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Review

Association between developmental defects of enamel and dental caries: A systematic review and meta-analysis

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ABSTRACT

Background: Dental caries is the main problem oral health and it is not well established in the literature if the enamel defects are a risk factor for its development.
Objective: Studies have reported a potential association between developmental defects enamel (DDE) and dental caries occurrence. We investigated the association between DDE and caries in permanent dentition of children and teenagers.
Data sources: A systematic review was carried out using four databases (Pubmed, Web of Science, Embase, and Science Direct), which were searched from their earliest records until December 31, 2014.
Study selection: Population-based studies assessing differences in dental caries experience according to the presence of enamel defects (and their types) were included. PRISMA guidelines for reporting systematic reviews were followed. Meta-analysis was performed to assess the pooled effect, and meta-regression was carried out to identify heterogeneity sources. From the 2558 initially identified papers, nine studies fulfilled all inclusion criteria after checking the titles, abstracts, references, and complete reading. Seven of them were included in the meta-analysis with random model.
Results: A positive association between enamel defects and dental caries was identified; meta-analysis showed that individuals with DDE had higher pooled odds of having dental caries experience [OR 2.21 (95% CI 1.3; 3.54)]. Meta-regression analysis demonstrated that adjustment for sociodemographic factors, countries' socioeconomic status, and bias (quality of studies) explained the high heterogeneity observed.
Conclusion: A higher chance of dental caries should be expected among individuals with enamel defects.

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1. Introduction

Dental caries is a chronic disease, being considered the oral health problem worldwide.[1] Caries is also the cause of dental pain and could lead to tooth loss, affecting oral health related quality of life.[2–4] This condition has a multifactorial aetiology, where demographic, socioeconomic, behavioural, and biological risk factors could be enrolled.[5–7] Generally, children whose mothers are poorly educated have more dental caries experience,[6] as well as individuals from low socioeconomic position and/or in disadvantaged conditions.[5,7,8] In addition, epidemiological data have revealed a polarization of caries experience, a concept defined as the occurrence of a large number of disease-free individuals and the majority of the disease burden concentrated in a relatively small proportion of individuals, reflecting social inequalities in oral health conditions.[7] In such a context, identifying potential factors that could contribute to caries occurrence is relevant. When considering the biological influences on dental caries, there has been greater attention given to the role of developmental defects enamel (DDE).

Enamel defects are related to disturbances during enamel formation and could be seen as enamel hypoplasia or opacities. Enamel hypoplasia is a quantitative defect involving reduced thickness of enamel (formed during the secretory stage of amelogenesis).[9] Opacities are characterized by enamel with normal thickness and an intact surface, but there is a discrete area (or areas) of different enamel translucency, being classified as diffuse or demarcated opacities.[10]

Several studies have highlighted the possibility of enamel defects being an important biological influence on dental caries development in deciduous[11–13] and in permanent dentitions,[14–16] whereas others have failed to find this association.[11,17] It is important to consider that most of these studies have not accounted for important factors such as fluoride exposure[12] and/or sociodemographic characteristics. Thus, generalizing their findings should be done carefully.[16]

Enamel hypoplasia has been frequently associated with dental caries experience,[14–15] mainly due to the higher acid solubility of the affected enamel,[18] plaque accumulation,[19–20] and a higher degree of colonization by *Streptococcus mutans* and *Lactobacilli*.[21] Nevertheless, cross-sectional studies have demonstrated that demarcated opacities were significantly associated with dental caries experience in permanent incisors and molars.[22–23]

Even with a possible relationship between DDE and dental caries, this association remains unclear in the literature. Therefore, the aim of the present study was to systematically review the literature in order to evaluate the association between development defects of enamel and dental caries experience in the permanent dentition.

2. Material and methods

This systematic review was reported according to the PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) protocol.[24]

2.1. Search strategy and bibliographic sources

This literature review used the following four electronic bibliographic data sources: PubMed, Web of Science, Science Direct, and EMBASE. In PubMed, the terms used were: topic terms (enamel defects OR developmental defects of enamel OR Dental Enamel Hypoplasia[Mesh]) OR dental hypoplasia OR enamel hypoplasia OR opacities) AND (dental caries[Mesh] OR caries OR dental decay). The same terms were used in the Science Direct and EMBASE databases. In the Web of Science database, we needed to include 'TS=' before the parentheses for each subset of terms.

The use of independent keywords allows a broader search because it rules out potential mistyping and other errors when using MeSH Terms (Medical Subject Headings) in different databases.

The search was carried out on January 2015 and included all of the papers published until December 31, 2014, with no date limits.

2.1.1. Criteria for inclusion/exclusion of papers

To be included in the review, a paper should have met the following criteria: (a) be an epidemiologic study, without any restriction of design (such as cross-sectional, case-control, and longitudinal studies) with assessment of likely association between DDE and dental caries; (b) determine the presence of DDE in the permanent dentition; (c) include participants 8–19 years old; (d) and use a population-based sample rather than a clinical convenience sample.

The exclusion criteria were: studies where dental caries was not the outcome; articles without the evaluation of enamel defects; studies evaluating the deciduous dentition; studies evaluating the mixed dentition without separate information about the permanent dentition; case-reports; literature reviews; manuscripts evaluating specific sub-populations (such as congenital cardiac disease patients); guidelines; and papers not using the FDI criteria[9] to assess enamel defects.

2.2. Stages of reference selection

All references were imported into reference management software (EndNote X3; Thomson Reuters Inc., Philadelphia, PA, USA). Two authors (FVF, MMSS) independently performed the assessments, with the reading of the titles and the abstracts of the selected manuscripts in order to exclude papers not meeting the inclusion criteria. The same authors also performed the complete reading of the papers and when disagreements occurred, discussion was made to obtain consensus, without the need for a third evaluator.[24] In addition, the reference lists of the selected articles were checked in order to find any investigation not found in the database previously consulted by the authors.[24]

2.3. Data collection

A data extraction spreadsheet was developed and the two researchers (FVF, MMSS) collected the information independently. For each selected manuscript, the following information was collected: year of publication (dichotomized

in 1994–2005 and 2006–2014), first author institutional affiliation, country (dichotomized in high-income countries and medium- and low-income countries), study design (cross-sectional, case-control, cohort, or other), language, age, sample size (up to 1000; more than 1000), presence of enamel defects (hypoplasia and other types), other exposure variables assessed (such as fluoride status, socioeconomic and behavioural aspects), diagnostic criteria for DDE and dental caries, intra-oral examinations (conditions and teeth analysed), and the outcome of the defects-caries analysis. We analysed the presence of controlling for confounding such as sociodemographic in each study and discussed its influence on findings (dichotomized in crude results and those adjusted for socioeconomic factors). Additionally, crude and adjusted odds ratios (ORs) with respective 95% confidence intervals were collected. In two papers, the ORs and 95% CI were calculated based on data presented.[22,25]

2.4. *Quality assessment*

In order to evaluate the quality of studies that fulfil the inclusion criteria, an adapted version of Downs and Black checklist[26] was used.[27]

From the original 27 items regarding interventional studies, only 17 were employed. The items assessed, mainly, methodology section (sample size, statistical analysis, participants selection) and each item scored only one point, except one that could score at most two. Consequently, the total score could range from 0 to 18 points, being classified according to the obtained score as follows: high risk of bias (0–5 points); moderate risk of bias (6–11 points) and low risk of bias (more than 12 points). Articles were evaluated independently by two reviewers, and disagreements were discussed until a consensus was achieved. More details are in elsewhere.[27]

2.5. *Meta-analysis*

The pooled effect of DDE on dental caries experience was calculated using a fixed and a random model (pooled OR and 95% CI). When heterogeneity was statistically significant ($P < 0.05$), the random model was preferred.[28] Meta-regression analysis was used to identify individual contribution of some possible variables to the heterogeneity between included studies (adjusted R^2 percentage). This analytical approach assessed which methodological variables affected the results. All analyses were performed using the software STATA 12.0 (StataCorp, College Station, TX, USA).

3. Results

Initially, 2558 abstracts were identified in total. After reading the titles, abstracts, and full text (the latter only when an abstract was not available), 40 were selected. Twelve studies were identified from sources and two identified from reading the references of the selected manuscripts. Studies involving mixed dentition and assessing only prevalence (enamel defects and dental caries experience) and not the association of interest were excluded after reading the entire manuscript. In the end, nine papers were included (Fig. 1) in the systematic review and seven were used in the meta-analytic approach. The reasons for exclusion of those papers were either that the data were not available[14] or one study used individuals who were free of dental caries as a reference category.[29]

Table 1 summarizes the main features and findings of the seven selected studies included in the meta-analysis. Of those, five were in English, one in Spanish, and one in Portuguese, and all were cross-sectional in design. Three studies were carried out in Brazil, two in Mexico, and one in Sri Lanka and Poland. The studies were published between 1994 and 2014, with sample sizes ranging from 245 to 3538 individuals.

Even though the enamel defects measure used in the included studies was the FDI (Fédération Dentaire Internationale) DDE index (1982 or 1992), there were differences in relation to the assessment and number of examined teeth. Some studies investigated teeth with natural lighting[16,22,25,30]; others[16,25] used sterile gauze and/or cotton wool to remove debris when necessary; and others employed a flashlight for illumination.[16,31] Three studies assessed only index teeth[16,22,25]; while two others evaluated all permanent teeth that were present.[15,30,31] There is not a standardized intra-oral examination for enamel defects; this may affect the findings, with, for example, an underestimated prevalence. However, for the outcome dental caries, all studies assessed dental caries experience using WHO[10] guidelines, with data reported as DMF or DMF scores. In relation to the assessment of quality, four studies scored more than 12 points, being classified as low risk for bias, and two studies presented a moderate risk for bias.[22,25]

A positive association between developmental defects of enamel and permanent dentition caries experience was identified in six studies.[15,22,25,30,31] It is important to mention that most studies assessed enamel defects, regardless of the type of enamel defect (whether opacity or hypoplasia) and their association with dental caries. The pooled effect obtained with the random model was 2.21 (95% CI 1.39; 3.54). When the individual contribution of each variable in the heterogeneity by meta-regression was analysed (Table 2), we observed that including variables related to adjustment for socioeconomic factors, socioeconomic status of countries, and quality of studies in the model resulted in a reduction of 30.3%, 14.1%, and 55.0%, respectively. Consequently, the combination of these methodological variables in the meta-regression analysis explained almost 100% of the heterogeneity. Fig. 3 presents the pooled effect stratified by study quality, demonstrating that this characteristic influences the magnitude of the association.

4. Discussion

To the best of our knowledge, this is the first systematic review and meta-analysis exploring the potential relationship between dental caries and enamel defects. Our findings demonstrated a positive association between caries experience and enamel defects, which could be considered a potential predictor for dental caries.

The literature has pointed that teeth with enamel defects (mainly hypoplastic lesions) can allow additional plaque accumulation[19–20] due to the presence of subsurface porosities,[25] facilitating caries progress.[19] However, other investigations

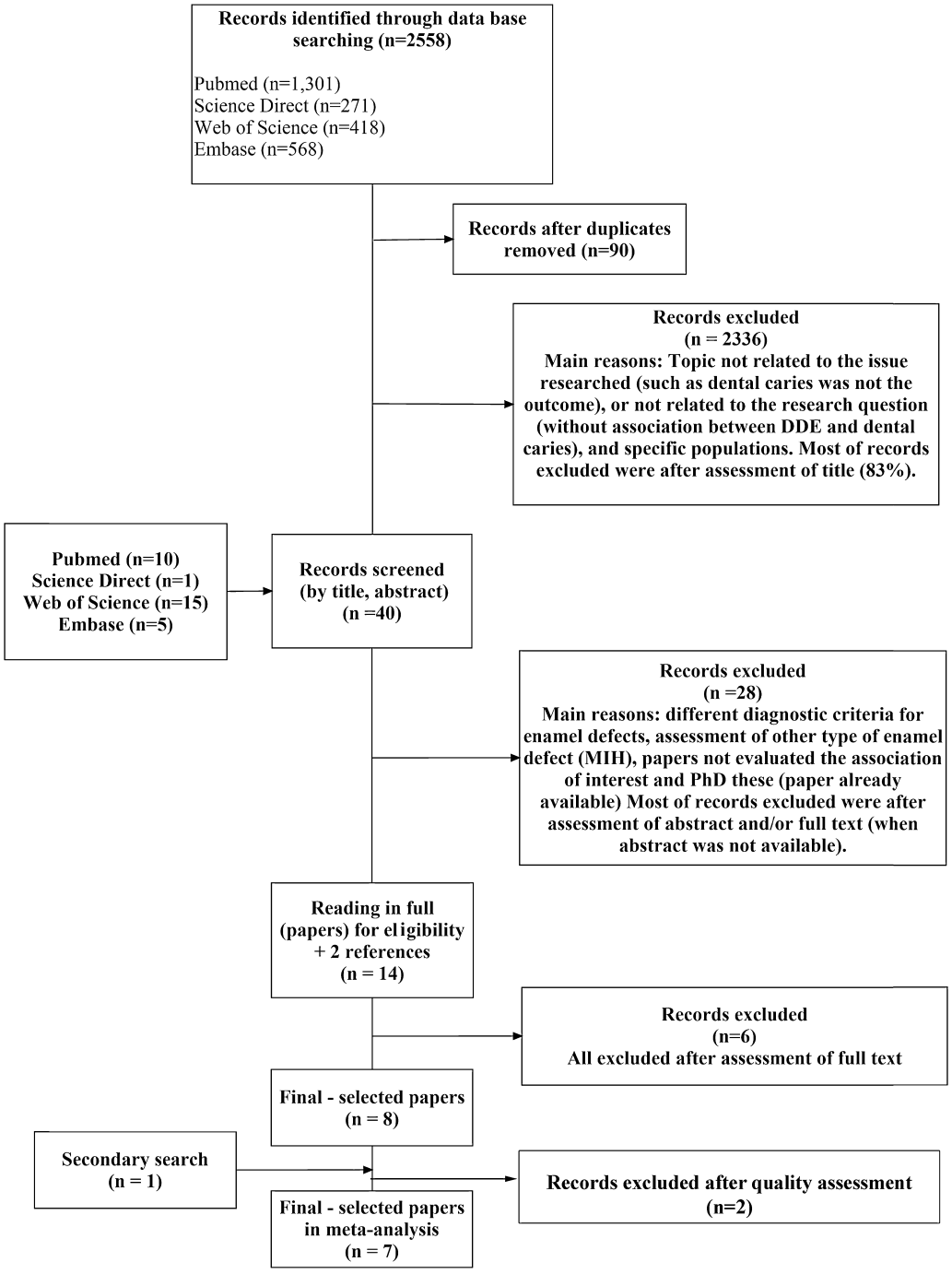

Fig. 1 – Flowchart of identification and selection process.

also showed that enamel opacities increase the chance of having dental caries.[15,22]

It is important to mention that most of the studies analysed have not elucidated the link between the outcome and enamel defects. In addition, their authors had pointed out several variables that could influence the association between dental caries and enamel defects, such as maternal schooling[16,32] and parental occupation.[14] The literature has suggested that enamel defects are influenced by maternal and child conditions early in the life course.[33–34] Children with a history of low birth weight were more likely than their normal birth weight counterparts to present with enamel hypoplasia.[34–35] Other studies[12,36] have demonstrated that the presence of enamel hypoplasia is a predictor for dental caries in deciduous teeth. A conceptual model has been proposed that connects the social, psychological, and behavioural mediating factors involved in caries experience.[37] Similarly to dental caries, variables such as *per capita* family income and birth weight may be considered

Table 1 – Main findings of studies that fulfil the inclusion criteria.

Author(s) and paper language	Year	Study site	Age (years)	Sample size	Study design	Main exposure definition	Outcome definition	Buccal exam (conditions)	Other measures	Main findings
Vargas-Ferreira et al. English	2014	Brazil	8–12	1210	Cross-sectional	FDI	WHO	Index teeth (14,13,14,12, 11,21,22,23, 24,36,46) Gauze to remove debris Non-natural light	Age Gender Skin colour Using of toothpaste earlier Maternal schooling	Children with enamel hypoplasia had almost three times the odds of having dental caries in posterior teeth than those with no hypoplasia (OR 2.79 95% CI 1.05; 6.51). Results adjusted for confounding variables.
Opydo-Szymaczek and Gerreth English	2014	Poland	12–14	245	Cross-sectional	FDI	WHO	Incisors and Molars Gauze to remove debris Non-natural light	–	The mean number of teeth with caries and the mean number of molars and incisors with caries were higher in subjects with enamel hypoplasia and/or demarcated opacity than in subjects without DDE or with diffuse opacities ($P < 0.05$).
Hoffmann et al. Portuguese	2007	Brazil	12	309	Cross-sectional	FDI	WHO	All teeth Natural light Wet teeth	Type of school Gender	There was no difference between the prevalence of DDE and gender/type of school ($P > 0.05$); children with enamel hypoplasia had more chance of dental caries than their counterparts (OR 11.01 95% CI 1.51; 225.57) and also with demarcated opacity (OR 2.32 95% CI 1.18; 4.59). Teeth with hypoplasia (75.9% had caries) and with opacity (55.8% showed dental caries).
Vallejos-Sánchez et al. Spanish	2007	Mexico	6–12	713	Cross-sectional	FDI	WHO	Without description	Age Gender Tooth brushing frequency Dental caries in deciduous teeth Maternal schooling	Children with enamel defects had a higher chance of dental caries than those without DDE. Crude analysis (OR 3.0 95% CI 1.99; 4.51) and in adjusted (4.03 95% CI 2.03; 7.99).
Casanova et al. English	2005	Mexico	9	1640	Cross-sectional	FDI	WHO	All teeth Natural light	Gender Family size Current occupation Socioeconomic level Tooth brushing frequency Plaque	The presence of enamel defects (OR 4.17; 95% CI 2.36; 7.39) was also positively associated with caries.

Table 1 (*Continued*)

Author(s) and paper language	Year	Study site	Age (years)	Sample size	Study design	Main exposure definition	Outcome definition	Buccal exam (conditions)	Other measures	Main findings
Ekanayake and Van der Hoek English	2002	Sri Lanka	14	486	Cross-sectional	FDI	WHO	Index teeth (14,13,14,12, 11,21,22,23, 24,36,46) Natural light Gauze to remove debris	Gender Water fluoridated	No difference between gender and enamel defects/ dental caries. Caries prevalence and the mean caries experience were significantly higher in children with diffuse opacities than in those without in the group consuming water containing $>$ 0.70 mg/l of fluoride ($P < 0.001$).
Ellwood and Mullane English	1994	North Wales	12	3538	Cross-sectional	FDI	WHO	Index teeth (14,13,14,12, 11,21,22,23, 24,36,46) Wet teeth Natural light	–	Children with diffuse opacities had a mean DMFS of 2.0 compared with 3.0 for those who were free from these. Subjects with demarcated opacities had a DMFS of 3.2 compared with 2.5 for those without defects, a difference in dental caries of 28% in the other direction ($P < 0.05$).

Table 2 – Individual contribution of each variable in the decrease of heterogeneity, measured by meta-regression analysis.

	Adjusted R^2 (%)
Socioeconomic status of countries	14.1
Sample size	0
Type of enamel defect	0
Adjustment for socioeconomic factors	30.3
Year of publication	0
Quality of studies	55.0

relevant factors thus could indirectly influence the formation of dental enamel.[33] In summary, a disadvantaged background seems to be associated with DDE occurrence in permanent teeth, as with dental caries.[38] This fact could explain the individual contribution of countries' socioeconomic status so as the adjusted results by socioeconomic factors. It is beyond dispute that medium- and low-income countries have improved their social conditions, and this is especially so in Latin America,[38] and reflected in a relevant decline in dental caries prevalence among children.[8] However, given that dental caries and DDE are associated with a disadvantaged background, it is possible to presume that children enrolled in these studies did not experience the benefits of this social development. Additionally, once dental caries and DDE present as common risk to the socioeconomic background, it is possible to observed a more evident association if the model is adjusted by this variable, as demonstrated by our findings.

In relation to enamel defects, all the types of defects can be associated with dental caries. Enamel hypoplasia is more susceptible to dental caries,[14,31] but another studies showed that enamel opacities are also associated with the outcome.[15,22] In opposite, individuals with diffuse opacities decurrently of greater fluoride exposure are less prone to exhibit dental caries.[29] The amount of fluoride contained in drinking water should be considered, especially if 0.70 mg/l or more of fluoride is present in the water.[15,22] The results of our study, however, demonstrated that the type of DED could not explain the heterogeneity, probably because the aetiology of these defects share some similar influencing factors.

All of the studies showed a positive association between enamel defects (regardless of the type) and dental caries. Fig. 2 shows clearly that the presence of enamel defects increases the chance of having dental caries. One difference found in the studies is in respect of the intra-oral examination. For the DDE, there is no standardization of clinical examinations and this may influence the findings of studies (underestimated prevalence, for example). As demonstrated in Fig. 3, studies classified as having a moderate risk of bias underestimated the association between DDE and dental caries. We hypothesize that, given their methodological issues, these studies' findings could misrepresent the association, as demonstrated by the difference in the magnitude of the pooled result for each subgroup.

In fact, in the meta-regression analysis aspects linked to the clinical examination did not explain the heterogeneity across the included studies. Nevertheless, as a small number of studies were included in our review, it was not possible to determine whether the clinical examination aspects did not actually influence the heterogeneity or whether our analysis did not have power enough to detect such statistical approach.

This analysis, however, revealed that other factors, such as the socioeconomic position and the country where the study was conducted influenced the heterogeneity of the model. It highlights the relevance of including these conditions when the association between dental caries and DDE is considered. Thus, researchers investigating such association should take into consideration not only the biological aspect of this relationship, but also the social one.

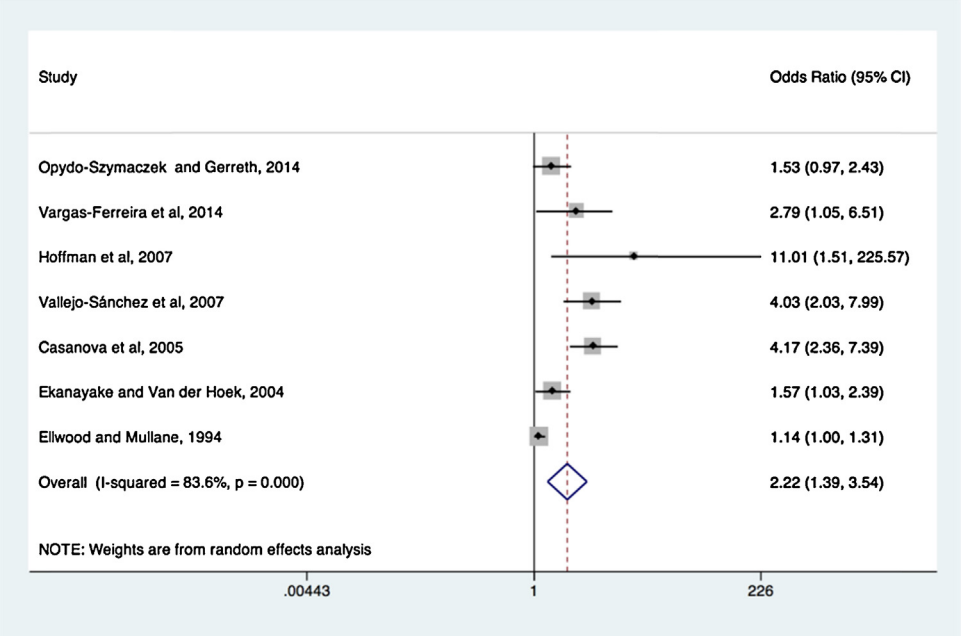

Fig. 2 – Pooled effect of enamel defects on chance of development of dental caries.

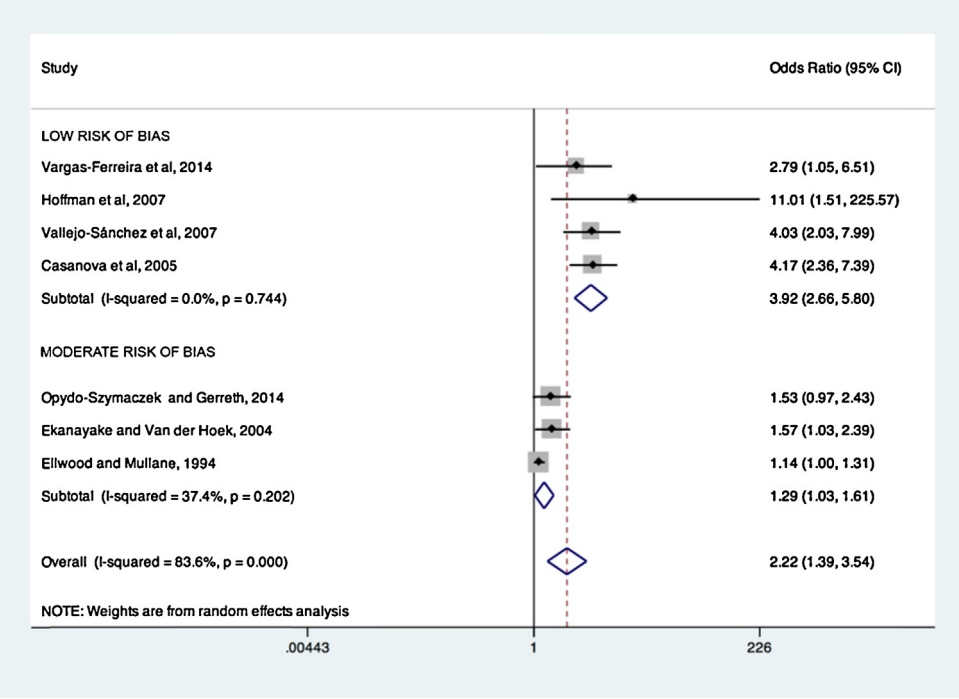

Fig. 3 – Stratified analysis by risk of bias of included studies.

A limitation found in the selected studies refers to the lack of investigation in relation to access to oral health services, dietary aspects and maternal-child factors in the studies included in the systemic review. These factors may be considered as potential effect modifiers that may lead to a weak or negative association between dental caries and enamel defects.[11,34,35]

An important limitation of this study refers to the quality assessment. There is not a standardized scale to assess observational cross-sectional studies instead of randomised trials. One alternative would be not to set thresholds for categories of risk of bias. The suggestion would be to adopt a scale more flexible, assuming a linear indirect effect of the number of adequately answered questions and risk of bias. The higher the number of adequate answers, the lower the risk of bias. However, a scale used in the literature uses thresholds to assess the quality and it has been well accepted.

This study adds to knowledge of the relationship between enamel defects and dental caries. Our findings indicated that more studies exploring this specific topic are needed, in order to elucidate the different mechanisms that may be involved in this association. Additionally, we believe that these findings can be useful in the prevention of early childhood dental caries, once it is possible to identify the potential risk factors in the very early stages of life. Such information is essential for planning dental health education programmes aimed to reduce the occurrence of dental caries. However, it is important to mention that the design of all included studies was cross-sectional, making it impossible to determine the temporal relationship between diseased states.[39] There is need to carry out other investigations (prospective) to assess this association between DDE and dental caries, and mainly, the directionality of this relationship.

Finally, because dental caries and DDE may share key risk factors, such as a disadvantaged background, a common risk approach should be more rational instead of focusing one specific condition.[40]

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