194
Other	1.58 (1.07 – 2.34)	0.020
Behavioral variable		
Dental visit in the last 6 months		
Yes	1	
No	0.57 (0.28 – 1.14)	0.115
Clinical variables		
MIH		
No	1	
Yes	1.42 (1.08 – 1.88)	0.011
Gingivitis		
No	1	
Yes	0.98 (0.74 – 1.29)	0.923

PR, prevalence ratio; 95% CI, 95% confidence intervals;

Table 3. Poisson regression with robust variance on the association between socioeconomic, demographic, clinical variables and presence of dental caries.

Variables	**Model 1[a] PR (95% CI)**	**Model 2[b] PR (95% CI)**	**Model 3[c] PR (95% CI)**
Fixed component			
Intercept	0.31 (0.27 – 0.35)	0.21 (0.15 – 0.28)	0.19 (0.14 – 0.27)
Demographic and socioeconomic			
Sex			
Female		1	1
Male		0.85 (0.65 – 1.11)	0.85 (0.65 – 1.11)
Age			
≤ 12 years		1	1
> 12 years		1.47 (1.12 – 1.93) *	1.47 (1.12 – 1.93) *
Social Program			
No		1	1
Yes		1.97 (1.47 – 2.64) *	1.97 (1.47 – 2.64) *
Head of the family			
Wife		1	1
Husband		1.26 (0.94 – 1.69)	1.26 (0.94 – 1.69)
Other		1.56 (1.06 – 2.30) *	1.56 (1.06 – 2.30) *
Clinical variables			
MIH			
No			1
Yes			1.39 (1.05 – 1.85) *
Random component			
Deviance (− 2 log likelihood)	697.46	631.45	628.36

[a] Model 1: empty model, unconditional model.

[b] Model 2: adjusted for demographic and socioeconomic variables.

[c] Model 3: adjusted for clinical variables.

PR, prevalence ratio; 95% CI, 95% confidence intervals; * $p < 0.05$

3. ARTIGO 2

Molar incisor hypomineralization and oral health-related quality of life: A systematic review and meta-analysis

Esse artigo será submetido ao periódico *Brazilian Oral Research* (ISSN 1517-7491) – Fator de Impacto: 1.223; Qualis CAPES A2. As normas para publicação estão descritas no ANEXO C.

Original Research Report

Brazilian Oral Research

Molar incisor hypomineralization and oral health-related quality of life: A systematic review and meta-analysis

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Abstract

The association between molar incisor hypomineralization (MIH) and oral health-related quality of life (OHRQoL) is still not well established. The aim of this review was to investigate the impact of MIH on the OHRQoL in children and adolescents, by synthesizing the available evidence. The literature was screened via PubMed/MEDLINE, Scopus, Web of Science, Embase, Trip and Lilacs databases until November 2020. Two independent reviewers selected the studies, extracted the data and assessed the bias risk, using Newcastle-Ottawa Scale. The meta-analysis was performed to obtain pooled estimates of prevalence ratio (PR) with 95% confidence intervals (CI). The data search identified 1.771 records. After applying eligibility criteria, 5 studies were included in this systematic review and 3 in the meta-analysis. Only two studies considered the MIH severity in the adjusted analysis. Most studies presented low risk of bias. Children with MIH had a 27% higher prevalence of negative impacts on OHRQoL; however, the association was not significant (PR 1.27; 95% CI 0.68 – 2.36). In conclusion, our findings suggest that the presence of MIH is not related whit poorer scores of OHRQoL in children and adolescents. Prospective cohort studies are recommended to understand if the impact of MIH changes with time.

Key-words: Molar-Incisor Hypomineralization, Quality of life, Oral health, Systematic review.

Introduction

Molar incisor hypomineralization (MIH) is defined as a qualitative demarcated enamel defect of tooth enamel affecting at least one first permanent molar, and may also affect permanent incisors, being the prtesence in molars, mandatory of the condition[1]. Less frequently, MIH-like defects have been described in permanent canines, premolars and in second primary molars (hypomineralized second primary molar)[2]. Teeth that present MIH have a demarcated opacity with defined limits and can cause post-eruptive breakdown according to the severity[3].

The MIH prevalence varies from 2% to 40% worldwilde[4]. According to a systematic review that evaluated possible risk factors, none of the potential factors analyzed presented convincing causality, besides the available evidence being weak[5]. Studies concluded that the etiology is likely to be multifactorial[6] and other study suggests investigating the biological and genetic factors[7].

Although MIH still has an unknown etiology, the association with dental problems, such as pain, difficulties in chewing, hypersensitivity, a greater probability of developing caries and recurrent dental treatment needs are consensus in the literature[8,9]. In addition, in the last decade studies have reported a greater impact on the oral health quality of life (OHRQoL) in patients with MIH and other enamel defects[10–12]. The OHRQoL has been defined as a multidimensional construct, which reflects people's comfort when eating and engaging in social interactions, their self-esteem, and their satisfaction with their oral health[13].

Studies evaluating MIH have indicated whether this condition has an impact on OHRQoL of children and adolescents[14]. The results, however, are conflicting. The clarification of this issue could contribute to the identification of oral problems that should be prioritized in the planning and definition of cost-effective prevention and treatment strategies on both the individual and collective levels. Therefore, the aim of this study was to perform a systematic review and meta-analysis to investigate the impact of MIH on the OHRQoL of children and adolescents. We hypothesized that individuals with highs levels of MIH are more likely to report poorest scores of OHRQoL.

Methods

This study was performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis[15] (PRISMA) and recorded in the International

Prospective Register of Systematic Reviews (PROSPERO: protocol number: CRD42020200797).

Focused PECOS strategy

The following research question was determined to access the literature and built the search strategy: "Does the molar incisor hypomineralization impacts on the OHRQoL in children and adolescents?" It was performed through the PECO strategy: Population (P): children and adolescents; exposure (E): patients with MIH; comparison (C): patients without MIH; outcome (O): OHRQoL; (S): epidemiological studies.

Search Strategy

A comprehensive literature search was performed through PubMed/MEDLINE, Scopus, Web of Science, Embase, Trip and Lilacs databases. The literature was screened until November 2020, with no restriction of language or year of publication. The subject search used a combination of controlled vocabulary and text words based on the search strategy in the PubMed/MEDLINE and adapted for other databases (Table 1). The results of searches of various databases were cross-checked to locate and eliminate duplicates.

Eligibility criteria

The inclusion criterion was observational studies that evaluated the impact of the MIH on the OHRQoL in children and adolescents. The exclusion criteria were: 1) studies that did not use a validated clinical criterion to evaluate MIH; 2) did not consider a validated parameter to measure OHRQoL; 3) studies that did not present control group (without MIH).

Screening and selection

Two authors (JKK and LILB) independently screened the titles and abstracts of publications identified by the electronic search. The inter-examiner reliability calculation was tested on 10% of the papers and indicated excellent agreement (Kappa = 1.00). In the second moment, de same authors evaluated the full-text articles selected, following exclusion criteria. The reference lists of included studies in this step were also evaluated. Disagreements were resolved by discussion with a third author (TMA).

Data extraction

Two authors (JKK and LILB) independently extracted publication details (authors, year of publication, country and language), sample characteristics (sample size and age of participants), MIH clinical criterion, MIH severity classification, MIH prevalence, OHRQoL scale and main outcome information. Data considered important, not available in the papers, were requested to the authors by email.

Assessment of the risk of bias

According to the Newcastle–Ottawa Scale (NOS)[16], two reviewers (JKK and LILB), conducted the risk of bias assessment independently. In this systematic review, it was used a modified version for assessing cross-sectional studies[17]. The NOS assesses the methodological quality of the primary study in three categories: selection of the study groups (maximum four stars), the comparability of the groups (maximum two stars), and the outcome (maximum three stars)[17]. To assess the risk of bias in a quantitative way, each category was classified in low, moderate and high risk, according to the sum of the number of stars of the three categories. Studies with seven or more stars were considered as low risk, studies with less than seven and more than four stars were considered as moderate risk and studies with less than four stars were considered as high risk of bias[18]. Studies with high risk of bias were be excluded from meta-analysis.

Data analysis

The prevalence of impact, severity level or general OHRQoL scores measured with validated instruments was set as the main outcome. The predictor considered was the presence or absence of MIH. If the study had classified more than one category (by severity), the measure of the most severe category was collected. Meta-analysis was performed to obtain pooled estimates using data from different studies that provided the necessary information. The pooled measurements were converted into a log-binomial and posteriorly transformed into the prevalence ratio (PR) with 95% confidence intervals (CI)[19]. Global meta-analysis was performed according to overall scores and specific-domains of questionnaires using random-effects model. Heterogeneity was evaluated through the I^2 statistic. An I^2 of 0 to 40% was interpreted as unimportant and > 40% was considered suggestive of moderate to considerable heterogeneity[20].

Results

Study Selection

The search strategy identified 1.771 records. The search on the references of selected papers did not retrieve any additional relevant paper. After exclusion of duplicates, 1.708 studies were considered potentially eligible and were screened based on title/abstract, in which 11 articles were selected for full text analysis. Finally, 5 studies have met the eligibility criteria and were included in this systematic review (Figure 1).

Study Characteristics

All studies were published in English and were cross-sectional design. Two studies were set in Brazil[10,12], one in Mexico[14], one in Colombia[21] and another in Nigeria[22]. The sample size ranged from 88 to 853 children across studies, and the age of children varied from 6 to 16 years old. For MIH, all studies considered the criteria proposed by the European Academy of Paediatric Dentistry (EAPD)[3] in which at least one permanent first molar should present a marked opacity, post-eruptive fracture, the presence of atypical restoration, or tooth extraction that was attributable to MIH. Two studies considered the MIH severity in the adjusted analysis[10,14]. In relation to the instrument used to measure OHRQoL, four studies used Child Perception Questionnaire (CPQ) in the validated versions in other languages (Brazilian Portuguese[10,12], Spanish[14] and Colombian[21]) and according to the age of the sample (CPQ_{8-10} or CPQ_{11-14}). One study[22] used Oral Impact on Daily Performance Questionnaire (Child-OIDP). A more detailed summary of the included studies is shown in Table 2.

Assessment of the risk of bias

The final assessment of the risk of bias was determined through the Newcastle-Ottawa Scale adapted for cross-sectional studies[17] and is shown in Table 3. Most studies[10,12,14,22] presented low risk of bias. Only one study[21] presented moderate risk of bias, once that not present answer rate and confounding factors did not controlled.

Meta-analysis

The pooled estimates of the association between MIH and OHRQoL of the studies included in the meta-analysis (n = 3)[10,12,14] are presented in Figure 2. Children with MIH had 27% higher prevalence of negative impacts on OHRQoL (PR 1.27; 95% CI 0.68 – 2.36). However, this association was not statistically significant. According to specific-domains of CPQ (Figure 3), the results were also no significant for oral symptoms (PR 1.95; 95% CI 0.92 – 1.97), functional limitations (PR 1.47; 95% CI 0.85 – 2.56),

emotional well-being (PR 1.24; 95% CI 0.73 – 2.10) and social well-being (PR 1.32; 95% CI 0.61 – 2.84). All analysis showed high heterogeneity ($I^2 > 97\%$).

Discussion

The present systematic review is the first that summarized in a quantitative meta-analysis the evidence from observational studies regarding the influence of MIH on OHRQoL in children and adolescents. All studies included in the meta-analysis used the Child Perceptions Questionnaire (CPQ)[23] for evaluating the quality of life. The CPQ scale is a validated and specific tool for measure impacts in the OHRQoL in children and contemplates 4 domains: "oral symptom," "functional limitation", "emotional well-being", and "social well-being". The number of questions varies according to the version and language. The total score is obtained through the sum of the scores of all questions, and the higher the score, the greater the impact on the quality of life.

The global meta-analysis showed a higher prevalence of impact on OHRQoL in children with MIH. Despite this higher prevalence, the association was not significant in the meta-analysis, neither in general scores nor in specific domains, refuting our conceptual hypothesis. A possible explanation for these findings is that in the included studies, the majority of MIH lesions were of mild opacity[10,12,14]. In this sense, despite being present, these injuries may often not be perceived and do not impact the individuals' daily lives, and consequently, their OHRQoL in general. Moreover, in the age group addressed, individuals tend to be affected by other oral conditions, such as dental caries and malocclusion[24,25], which can have a greater impact on their quality of life, overlapping the impact of MIH.

The enamel of teeth affected by MIH has greater porosity and less resistance when compared to the enamel of sound teeth[26]. This porosity is a result of the disorganization of the enamel prisms, less distinct hydroxyapatite crystals and reduced mineral content[26]. The lower hardness of the enamel of teeth affected by MIH can result in post-eruptive fracture when subjected to the masticatory effort, which can facilitate the accumulation of plaque and consequently lead to dental caries[9]. Another important factor is the absence of brushing due to due to hypersensitivity of the affected teeth[27], which explains the association of oral symptoms in the domain's CPQ[10,12,14] in three studies included.

When the functional limitation domain of the CPQ questionnaire was evaluated isolately, no significant association was found between MIH and OHRQoL in the meta-

analysis. Some studies have suggested that older children present more severe MIH[28] and more prevalence of hipomineralized teeth that younger children[29], which may explain the absence of association in the present review, since only one study[10] included children with more than 10 years old.

The emotional and social well-being domains address such issues as "being ashamed", "worrying about what people think", "not being so pretty" because of the teeth and mouth, avoidance of smiling, and difficulties in relationships with other children. In this context, the present review did not found a significant association in these domains, which may be related to the nature of the questionnaire, since studies that utilized sensitive tools for this outcome found a significant association in relation to aesthetic outcomes and MIH[30].

Two studies[21,22] were not included in the meta-analysis because did not present the adjusted values, measure of the effect of the association between MIH and OHRQoL and data inconsistency. Besides that, the direct association found in one study[21] may be overestimated due to the sampling process, moderate kappa coefficient values and absence of adjusted analysis. In this context, it is important that future studies consider these aspects in order to generate more robust results and more reproducible methodologies. The use of a defined protocol available in the literature and criteria validated will increase the quality of epidemiological studies of MIH.

The risk of bias was evaluated using the Modified Newcastle-Ottawa[17], and grouped quantitatively[18] as reported in other study[6]. As all studies included in the meta-analysis had low risk of bias and the authors controlled confounding variables[10,12,14], so we believe that the result found was not influenced by some possible bias. In addition, the selected studies did not report on any the sources of funding, and reported operator training, as well the calibration values satisfactory of Cohen's kappa coefficient for intra-examiner[10,12,14].

The heterogeneity of the included studies was considered high through I^2 test. Although the studies are methodologically similar and used the same diagnostic criteria, the high heterogeneity value may be explained by the difference in the sample number of each study, prevalence MIH distinct, and by the limited number of studies. The meta-analysis was performed used the random-effects model, which considers the studies' weighted with the inverse of their variance and the with heterogeneity context, being a better approach. In addition, differently from the MIH diagnostic criteria, the MIH severity criteria used in the included studies were conflicting. This divergence may be

related to an absence of the defined index for severity, while de diagnostic criteria are well defined by EAPD[3], still be gaps in the literature in relation to of the better parameter for classifying the MIH severity.

Although it was not possible to measure whether MIH severity impacts differently on OHRQoL because only 2 studies presented adjusted data considering severity, we believe that more severe injuries can have a greater impact than mild or moderate injuries. In both studies, children with severe MIH has a greater negative impact on the oral symptom and functional limitation domains than those without MIH[10,14]. More studies are needed to investigate the association between the MIH severity and its impact on OHRQoL. Furtheremore, it is important to emphasize that the present review does not have the presumption of modifying clinical decision-making. Although the meta-analysis has shown no association, each case must be assessed individually, considering biological and psychosocial aspects.

This systematic review has some limitations, such as the compilation of different questionnaires according to age groups. Despite this, the tools were developed with the same purpose and present the same domains, therefore, they measure the same construct[23]. Another limitation would be inherent to the study design, the data report the perception in a single moment. Thus, longitudinal studies are needed to elucidate the influence of MIH on OHRQoL in children and adolescents and how the impact of MIH changes with time.

Conclusion

Our findings suggest that the presence of MIH is not associated with poorer OHRQoL in children and adolescents, neither in general scores nor in specific domains. However, the scientific evidence is still inconclusive for draw definitive conclusions.

Conflict of interest

The authors declare no conflict of interest.

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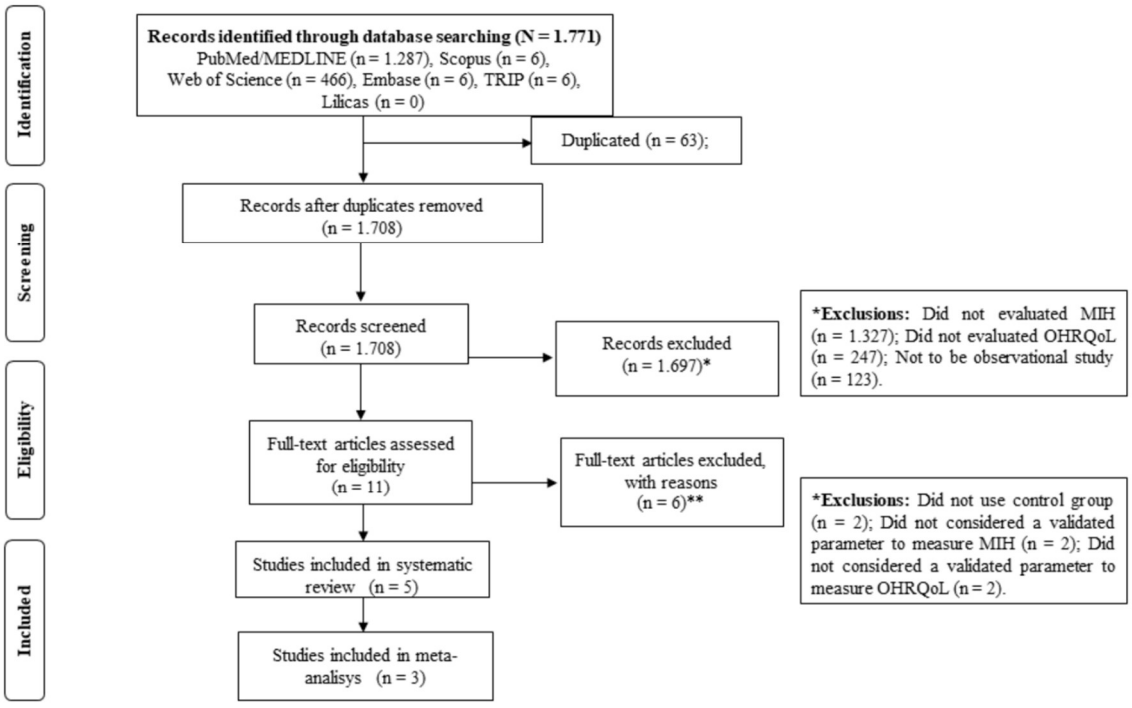

Figure 1. Flowchart of the screening process of studies included in the systematic review and meta-analysis.

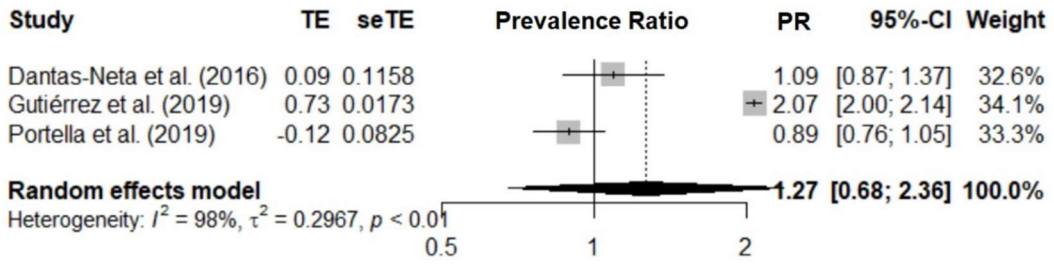

Figure 2. A general meta-analysis of the association of MIH on the overall CPQ scores.

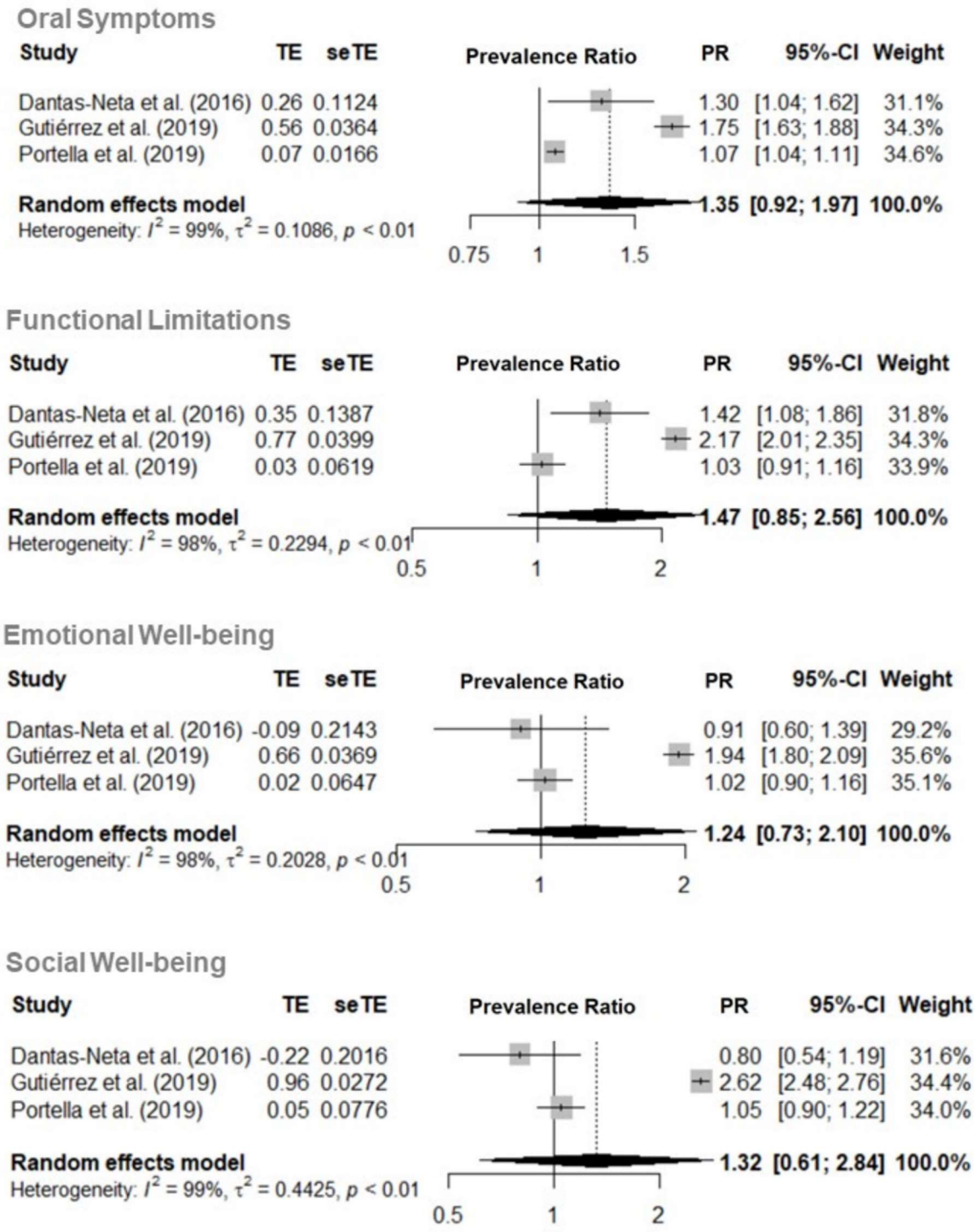

Figure 3. A meta-analysis of the association of MIH according to the specific domains of the CPQ.

Table 1. Eletronic databases searched and search strategies used in the systematic review (up to November 2020).

Database	Search strategy used	Hits
Pubmed/MEDLINE (https://www.ncbi.nlm.nih.gov/pubmed)	(((((((tooth, deciduous [MeSH Terms]) OR deciduous tooth) OR primary dentition) OR primary tooth)) OR Dentition, Permanent [MeSH Terms]) OR permanent dentition) OR permanent tooth)) AND (((molar incisor hypomineralization) OR hypomineralization, molar incisor) OR MIH)) AND (((((Quality of Life [MeSH Terms]) OR Health-Related Quality Of Life) OR oral health related quality of life) OR ohrqol) OR oral impact)	1.287
Web of Science (https://login.webofknowledge.com)	TOPIC: (deciduous tooth) OR TOPIC: (primary dentition) OR TOPICO: (primary tooth) OR TOPIC: (Dentition, Permanent) OR TOPIC: (permanent dentition) OR TOPIC: (permanent tooth) AND TOPIC: (molar incisor hypomineralization) OR TOPIC: (hypomineralization, molar incisor) OR TOPIC: (primary tooth) OR TOPIC: (MIH) AND TOPIC: (oral health related quality of life) OR TOPIC: (ohrqol) OR TOPIC: (oral impacts)	466
Scopus (https://www.scopus.com)	TITLE-ABS-KEY-AUTH (deciduous AND tooth) OR TITLE-ABS-KEY (primary AND dentition) OR TITLE-ABS-KEY (primary AND tooth) OR TITLE-ABS-KEY (dentition, AND permanent) OR TITLE-ABS-KEY (permanent AND dentition) OR TITLE-ABS-KEY (permanent AND tooth)) AND (TITLE-ABS-KEY (molar AND incisorAND hypomineralization) OR TITLE-ABS-KEY (hypomineralization, AND molar AND incisor) OR TITLE-ABS-KEY (mhi)) AND (TITLE-ABS-KEY (oral AND health AND related AND quality AND of AND life) OR TITLE-ABS-KEY (ohrqol) OR TITLE-ABS-KEY (oral AND impacts))	6
Embase (https://www.embase.com)	('molar'/exp OR molar) AND ('incisor'/exp OR incisor) AND ('hypomineralization'/exp OR hypomineralization) AND oral AND ('health'/exp OR health) AND related AND ('quality'/exp OR quality) AND of AND ('life'/exp OR life)	6
TRIP (https://www.tripdatabase.com/)	molar incisor hypomineralization AND oral health related quality of life	6
Lilacs (https://lilacs.bvsalud.org/)	hipomineralização molar incisivo [Palavras] and qualidade de vida [Palavras]	0
Total		1.771

Table 2. Main characteristics of the studies selected for this systematic review.

Study	Country	Study Design	Sample Size	Age	MIH criteria	MIH severity classification	MIH Prevalence	OHRQoL Questionaire	Main Result
Dantas-Neta et al., 2016	Brazil	Cross-sectional	594	11-14 years	EAPD	Mild (opacities without fracture); moderate (hard and fractured enamel); severe (loss of tooth structure affecting the enamel and dentine)	18.9%	CPQ_{11-14}	Severe MIH was associated with a greater negative impact in the oral sympton and functional limitation domain CPQ. In the overall score, there was no association.
Folayan et al., 2018	Nigeria	Cross-sectional	853	6-16 years	EAPD	Not reported	2.9%	C-OIDP	MIH had no significant impact on the overall oral health quality of life.
Velandia et al., 2018	Colombian	Cross-sectional	88	7-10 years	EAPD	Mild (demarcated opacities in non-stress-bearing area of molar); moderate (intact atypical restoration present); severe (posteruptive enamel breakdown present)	Not report	CPQ_{8-10}	MIH has negative impact on all dimensions of OHRQoL as reflected by the CPQ.
Portella et al., 2019	Brazil	Cross-sectional	728	8 years	EAPD	Mild Injury (opacity); severe injury (post-eruptive fractures, atypical restorations, and tooth extraction attributable to MIH)	12.1%	CPQ_{8-10}	MIH was associated with a greater impact

									on OHRQoL only in children's oral symptoms.
Gutiérrez et al, 2019	Mexico	Cross-sectional	411	8-10 years	EAPD	Mild (one white or creamy opacity with a >1 mm diameter and affecting less than one third of the tooth surface); moderate (one yellow or brown opacity with a >1 mm diameter and affecting less than one third of the tooth surface, two or more white or creamy opacities with a >1 mm diameter affecting at least one third but less than two thirds of the tooth surface, post-eruptive enamel breakdown ≤2 mm in diameter, or atypical restorations involving at least one third but less than two thirds of the affected tooth surface); severe (two or more yellow or brown opacities with a >1 mm diameter affecting at least one third or more of the tooth surface, two or more white or creamy opacities with a >1 mm diameter affecting at least two thirds of the tooth surface, post-eruptive enamel breakdown >2 mm in diameter, or atypical restoration involving more than two thirds of the affected tooth surface)	40.4%	CPQ_{8-10}	MIH was associated with a negative impact in the four CPQ domains.

Table 3. Assessment of the risk of bias of the selected studies.

Study	Selection (****)	Comparability (**)	Outcome (***)	Risk of bias
Dantas-Neta et al., 2016	****	**	**	Low
Folayan et al., 2018	***	**	**	Low
Velandia et al., 2018	**	-	**	Moderate
Portella et al., 2019	****	**	**	Low
Gutiérrez et al, 2019	***	**	**	Low

4. CONCLUSÃO

Com base nas investigações científicas apresentadas nessa dissertação, pode-se concluir que:

Existe uma associação entre HMI e experiência de cárie dentária.

A qualidade de vida associada à saúde bucal parece não ser afetada por HMI quando investigada através do questionário Child Perceptions Questionnaire. Entretanto, mais estudos são necessários.

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ANEXO A – APROVAÇÃO DO COMITÊ DE ÉTICA EM PESQUISA

UFRGS - PRÓ-REITORIA DE PESQUISA DA UNIVERSIDADE FEDERAL DO RIO GRANDE DO

PARECER CONSUBSTANCIADO DO CEP

Elaborado pela Instituição Coparticipante

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: AVALIAÇÃO DA SAÚDE DE ESCOLARES DO ENSINO FUNDAMENTAL DO SUL DO BRASIL

Pesquisador: ELIANA MARCIA DA ROS WENDLAND

Área Temática:

Versão: 1

CAAE: 70213717.1.3001.5347

Instituição Proponente: Faculdade de Odontologia

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 2.632.694

Apresentação do Projeto:

Trata-se de uma emenda a projeto aprovado no CEP-UFRGS em 11 de janeiro deste ano. A emenda tem por finalidade incluir teste pulmonar, a partir de medida simples de espirometria com medidas de volumes e fluxos pulmonares na expiração forçada (CVF, VEF 1 , VEF 1 /CVF, FEF 50% e FEF 75%). Também é incluída na equipe de pesquisa a professora Margaret Gerbase

Objetivo da Pesquisa:

Objetivo Primário:

Avaliar a prevalência dos principais problemas de saúde em crianças e adolescentes que frequentam a escola (2o ao 9o ano).

Objetivos Secundários:

* Avaliar a distribuição e prevalência de agravos de saúde bucal;
* Avaliar a relação entre fatores contextuais referentes ao local de moradia e o local de estudo e a saúde bucal de escolares;
* Identificar o padrão alimentar e fatores associados;
* Estimar a prevalência de sobrepeso e obesidade;
* Verificar associação entre padrão alimentar e gordura corporal (% de gordura;

Endereço: Av. Paulo Gama, 110 - Sala 317 do Prédio Anexo 1 da Reitoria - Campus Centro
Bairro: Farroupilha **CEP:** 90.040-060
UF: RS **Município:** PORTO ALEGRE
Telefone: (51)3308-3738 **Fax:** (51)3308-4085 **E-mail:** etica@propesq.ufrgs.br

* Verificar associação do padrão alimentar com determinantes socioeconômicos, demográficos e comportamentais (grau de escolaridade e idade dos responsáveis, tempo de aleitamento materno, tempo de introdução da alimentação complementar, tempo de permanência na escola);
* Avaliar a frequência de adesão dos escolares as indicações do Novo Guia Alimentar da População Brasileira;
* Avaliar a associação entre a prevalência de hipertensão arterial sistêmica e alimentação saudável;
* Avaliar a associação entre a prevalência de anemia e alimentação saudável;
* Avaliar a associação entre alimentação saudável e nível de atividade física;
* Mensurar a frequência de uso de medicamentos entre os escolares;
* Avaliar a associação entre alimentação saudável e saúde bucal.

Avaliação dos Riscos e Benefícios:

Riscos:

Os participantes envolvidos no estudo estarão submetidos aos possíveis riscos inerentes ao exame odontológico, às necessidades de procedimentos de odontologia minimamente invasiva e ao exame de coleta de hemoglobina capilar. Durante a realização do exame de hemoglobina capilar poderá ocorrer sangramento, que será manejado por enfermeira capacitada através de técnica padrão (compressão), bem como poderá ocorrer pequeno hematoma local.

Benefícios:

Os benefícios que se espera com o estudo são um melhor entendimento dos problemas apresentados pelos estudantes do município e fim de se planejar melhorias futuras para estes estudantes e os dados poderão ser utilizados para orientar as políticas públicas, nas áreas estudadas, no município.

Comentários e Considerações sobre a Pesquisa:

A emenda ao projeto apresenta justificativa adequada, anexada em documento próprio. O TCLE e TALE foram alterados para incluir o teste pulmonar.

O equipamento a ser utilizado será um espirômetro digital portátil para pesquisa de campo que será disponibilizado pela pesquisadora responsável pelo módulo respiratório deste projeto.

Considerações sobre os Termos de apresentação obrigatória:

Além dos documentos já apresentados no projeto original, a emenda inclui o TALE e o TCLE alterados.

Conclusões ou Pendências e Lista de Inadequações:

Não há pendências adicionais. Encaminha-se para aprovação pelo CEP-UFRGS.

Considerações Finais a critério do CEP:

Aprovação.

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
TCLE / Termos de Assentimento / Justificativa de Ausência	Termo_Assentimento_alterado.pdf	29/11/2017 17:38:52	Fernanda Henemann Barboza	Aceito
Outros	ProjetoEstanciaVelha_Justificativa.pdf	29/11/2017 17:35:33	Fernanda Henemann Barboza	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	Termo_Assentimento.pdf	29/11/2017 17:32:08	Fernanda Henemann Barboza	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TCLE_alterado.pdf	29/11/2017 17:10:28	Fernanda Henemann Barboza	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	Termo_Anuencia.pdf	06/10/2017 23:10:43	Larissa Edom Bandeira	Aceito
Outros	CARTA_RESPOSTA.pdf	09/08/2017 20:48:03	Larissa Edom Bandeira	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	APENDICE_E_TCLE_novo.pdf	09/08/2017 20:47:26	Larissa Edom Bandeira	Aceito
Projeto Detalhado / Brochura Investigador	2017_Projeto_Inqurerito_EV.docx	13/06/2017 17:19:13	ELIANA MARCIA DA ROS WENDLAND	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	APENDICE_F_Termo_Assentimento.pdf	07/06/2017 18:38:31	Larissa Edom Bandeira	Aceito
Outros	APENDICE_D_Ficha_Coleta_Exame_Bucal.pdf	07/06/2017 18:37:29	Larissa Edom Bandeira	Aceito
Outros	APENDICE_C_Ficha_Coleta_Indicadores_Saude.pdf	07/06/2017 18:36:32	Larissa Edom Bandeira	Aceito

UFRGS - PRÓ-REITORIA DE PESQUISA DA UNIVERSIDADE FEDERAL DO RIO GRANDE DO

Continuação do Parecer: 2.632.694

Outros	APENDICE_B_Questionario_Adolescentes.pdf	07/06/2017 18:35:51	Larissa Edom Bandeira	Aceito
Outros	APENDICE_A_Questionario_Familiares.pdf	07/06/2017 18:35:24	Larissa Edom Bandeira	Aceito
Outros	ANEXO_1_Questionario_Criancas_CAAFE.pdf	07/06/2017 18:26:33	Larissa Edom Bandeira	Aceito

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PORTO ALEGRE, 03 de Maio de 2018

Assinado por:
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ANEXO B – NORMAS DO PERIÓDICO *CARIES RESEARCH*

What are you looking for?

Caries Research

Author Guidelines

About the Journal

Aims and Scope

Caries Research publishes epidemiological, clinical and laboratory studies in dental caries, fluorosis, erosion and related dental diseases. Some studies build on the considerable advances already made in caries prevention, e.g. through fluoride application. Some aim to improve understanding of the increasingly important problem of dental erosion and the associated tooth wear process. Others monitor the changing pattern of caries in different populations, explore improved methods of diagnosis or evaluate methods of prevention or treatment. Studies using genetic methods to identify human genes or mutations associated with caries prevalence are welcome as are manuscripts using modern high-throughput sequencing methods to characterise microbial biofilms associated with oral health and active caries. The broad coverage of innovative research into dental caries is unique and has given the journal an outstanding international reputation as an indispensable source for both basic scientists and clinicians engaged in understanding, investigating and preventing dental diseases.

Journal Sections

Current Topics
Current topics are concise articles that present critical discussion of a topic of current interest, or a fresh look at a problem, and should aim to stimulate discussion.

Article Types

Research Article

Research Articles report on primary research. They must describe significant and original observations. Consideration for publication is based on the article's originality, novelty, and scientific soundness, and the appropriateness of its analysis.
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Documents

Research Article (DOCX, 27.22 KB)

Review Article

Review Articles are considered reviews of research or summary articles. They are state-of-the-art papers covering a current topic by experts in the field. They should give evidence on and provide answers to a well-defined aspect or question in a particular area. Review Articles must include a critical discussion of the reported data and give a clear conclusion with potential impacts on the standard of care.

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Documents

Review Article (DOCX, 23.06 KB)

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Documents

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ANEXO C – NORMAS DO PERIÓDICO *BRAZILIAN ORAL RESEARCH*

ISSN 1807-3107 *online version*

INSTRUCTIONS TO AUTHORS

Mission, scope, and submission policy

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