Special Article

Prevalence of Developmental Enamel Defects in Children with Cleft Lip and Palate: A Systematic Review

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Background: Developmental defects of the enamel [DDE] are a widespread problem among children with cleft lip/palate.

Objective: Our aim was to conduct a systematic literature review regarding the prevalence of DDE in children with cleft lip/palate.

Materials and Methods: A systematic literature search was conducted of PubMed for the years between 1961 and 2018. The key search terms were 'children with cleft lip palate' and 'developmental defect of enamel', or 'enamel defect'. Two trained reviewers conducted a risk of bias assessment using a nine-item checklist for prevalence studies.

Results: From the 7 selected full articles, the analysis of pooled prevalence of DDE in primary teeth was 53.3% vs. 32.4% in permanent teeth. Teeth adjacent to the cleft side had a higher occurrence of DDE. The risk of bias assessment revealed that most full articles were about the low-risk category.

Conclusion: The present study revealed that the prevalence of DDE in primary teeth was 53.3% vs.32.4%in permanent teeth. The prevalence of DDE in children with cleft lip/palate was high.Early detection of DDE, its effective preventive care, and tooth monitoring are appropriate management of enamel defects in these children.

Keywords: Developmental defect of enamel, Cleft lip, Cleft palate

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Tooth enamel is only formed during tooth development. Ameloblasts are secretory cells that produce dental enamel[(1)]. Development of the primary teeth starts in the 15th gestational week and completes 12 months after birth (second deciduous molar). During enamel formation, the ameloblasts, which are sensitive to environment changes, are susceptible to several external factors that affect development of the organic matrix and its calcification,leading to developmental defects of the enamel [DDE][(2)].

DDE are common in deciduous and permanent maxillary incisors of children.These defects may be classified according to their macroscopic appearance in two main categories. First, hypoplasia is a defect involving the surface of the enamel and is associated with a reduced thickness of the enamel. Hypoplasia can occur in the form of (a) pits, (b) grooves, or (c) large areas of missing enamel. Second, hypomineralized enamel comprises (a) demarcated opacity, and (b) diffuse opacity. In the former,the defective enamel is of normal thickness with a smooth surface; it has a clear boundary with the adjacent normal enamel and can be white, cream, yellow, or brown; the lesions vary in extent, position on the tooth surface, and distribution in the mouth[(2)]. In the latter, the defect involves an alteration in the translucency of the enamel, variable in degree; the defective enamel is of normal thickness and at eruption has a smooth surface and is white; it can have a linear, patchy, or continuous distribution,

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but there is no clear boundary with the adjacent normal enamel, and part or all the tooth surface can be affected[2-3].

The effects of DDE may include tooth sensitivity or an increased risk of caries. The affected children may also experience low self-esteem or stigma because they perceive DDE as being disfiguring[4,5]. Previous studies reported that developmental of DDE was common in deciduous and permanent maxillary incisors of individuals with cleft lip/palate, and their occurrence was associated with the cleft, especially when the alveolus was affected[6,7].

The objective of the current systematic review was to assess the prevalence of DDE in children with cleft lip/palate.

Materials and Methods

A systematic literature search was conducted for the years between 1961 and 2018, using PubMed. The key search terms were 'children with cleft lip palate', 'developmental defect of enamel', and 'enamel defect'.

Selection criteria

Studies published about children with cleft lip/palate where the prevalence of DDE was reported were included in the review. The inclusion criteria were: 1) observational studies; 2) studies where prevalence data can be extracted or calculated. The exclusion criteria were: 1) conference proceedings; 2) editorials or letters; and 3) case reports. Only articles published in English were included. Both authors performed the search independently using these criteria. Disagreements were resolved by consensus.

Search strategy

Papers containing these terms in any language were included and searched. The titles and abstracts of 65 relevant articles were screened independently by WW and WWb to identify articles for which there were full text publications. The authors then selected relevant articles, including those reporting on the prevalence of DDE in children with cleft lip/palate. Reference lists of included papers were screened for additional papers that may have been missed in the database search[6].

Definitions

The definition of developmental defects of enamel [DDE] was "a defect of enamel which disturbs enamel formation and may manifest as enamel hypoplasia or hypomineralized enamel"[7]. Enamel hypoplasia was defined as a quantitative defect associated with a reduced or altered amount of enamel, appearing as grooves and pits or a partial or total lack of surface enamel. Hypomineralized enamel was defined as a defect involving alteration in the translucency of the enamel[7].

Study selection

Two reviewers (WW, WWb) selected relevant articles by critical appraisal of the full text of each study. Disagreements between reviewers were discussed with reference to the protocol or a third reviewer (WS) was consulted.

Risk of bias assessment

All of the articles after full-text screening were subjected to a risk of bias assessment, using a nine-item checklist adapted from Hoy et al[8]. Based on the assessment checklists, studies were identified as reporting on a high (7 to 9), moderate (4 to 6), or low-risk (0 to 3). The risk of bias assessment was done by two trained and calibrated reviewers (WW and WWb). Disagreements were resolved by consensus.

Data extraction

A specially designed data extraction form was used to record information from each study. Information included were types of study design, years, location, number of children with cleft lip/palate, age, number of children with DDE in primary teeth in cleft lip/palate,number of children with DDE in permanent teeth in cleft lip/palate, DDE by type of cleft lip/palate, and location of DDE. The extracted information was reported and the prevalence of DDE in children with cleft lip/palate calculated.

Statistical analysis

The summary measure was the prevalence rate of DDE in children with cleft lip/palate. The statistical analyses included frequency and prevalence. DDE was divided into two subgroups, according to the type of teeth (i.e., primary or permanent). Calculation of the pooled prevalence rate of each subgroup was performed. Evaluation of the prevalence of DDE by location was determined by magnitude of percentage.

Results

The search combination in the databases identified 65 relevant articles. After a thorough evaluation of each article using the title and study selection criteria, the authors excluded 47 articles. Of

the 18 remaining articles, 12 were excluded due to incomplete data. From among the 6 remaining papers, 1 additional study was found after checking the references. The additional study was not initially retrieved by the original search because it was not indexed in the databases. In total, 7 reports were eligible for inclusion into the systematic review (Figure 1).

From among the 7 selected full articles, 876 children were identified with cleft lip/palate; these were divided into 3 groups. The respective number of children who had primary, mix dentition, and permanent teeth was 193, 530, and 153. The number of children with DDE in primary teeth in the cleft lip/palate was 385. The total number of children with primary teeth was 723. The pooled prevalence rate of DDE in the primary teeth was 53.3%. The number of children with DDE in permanent teeth in cleft lip/palate was 221. The number of children who had permanent teeth was 683, so the pooled prevalence rate of DDE in permanent teeth was 32.4%. Teeth adjacent to the cleft side had a greater occurrence of DDE (Table 1).

Risk of bias assessment

The risk of bias assessment was done for 7 publications of which 5 were low-risk studies. Two were moderate risk due to (1) use of a of non-representative population, (2) the samples were not selected by random sampling, or (3) the same mode of data collection was not used for all individuals.

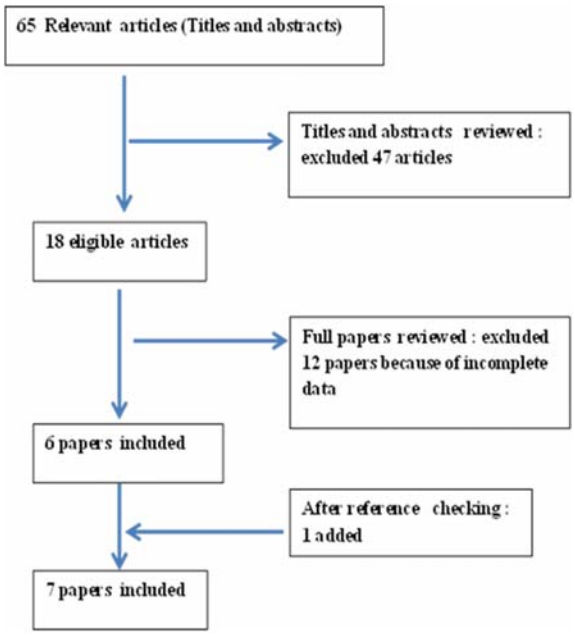

Figure 1. Flow diagram of papers searched and included in the systematic review.

Discussion

The present study revealed that the prevalence of DDE in primary teeth ranged between 34.4% and 82.8% vs. between 24% and 92.5% for permanent teeth. Salanitri and Seow found that among healthy children, the prevalence of DDE in primary teeth ranges between 4% and 49%[14]. Basha et al reported that among healthy children, the prevalence of DDE in permanent teeth varies between 20% and 77%[15]. The prevalence of DDE trended to be more frequent among children with clefts than children without. DDE affected teeth adjacent to the cleft more often than teeth on the non-cleftside[6,10], especially anterior teeth. In individuals with cleft lip/palate, a specific etiological factor for development of enamel defects is uncertain[10]. Ruiz et al suggested that because of the association between chronological development of cleft lip/palate (in the 3rd to 12th embryological week) and dental development (in the 6th to 20th embryological week), it is possible that a metabolic disorder could cause development of the cleft and enamel defect of the teeth adjacent to the cleft side[10].

A quality assessment tool was developed and modified by Hoy et al in 2012[8]. It was reportedly easy to use with good reliability. To eliminate any chance of subjectivity in the quality assessment, two calibrated reviewers conducted the exercise with disagreements resolved by consensus.

The etiology of enamel defects could be caused by local, systemic, environmental, or genetic factors, and most cases were multifactorial in nature. The rank of most common causes of localized enamel defects were surgery in the area adjacent to the cleft palate repair, infection, and trauma. Cleft palate repair caused localized enamel defects in the permanent teeth;the defects ranged from demarcated opacities to hypoplastic defects[16,17]. Chronic radicular infection resulting from pulpal necrosis in a primary tooth may result in pulpal necrosis, resulting in DDE in the succedaneous permanent teeth[18,19]. Trauma to the developing tooth germ such as exerted through the laryngoscope or endotracheal intubation is known to cause damage to the ameloblasts, and result in opacities or hypoplasia in pre-term children[20].

Systemic peri-natal factors and post-natal problems, hypoxia, and malnutrition may be related to the occurrence of DDE in primary and permanent teeth.

Table 1. Prevalence of DDEin children with cleft lip/palate

Authors/Year/ Location of study	Type of study design	Age (years)	Children with cleft (N)			Children with DDE in primary teeth N (%)	Children with DDE in permanent teeth N (%)	DDE by type of cleft lip/palate	Location of DDE
			Primary teeth	Mix dentition	Permanent teeth				
Kulas et al/2016/ Germany[9]	a case-control study	6 to 18	-	73	-	NA	- 29 (39.7) % opacity of enamel	NA	NA
Ruiz et al/2013/ Brazil[10]	cross-sectional study	>12	-	-	80	NA	-74 (92.5%) of total included: - 41 (51.25%) enamel hypoplasia - 33 (41.25%) opacity of enamel	- 47.4% bilateral cleft lip and palate - 52.6% unilateral cleft	- 40% middle third of anterior teeth was highest - 33% incisal third - 27% cervical third - 51.6% on right cleft side - 48.4% on left cleft side;
Pegelow et al/2012/ Sweden[11]	retro-spective study	5, 7, 10	-	129	-	NA	- 62 (48.05%) of total included: - 34 (26.35%) enamel hypoplasia in central incisor - 28 (21.7%) opacity of enamel in central incisor	- 52.0% unilateral cleft lip and palate - 36.4% unilateral cleft 52.6% unilateral cleft lip and alveolus	- 48.5% central incisor on cleft side
Gomes et al/2009/ Brazil[12]	cross-sectional study	1 to 3	101	-	-	- 43 (42.6%) of total included: - 15 (14.8%) of demarcated opacity - 13 (12.8%) of diffuse opacity - 12 (11.8%) of hypoplasia - 3 (3%) of mixed lesions	NA	NA	- 90.7% of DDE at buccal surface of maxillary central incisor teeth on cleft side,

DDE = developmental defects of enamel, NA = not available

Table 1. cont.

Authors/Year/ Location of study	Type of study design	Age (years)	Children with cleft (N)			Children with DDE in primary teeth N (%)	Children with DDE in permanent teeth N (%)	DDE by type of cleft lip/palate	Location of DDE
			Primary teeth	Mix dentition	Permanent teeth				
Galante et al/2005/ Brazil[7]	cross-sectional study	3 to 10	-	312	-	- 258 (82.8%) hypoplasia in canines	NA	- 43.8% unilateral cleft - 39% bilateral cleft	- 82.8% canine teeth
Maciel et al/2001/ Brazil[6]	cross-sectional study	2 to 11	42	-	48	- 31 (73.8%) opacity of enamel	- 44 (91.6%) opacity of enamel	NA	- 47.6% cleft-adjacent central incisors - 66.66% cleft-adjacent central incisors - 34.1% anterior teeth - 12.2% posterior teeth
Chapple et al/2001/ United Kingdom[13]	cross-sectional study	-4 -8 -12	50 - -	- 16 -	- - 25	-28 (56%) of opacity of enamal in 4 years old - 25 (100%) of opacity of enamel in 12 years old	- (6) 37.5% of enamel hypoplasia in 8 years old - (6) 24% of enamel hypoplasia in 12 years old		
Total			193	530	153				
Percent of DDE						(385/723) x100 = 53.25%	(221/683) x100 = 32.36%		

DDE = developmental defects of enamel, NA = not available

Pre-natal conditions possibly associated with enamel hypoplasia in children include maternal vitamin D deficiency, maternal smoking, increased maternal weight gain, and failure to access antenatal care. Nutritional deficiencies in the infant, particularly those associated with insufficient supply and absorption of calcium and vitamins A, C, and D are well-known risk factors for enamel hypoplasia in pre-term children. Children born prematurely and of low or very low birth weight had a higher prevalence of enamel hypoplasia than full-term children with normal birth weights[21,22].

In regions with high natural levels of fluoride in the drinking water, ingestion of excess fluoride during tooth development could result in dental fluorosis, a form of enamel hypomineralization where the white striations contain less mineral and retain more developmental enamel proteins. The hypomineralization can vary from minor white striations to small or more extensive opacities[23].

The genetic factor involving enamel only is known as amelogenesis imperfecta and defects may present as enamel hypoplasia and/or hypo-mineralization. There is evidence that amelogenesis imperfecta may present as part of a hereditary syndrome[24].

Teeth with DDE often lead to poor self-image and tooth sensitivity. These problems are especially true of hypoplasia, in which the teeth are more susceptible to plaque accumulation and caries. Parents need to know that teeth with enamel defects are highly susceptible to decay and erosion from acids in foods and drinks. Preventive advice given to parents should include replacing cariogenic snacks with healthy foods, twice daily tooth brushing, and topical fluoride application. To reduce sensitivity from tooth brushing, a very soft toothbrush and lukewarm water for mouth rinsing is suggested[14]. Management of enamel defects includes early detection, preventive care, and tooth monitoring.

Limitations

1) The etiology of DDE includes local, systemic, environmental, and genetic factors. Enamel defect can affect both anterior and posterior teeth. Most of the full papers included in this systematic review only examined enamel defects of anterior teeth. If enamel examination included all anterior and posterior teeth, the epidemiological data of enamel defect would be more complete.

2) Data for all individual studies were collected in hospital-based studies, so there was limited generalizability of the results.

3) The prevalence estimates were calculated based on the information from the publications, and no attempt was made to contact the individual authors for the data. The estimates that were presented must be interpreted with caution.

Conclusion

The present study revealed that the prevalence of DDE in primary teeth was 53.3%. The prevalence of DDE in permanent teeth was 32.4%. The prevalence of DDE in children with cleft lip/palate was high. The effects of DDE include tooth sensitivity, increased risk of caries, and affected children experience low self-esteem. Management of enamel defects includes early detection, preventive care, and monitoring.

What is already known on this topic?

Developmental defect of enamel is a widespread problem among children with cleft lip/palate

What this study adds?

The current study presents the prevalence of DDE in primary and permanent teeth. Teeth adjacent to cleft side had a higher occurrence of DDE, especially the anterior teeth.

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Potential conflict of interest

The authors no declare conflicts of interest.

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