

Diagnostic and Preventive Approaches for Dental Caries in Children: A Review

Shahryar Karami,¹ Nazanin Ghobadi,¹ and Hasan Karami^{2,*}

¹Department of Dentistry, Faculty of Dentistry, Mazandaran University of Medical Sciences, Sari, IR Iran

²Department of Pediatric Gastroenterology, Faculty of Medicine, Mazandaran University of Medical Sciences, Sari, IR Iran

*Corresponding author: Hasan Karami, MD, Pediatric Gastroenterologist, Department of Pediatric Gastroenterology, Bouali Sina Hospital, Pasdaran Bulevard, IR Iran. Tel/Fax: +98-1133344506, E-mail: dr_hkarami87@yahoo.com

Received 2017 January 26; Revised 2017 March 05; Accepted 2017 March 07.

Abstract

Context: Oral health status plays an essential role in human health. Recently, enhancement in oral health caries has been noted in both developed and developing countries. Dental caries is still very common among children. Screening and preventive interventions is necessary. The aim of this study was to review the diagnostic and preventive approaches for dental caries in children.

Evidence Acquisition: Searching PubMed, Medline, the Cochrane Library (for 5 recent years from 2011-2016), and reference lists for keywords and phrases such as “dental caries in children” and prevention and diagnosis, we included trials and controlled observational studies regarding the diagnosis and preventive techniques for dental caries in children.

Results: We found no study demonstrating the effects of screening by primary care providers on clinical outcomes. In a cohort study, pediatrician examination associated with a sensitivity of 0.76 was reported to identify dental caries in children. The results of the new randomized trials that were confirmed by previous studies showed that the efficacy of fluoride varnish is more than no varnish in reduction of dental caries from 18% to 59%. Some of the trials regarding xylitol had no results regarding the effects on dental caries. New observational studies have shown an association between early childhood fluoride use and enamel fluorosis. There is no evidence on the accuracy of prediction instruments in primary care settings.

Conclusions: We found no direct evidence that reveals that screening by primary care clinicians can decrease early childhood caries. Previous evidences reviewed by the United State Preventive Services Task Force demonstrated that oral fluoride supplementation is effective in decreasing caries incidences, and recent evidences supported the effectiveness of fluoride varnish in higher-risk children.

Keywords: Dental Caries, Preventive Dentistry, Dental Care for Children

1. Context

Dental caries is known as one of the most common chronic childhood diseases in children (1, 2). The disease remains a predominant oral disease and cavities and also a worldwide public health problem (1). The past 2 decades of researches regarding caries have advanced our knowledge about the disease. Furthermore, in particular, it has demonstrated that caries is a dynamic, multi-factorial disease process involving the interface of the undisturbed plaque biofilm and the surface of the tooth when dietary sugars are present (3). Over the past 20 years, oral health status of populations in industrialized countries has improved significantly, including a significant decline in the prevalence of caries and periodontal diseases due to preventive strategies (1). Dental caries are preventable and can theoretically be controlled by altering bacterial flora in the mouth, modifying diet, and increasing Oral health education (awareness and motivation). Therefore, it is an important element for improving oral hygiene. It must start early from the preschool. In fact, the first permanent mo-

lar (tooth of 6 years) tends to be decayed since its eruption if the child does not brush regularly (4).

The early incidence of dental caries during lifetime, specifically early childhood caries (ECC), is of particular concern. Though generally preventable, and in spite of the significant enhancement of oral health during the past few decades, dental caries is still known as the most common chronic disease among children and adolescents. Indeed, oral health of the children is considered to be related to several factors such as their families, their socioeconomic condition, as well as the parents' education level, occupation, and attitude towards health. The chances for cavities increase by dry mouth, frequent intake of sweets, and poor oral hygiene. The timing of tooth eruption, the duration of harmful dietary habit and the type of muscle movements during sucking and swallowing are the common risk factors of dental caries. The pattern of early childhood caries varies at age 3 and begins to affect the first and second primary molars (1, 2, 5-7). According to mentioned above, this study was conducted to review the diagnostic and preven-

tive approaches for dental caries in children.

2. Evidence Acquisition

We searched PubMed, Medline, and the Cochrane Library Database for relevant articles, and reviewed reference lists for additional citations in 5 recent years from 2011 to 2016. The inclusion criteria were articles published in peer-reviewed journals addressing questions related to dental caries in children population with focus on diagnosis and preventive approaches using phrase and keywords such as “dental caries in children”, prevention, and diagnosis. All abstracts and articles not related to children, surgical intervention of cleft lip and cleft palate, and speech-related interventions were excluded. Herein, we discuss the qualitative results derived from the reviewed articles.

3. Results

3.1. Incidence

In several studies conducted in Europe, the prevalence of ECC reported ranging from 11.4% in 3 - 6 year old Swedish children, to 55.1% in 5 years old children in the Czech Republic, and ranged from 8% to 31.6% in Italy (7-10). In developing countries, an increase of these conditions is observed due the observed changes in eating habits and lack of other prevention policies. Thus, 80% of the people carrying carious lesions around the world are living in these countries (5, 8, 10).

In the Italian population, dental caries demonstrated a consistent burden, interesting almost 20% of 3 - 5 years old children, where as almost 3% were affected by the more severe disease (4). It is also the most common chronic disease of children in the United States, and its prevalence is increasing among 2 to 5 year old children (5).

3.2. Etiology

Dental caries is a disease caused by a number of factors, however, there is no specific method for its assessment that included all etiologic factors of caries (11). These factors consist of consumption of sugar and sugar-containing foods, plaque, inflammation of the gums, high salivary counts of *Streptococcus mutans* in children and mothers, and the attitude of parents towards health (2, 12). When acid-producing species, such as the mutans streptococci, present in plaque biofilm, the process is beginning and they metabolize these dietary sugars to produce lactic and other acids, causing initial demineralization, i.e., the first calcium and phosphate ions loss from the hydroxy apatite structure of the tooth's enamel. This initial step can lead to a reversible early caries lesion. Therefore, inadequate

oral hygiene assessed by the presence of biofilm that adhered to the tooth surface, is associated with new carious lesions in the bivariate analysis (13). Biofilm is related to the presence of cariogenic bacteria and fermentable substances, which leads to demineralization and dental caries. The counts of *Streptococcus mutans* in saliva are widely known as the main etiological factor in the development of caries (14).

Early colonization can increase the risk of caries. Mother's saliva is the most commonly possible rout of streptococcus mutans transmission to an infant (15). By determining the salivary concentration of streptococcus mutans, we can evaluate the rate of caries development (16).

Several risk factors are identified for dental caries including high levels of cariogenic bacteria colonization, inappropriate bottle feeding, frequent exposure to dietary sugar, decreased saliva flow rates, developmental tooth enamel defects, low community water fluoride levels, inadequate tooth brushing or use of fluoride containing toothpastes, and maternal risk factors such as caries, or poor maternal oral hygiene, and lack of parental knowledge related to oral health (17, 18).

The interaction of a number of factors including Inflammation of the gums, dental plaque, counts of streptococcus mutans and attitude towards the child's care are considered to be caries risk-modifying factors. Among these factors, dental plaque is one of the factors that promote caries development (19).

Another predisposing and causative factor for tooth decay is chemical composition of saliva. It is generally accepted that the process of tooth decay is controlled largely by natural immune mechanism of saliva. Salivary pH, Calcium, Phosphorus, and Fluoride are important. In addition, salivary flow rate and concentration is also involved in development of caries. Normal salivary flow eliminates the food debris on which microorganisms thrive. In addition, saliva has antibacterial and antiseptic properties. Disturbing the natural salivary flow, salivary composition, and viscosity, caries develop. Conditions that decrease salivary flow include immune disorders, genetic conditions, drug consumption, and neuropsychiatric disturbances. Medications, such as antihistamines and antidepressants, can also impair salivary flow. Studies have shown that the minimum effective dose of antihistamines can reduce salivary flow by as much as 50% (20, 21).

Several studies reported the use of bottle feeding and breastfeeding as ECC risk factors, whereas the results of other studies found no effect by the 2 risk factors or differences between them (22-26). The length of breast and bottle feeding may play a role to caries development. Various studies have been demonstrated late weaning e.g., between 12 and 36 months was associated with caries (27).

However, other studies reported no relationship between the age of weaning from breast or bottle with caries (28-30). Higher risk for ECC was reported in children who received nocturnal bottle feeding (22, 26).

Another risk factor for dental caries in children is nocturnal breastfeeding, and its frequency, particularly if more than twice throughout the night with a duration more than 15 minutes (31). However other studies did not show an association between nocturnal feeding and caries (22, 32).

The nutritional assessment is an important part of clinical evaluation in children with dental caries. Long term Ca+Vitamin D malabsorption can lead to reduced bone mineral density and increased dental caries. Vitamin deficiency, especially vitamin A and vitamin C, increase periodontal disease. Clinical findings same as diarrhea, steatorrhea, FTT, and specific lab test may be useful for the detection of malabsorption disease such as celiac (33-37).

Delayed starting of tooth brushing for example, after 12 months of age, is slightly controversial. Frequency of brushing, bedtime brushing, and time spending for brushing were found to be associated with ECC in some studies, however, no association between frequency of tooth brushing and caries has been reported by other studies (29, 32, 38, 39).

3.3. Diagnosis

The manifestations of ECC are included pain, tooth loss, as well as growth impairment, weight loss, and negative effects on speech, appearance, self-esteem, school performance, and quality of life (3, 5).

Traditionally, visual and tactile inspection along with radiographs (X-rays) are employed frequently for dental caries diagnosis. This approach requires visual identification of demineralized areas (typically white spots), pits, or fissures, and using a dental explorer to evaluate the softness of dental enamel or breaks in it. Advanced methods for early decay detection is infrared laser fluorescence. It has a stabilized diode laser and a fiber optic cable that transmits light to the probe that emits light directed on the mineralized surface to be examined. Dental enamel absorbs infrared light, causing infrared fluorescence. Fluorescence light emitted will be captured back by the probe and processed. The device will display values ranging from 0 to 99. Elevated fluorescence reading values, especially above 20, is sign of tooth decay. Techniques for the assessment and early detection of caries are infrared and red fluorescence (Other advanced Midwest caries ID), measurable fluorescence (Quantitative light-induced fluorescence), caries ID, and measurable fluorescence (quantitative light-induced fluorescence) (20).

3.4. Prevention

Brushing with fluoridated toothpaste is one of the measures for caries prevention (40). However, this preventive measure may be inadequate in young children, due to their poor dexterity (41). Thus, brushing should be practiced or supervised by parents/caregivers until the child is able to perform it alone (42). Indeed, the association between dental caries and the recurrence of visible plaque may be related to a lack of oral hygiene monitoring by parents/caregivers. However, the multivariate model revealed that oral hygiene did not remain associated with new carious lesions (43). In 2004, the US preventive services task force (USPSTF) has recommended the primary care clinicians to prescribe dietary fluoride supplementation for children 6 months of age whose primary water source is deficient in fluoride (44). No trial specifically evaluated the effectiveness of oral health education or counseling intervention by a primary care clinician in preventing dental caries. Non-randomized clinical trials reported multifactorial interventions including an educational component that is associated with decreased caries outcomes in deprived, 5 years old children (40, 45, 46).

Further pediatrician training, electronic medical record reminders, and providing of tooth-brushing materials are other components of the interventions. No study directly assessed the effects of dental referral by a primary care clinician to a dentist on caries incidence (47).

Several chemotherapeutic agents such as antibiotics, various types of fluoride agents, and metal ions have been tested for preventing and arresting caries (48, 49). It is shown that dietary fluoride supplementation with water fluoridation levels below 0.6 ppm reduced caries incidence versus no fluoridation ranging from 48% to 72% for primary teeth and 51% to 81% for primary tooth surfaces (50). The results of 2 trials with prolonged follow-up also revealed that consumption of dietary fluoride supplement was associated with lower incidence of caries at 7 to 10 years of age ranged from 33% to 80% (50, 51).

Comparison of fluoride varnish (2.26% F) used every 6 months with no fluoride varnish has been reevaluated by the trials published since the 2004 USPSTF. The results of all trials in the 2004 USPSTF review showed that the incidence of caries decreased following use of fluoride varnish after 2 years. The reduction rates of the decay-missing-filled (DMF) increment were reported as 18% and 24% in the 2 trials, 59% in 1 trial, and the absolute mean reductions reported in the number of affected surfaces ranged from 1.0 to 2.4 (51-54).

The results of the new studies found an association between consumption of fluoride supplements before 7 years of age (primarily before 3 years of age) and increasing risk

of fluorosis (55). Updated systematic review on the professionally, acidulated phosphate fluoride (APF) has been used to control dental caries since the 1970s, and its anti-carries effectiveness has been approved (56). The application of the APF gel has been suggested as a therapeutic approach for dental caries in specific risk situations, such as compensation for lack of self-use of fluoride products or in individuals with history of caries experience (44, 46, 48, 49, 57). Another alternative for safe gel use in children is reducing the time of gel application from 4 minutes to 1 minute, because both time periods lead to equally efficient enamel retention and reduction of demineralization. Compared to other types of topical fluorides, fluoride gel has the best cost benefit relationship (58). However, adverse effects following use of fluoride gel depending upon the method of application have been reported especially in children. For example, gastrointestinal side effects such as nausea, vomiting, and abdominal pain have been reported following ingestion of 15 to 31 mg of fluoride (17, 19, 59).

Although the results of a study on anticaries effect of salivary retention of fluoride does not necessarily reveal the anticaries effect of topical fluoride application, they can provide some indication of dose-effective methods of application (60). The low dose of fluoride (6.4 mg) used in this experiment on a toothbrush was much lower than an acute toxic dose (5.0 mg fluoride/kg) in a child weighing about 20 kg. Thus, application of gel with a toothbrush offers more safety, especially when it's indicated for public health plans (45), such as school programs. Xylitol is a naturally-occurring 5-Carbon Polyol Sugar Substitute that has been widely studied during the last 40 years for treatment of dental caries. The mechanism of action of Xylitol as a low-calorie sweetener, which is found in toothpaste, foods, and widely in gums, is inhibiting the growth of *S. mutans* (46, 47).

The result of a randomized trial showed that Xylitol wipes used 3 times per day for 1 year markedly was more effective than placebo wipes to reduce caries in children between 6 to 35 months of life (61). Although the results of a clustered randomized trial showed no difference between the use of 65% xylitol gum 3 times per day and tooth brushing with fluoride, performing in a supervised day care setting, and enrolled children up to 6 years of age, potentially had limited its applicability to younger children (62). In a trial, diarrhea was reported by 11% of children allocated to xylitol chewing gum or syrup (63). Nano Silver Fluoride 1 (NSF) is a novel experimental formulation, which contains silver nanoparticles, chitosan, and fluoride. These combinations provide preventive and antimicrobial properties against Mutans streptococci and Lactobacilli with as effective as an anti-carries agent without staining the porous dental tissues black, as does silver diamine fluoride (SDF)

and amalgam. NSF is low in cost substance and available as a yellow solution that proves to be stable for 3 years (64). SDF has been shown to be more effective than fluoride varnish (63). It is suggested that this superior effect could be due to the fluoride concentration on SDF, which is greater than what is found in the fluoride varnish (65).

Though, the effect of SDF on caries lesions could be described by both fluoride action, and by the silver ions, due to reaction with thiol groups in amino and nucleic acids leading to bacterial lysis (66). Thus consequently leading to probable quicker caries arrestment (67), especially compared to other options of arresting initial caries lesions such as other fluorides. The use of SDF causes some aesthetic concerns such as black staining on carious lesions caused by precipitation of silver (68). Nevertheless, aesthetics was not considered to be threatened in the case of initial caries lesions on proximal surfaces of posterior teeth due to their localization. Comparison of the new dentifrice containing 1.5% arginine, an insoluble calcium compound, and 1450 ppm fluoride, as MFP, with conventional 1450 ppm fluoride dentifrice have demonstrated a significant improvement in the anti-carries efficacy (29). The basis of this therapeutic approach, which uses a combination of arginine and an insoluble calcium compound, is to complement and improve the effects of fluoride by specifically targeting dental plaque, modifying its metabolism to decrease the production, and effects of bacterial acid that result in reducing its pathogenicity (69). Non-pathogenic arginolytic organisms, metabolize the arginine component to ammonia that has an arginine deiminase pathway. This ammonia neutralizes plaque acids and stabilizes the residual plaque biofilm on vulnerable tooth surfaces. Thus, arginine can prevent a shift in oral flora to aciduric bacterial species, such as *S. mutans*, by maintaining a more basic plaque pH, encouraging re-mineralization, and reducing de-mineralization due to less acid production. Furthermore, the insoluble calcium compound is accessible as a source of free calcium ions to add on the re-mineralization process (69, 70).

Caries vaccine is another preventive method against tooth decay, which has used from 1940. Since *S. mutans* is known as the main etiological agent of human dental caries, the caries vaccine is also provided from the killed form of the microbe injected in mouth of animal samples. The vaccine is usually administered by absorbing the inner lining of the mouth or nose, which requires more research and more comprehensive researches to use in humans (71).

4. Conclusions

In the current health care plan, caries risk assessment is a useful component in providing dental care in children.

Risk assessment procedures in children consists of evaluating risk factors in children and oral examination. In evaluating risk factors, clinical evaluation by examination, treatment, and diagnosis assessment are done. Assessment of risk factors include salivary secretion disorders, benefit from dental services, family history of dental caries, socio-economic status of the family, snack and sugar consumption, exposure to fluoride, and toothbrushes. In the oral examination, visible dental plaque, gingivitis, and tooth enamel defects are evaluated. When caries-risk assessment tool (CAT) and routine examination or symptomatic signs of the child results in tooth decay detection, restorative treatment should be done.

Footnotes

Financial Disclosure: None.

Funding/Support: None.

References

- Petersen PE. The World Oral Health Report 2003: continuous improvement of oral health in the 21st century—the approach of the WHO Global Oral Health Programme. *Community Dent Oral Epidemiol.* 2003;**31**(Suppl 1):3-23.
- Sheiham A. Dietary effects on dental diseases. *Public Health Nutr.* 2001;**4**(2B):569-91. [PubMed: [11683551](#)].
- Wigen TI, Espelid I, Skaare AB, Wang NJ. Family characteristics and caries experience in preschool children. A longitudinal study from pregnancy to 5 years of age. *Community Dent Oral Epidemiol.* 2011;**39**(4):311-7. doi: [10.1111/j.1600-0528.2010.00596.x](#). [PubMed: [21114517](#)].
- Nobile CG, Fortunato L, Bianco A, Pileggi C, Pavia M. Pattern and severity of early childhood caries in Southern Italy: a preschool-based cross-sectional study. *BMC Public Health.* 2014;**14**:206. doi: [10.1186/1471-2458-14-206](#). [PubMed: [24571668](#)].
- Benjamin RM. Oral health: the silent epidemic. *Public Health Rep.* 2010;**125**(2):158-9. doi: [10.1177/003335491012500202](#). [PubMed: [20297740](#)].
- Ismail AI, Sohn W. The impact of universal access to dental care on disparities in caries experience in children. *J Am Dent Assoc.* 2001;**132**(3):295-303. [PubMed: [11258086](#)].
- Wennhall I, Matsson L, Schroder U, Twetman S. Caries prevalence in 3-year-old children living in a low socio-economic multicultural urban area in southern Sweden. *Swed Dent J.* 2002;**26**(4):167-72. [PubMed: [12611146](#)].
- Stromberg U, Holmn A, Magnusson K, Twetman S. Geo-mapping of time trends in childhood caries risk—a method for assessment of preventive care. *BMC Oral Health.* 2012;**12**:9. doi: [10.1186/1472-6831-12-9](#). [PubMed: [22510486](#)].
- Lencova E, Pikhart H, Broukal Z. Early childhood caries trends and surveillance shortcomings in the Czech Republic. *BMC Public Health.* 2012;**12**:547. doi: [10.1186/1471-2458-12-547](#). [PubMed: [22828200](#)].
- Panetta F, Dall'Oca S, Nofroni I, Quaranta A, Polimeni A, Ottolenghi L. Early childhood caries. Oral health survey in kindergartens of the 19th district in Rome. *Minerva Stomatol.* 2004;**53**(11-12):669-78. [PubMed: [15894942](#)].
- Reich E, Lussi A, Newbrun E. Caries-risk assessment. *Int Dent J.* 1999;**49**(1):15-26. [PubMed: [10887469](#)].
- Hansel Petersson G, Twetman S, Bratthall D. Evaluation of a computer program for caries risk assessment in schoolchildren. *Caries Res.* 2002;**36**(5):327-40. [PubMed: [12399693](#)].
- Stokes E, Ashcroft A, Burnside G, Mohindra T, Pine CM. Randomised controlled trial of the efficacy of a high-fluoride gel self-applied by toothbrushing in children at high caries risk. *Caries Res.* 2011;**45**(5):475-85. doi: [10.1159/000331205](#). [PubMed: [21912128](#)].
- Harris R, Nicoll AD, Adair PM, Pine CM. Risk factors for dental caries in young children: a systematic review of the literature. *Community Dent Health.* 2004;**21**(1 Suppl):71-85. [PubMed: [15072476](#)].
- Berkowitz RJ. Mutans streptococci: acquisition and transmission. *Pediatr Dent.* 2006;**28**(2):106-9. [PubMed: [16708784](#)] discussion 192-8.
- Petti S, Bossa MC, Tarsitani G, Falcolini G, Lumbau A, Campus G. Variables affecting salivary Streptococcus mutans counts in a cohort of 12-year-old subjects. *Minerva Stomatol.* 1999;**48**(9):361-6. [PubMed: [10638169](#)].
- Tinanoff N, Reisine S. Update on early childhood caries since the Surgeon General's Report. *Acad Pediatr.* 2009;**9**(6):396-403. doi: [10.1016/j.acap.2009.08.006](#). [PubMed: [19945074](#)].
- Marsh PD. Microbiologic aspects of dental plaque and dental caries. *Dent Clin North Am.* 1999;**43**(4):599-614. [PubMed: [10553246](#)] v-vi.
- Dietary effects on dental diseases. *Public Health Nutr.* 2001;**4**(2B):569-91. [PubMed: [11683551](#)].
- Busscher HJ, van der Mei HC. Physico-chemical interactions in initial microbial adhesion and relevance for biofilm formation. *Adv Dent Res.* 1997;**11**(1):24-32. doi: [10.1177/08959374970110011301](#). [PubMed: [9524439](#)].
- Ramos-Gomez FJ, Weintraub JA, Gansky SA, Hoover CI, Featherstone JD. Bacterial, behavioral and environmental factors associated with early childhood caries. *J Clin Pediatr Dent.* 2002;**26**(2):165-73. [PubMed: [11878278](#)].
- Menghini G, Steiner M, Thomet E, Roos M, Imfeld T. Caries prevalence in 2-year-old children in the city of Zurich. *Community Dent Health.* 2008;**25**(3):154-60. [PubMed: [18839721](#)].
- Al-Jewair TS, Leake JL. The prevalence and risks of early childhood caries (ECC) in Toronto, Canada. *J Contemp Dent Pract.* 2010;**11**(5):001-8. [PubMed: [20978718](#)].
- Nunes AM, Alves CM, Borba de Araujo F, Ortiz TM, Ribeiro MR, Silva AA, et al. Association between prolonged breast-feeding and early childhood caries: a hierarchical approach. *Community Dent Oral Epidemiol.* 2012;**40**(6):542-9. doi: [10.1111/j.1600-0528.2012.00703.x](#). [PubMed: [22725605](#)].
- Declerck D, Leroy R, Martens L, Lesaffre E, Garcia-Zattera MJ, Vandenberghe S, et al. Factors associated with prevalence and severity of caries experience in preschool children. *Community Dent Oral Epidemiol.* 2008;**36**(2):168-78. doi: [10.1111/j.1600-0528.2007.00385.x](#). [PubMed: [18333881](#)].
- Seow WK, Clifford H, Battistutta D, Morawska A, Holcombe T. Case-control study of early childhood caries in Australia. *Caries Res.* 2009;**43**(1):25-35. doi: [10.1159/000189704](#). [PubMed: [19136829](#)].
- Hallonsten AL, Wendt LK, Mejare I, Birkhed D, Hakansson C, Lindvall AM, et al. Dental caries and prolonged breast-feeding in 18-month-old Swedish children. *Int J Paediatr Dent.* 1995;**5**(3):149-55. [PubMed: [9601235](#)].
- Hallett KB, O'Rourke PK. Pattern and severity of early childhood caries. *Community Dent Oral Epidemiol.* 2006;**34**(1):25-35. doi: [10.1111/j.1600-0528.2006.00246.x](#). [PubMed: [16423028](#)].
- Tiberia MJ, Milnes AR, Feigal RJ, Morley KR, Richardson DS, Croft WG, et al. Risk factors for early childhood caries in Canadian preschool children seeking care. *Pediatr Dent.* 2007;**29**(3):201-8. [PubMed: [17688016](#)].
- Cogulu D, Ersin NK, Uzel A, Eronat N, Aksit S. A long-term effect of caries-related factors in initially caries-free children. *Int J Paediatr Dent.* 2008;**18**(5):361-7. [PubMed: [18802994](#)].

31. van Palenstein Helderma WH, Soe W, van 't Hof MA. Risk factors of early childhood caries in a Southeast Asian population. *J Dent Res.* 2006;**85**(1):85-8. doi: [10.1177/154405910608500115](https://doi.org/10.1177/154405910608500115). [PubMed: [16373687](https://pubmed.ncbi.nlm.nih.gov/16373687/)].
32. Tsai AI, Chen CY, Li LA, Hsiang CL, Hsu KH. Risk indicators for early childhood caries in Taiwan. *Community Dent Oral Epidemiol.* 2006;**34**(6):437-45. doi: [10.1111/j.1600-0528.2006.00293.x](https://doi.org/10.1111/j.1600-0528.2006.00293.x). [PubMed: [17092272](https://pubmed.ncbi.nlm.nih.gov/17092272/)].
33. Mehrani J, Karami H, Karami S, Ghobadi N. Effects of Nutritional Composition on Periodontal Disease. *JCE.* 2015;**3**(2):34-55.
34. Karami Sh, Ghobadi N, Karami H. Diagnostic Approach and Treatment in Children's Dental Fracture [Persian]. *JCE.* 2016;**5**(1):123-13.
35. Shahraki T, Farahmand F, Shahraki M, Karami H. Clinical and laboratory findings of celiac disease in patients referred to children medical center (tehran; Iran). *JBUMS.* 2009;**11**(4):69-74.
36. Van der Velden U, Kuzmanova D, Chapple IL. Micronutritional approaches to periodontal therapy. *J Clin Periodontol.* 2011;**38** Suppl **11**:142-58. doi: [10.1111/j.1600-051X.2010.01663.x](https://doi.org/10.1111/j.1600-051X.2010.01663.x). [PubMed: [21323711](https://pubmed.ncbi.nlm.nih.gov/21323711/)].
37. Karami H, Kianifar HR, Karami S. Principle of Nutrition in Infant and children [Persian]. Sari: Mazandaran University of Medical Sciences; 2015.
38. Aida J, Ando Y, Oosaka M, Niimi K, Morita M. Contributions of social context to inequality in dental caries: a multilevel analysis of Japanese 3-year-old children. *Community Dent Oral Epidemiol.* 2008;**36**(2):149-56. doi: [10.1111/j.1600-0528.2007.00380.x](https://doi.org/10.1111/j.1600-0528.2007.00380.x). [PubMed: [18333879](https://pubmed.ncbi.nlm.nih.gov/18333879/)].
39. Gao XL, Hsu CY, Xu YC, Loh T, Koh D, Hwang HB. Behavioral pathways explaining oral health disparity in children. *J Dent Res.* 2010;**89**(9):985-90. doi: [10.1177/0022034510372896](https://doi.org/10.1177/0022034510372896). [PubMed: [20554887](https://pubmed.ncbi.nlm.nih.gov/20554887/)].
40. Kressin NR, Nunn ME, Singh H, Orner MB, Pbert L, Hayes C, et al. Pediatric clinicians can help reduce rates of early childhood caries: effects of a practice based intervention. *Med Care.* 2009;**47**(11):1121-8. doi: [10.1097/MLR.0b013e3181b58867](https://doi.org/10.1097/MLR.0b013e3181b58867). [PubMed: [19786919](https://pubmed.ncbi.nlm.nih.gov/19786919/)].
41. Casamassimo PS, Thikkurissy S, Edelstein BL, Maiorini E. Beyond the dmft: the human and economic cost of early childhood caries. *J Am Dent Assoc.* 2009;**140**(6):650-7. [PubMed: [19491160](https://pubmed.ncbi.nlm.nih.gov/19491160/)].
42. Calonge N, U. S. Preventive Services Task Force . Prevention of dental caries in preschool children: recommendations and rationale. *Am J Prev Med.* 2004;**26**(4):326-9. doi: [10.1016/j.amepre.2004.01.008](https://doi.org/10.1016/j.amepre.2004.01.008). [PubMed: [15110060](https://pubmed.ncbi.nlm.nih.gov/15110060/)].
43. Correa-Faria P, Martins-Junior PA, Vieira-Andrade RG, Marques LS, Ramos-Jorge ML. Factors associated with the development of early childhood caries among Brazilian preschoolers. *Braz Oral Res.* 2013;**27**(4):356-62. doi: [10.1590/S1806-83242013005000021](https://doi.org/10.1590/S1806-83242013005000021). [PubMed: [23780495](https://pubmed.ncbi.nlm.nih.gov/23780495/)].
44. Bader JD, Rozier RG, Lohr KN, Frame PS. Physicians' roles in preventing dental caries in preschool children: a summary of the evidence for the U.S. Preventive Services Task Force. *Am J Prev Med.* 2004;**26**(4):315-25. doi: [10.1016/j.amepre.2003.12.001](https://doi.org/10.1016/j.amepre.2003.12.001). [PubMed: [15110059](https://pubmed.ncbi.nlm.nih.gov/15110059/)].
45. Davies GM, Duxbury JT, Boothman NJ, Davies RM. Challenges associated with the evaluation of a dental health promotion programme in a deprived urban area. *Community Dent Health.* 2007;**24**(2):117-21. [PubMed: [17615828](https://pubmed.ncbi.nlm.nih.gov/17615828/)].
46. Davies GM, Duxbury JT, Boothman NJ, Davies RM, Blinkhorn AS. A staged intervention dental health promotion programme to reduce early childhood caries. *Community Dent Health.* 2005;**22**(2):118-22. [PubMed: [15984138](https://pubmed.ncbi.nlm.nih.gov/15984138/)].
47. Beil H, Rozier RG, Preisser JS, Stearns SC, Lee JY. Effect of early preventive dental visits on subsequent dental treatment and expenditures. *Med Care.* 2012;**50**(9):749-56. doi: [10.1097/MLR.0b013e3182551713](https://doi.org/10.1097/MLR.0b013e3182551713). [PubMed: [22525611](https://pubmed.ncbi.nlm.nih.gov/22525611/)].
48. US Department of Health and Human Services . Oral Health in America: A report of the Surgeon General. Rockville: National Institutes of Health; 2000.
49. Dye BA, Tan S, Smith V, Lewis BG, Barker LK, Thornton-Evans G, et al. Trends in oral health status: United States, 1988-1994 and 1999-2004. *Vital Health Stat 11.* 2007;**248**:1-92. [PubMed: [17633507](https://pubmed.ncbi.nlm.nih.gov/17633507/)].
50. Lin YT, Tsai CL. Comparative anti-caries effects of tablet and liquid fluorides in cleft children. *J Clin Dent.* 2000;**11**(4):104-6. [PubMed: [11460274](https://pubmed.ncbi.nlm.nih.gov/11460274/)].
51. Margolis FJ, Reames HR, Freshman E, MacCauley CD, Mehaffey H. Fluoride. Ten-year prospective study of deciduous and permanent dentition. *Am J Dis Child.* 1975;**129**(7):794-800. [PubMed: [1096595](https://pubmed.ncbi.nlm.nih.gov/1096595/)].
52. Slade GD, Bailie RS, Roberts-Thomson K, Leach AJ, Raye I, Ender C, et al. Effect of health promotion and fluoride varnish on dental caries among Australian Aboriginal children: results from a community-randomized controlled trial. *Community Dent Oral Epidemiol.* 2011;**39**(1):29-43. doi: [10.1111/j.1600-0528.2010.00561.x](https://doi.org/10.1111/j.1600-0528.2010.00561.x). [PubMed: [20707872](https://pubmed.ncbi.nlm.nih.gov/20707872/)].
53. Chou R, Cantor A, Zakher B, Mitchell JP, Pappas M. Preventing dental caries in children <5 years: systematic review updating USPSTF recommendation. *Pediatrics.* 2013;**132**(2):332-50. doi: [10.1542/peds.2013-1469](https://doi.org/10.1542/peds.2013-1469). [PubMed: [23858419](https://pubmed.ncbi.nlm.nih.gov/23858419/)].
54. Chou R, Cantor A, Zakher B, Mitchell JP, Pappas M. Prevention of dental caries in children younger than 5 years old. Rockville: Agency for Healthcare Research and Quality; 2014.
55. Bottenberg P, Declerck D, Ghidry W, Bogaerts K, Vanobbergen J, Martens L. Prevalence and determinants of enamel fluorosis in Flemish schoolchildren. *Caries Res.* 2004;**38**(1):20-8. doi: [10.1159/000073916](https://doi.org/10.1159/000073916). [PubMed: [14684973](https://pubmed.ncbi.nlm.nih.gov/14684973/)].
56. Selwitz RH, Ismail AI, Pitts NB. Dental caries. *Lancet.* 2007;**369**(9555):51-9. doi: [10.1016/S0140-6736\(07\)60031-2](https://doi.org/10.1016/S0140-6736(07)60031-2). [PubMed: [17208642](https://pubmed.ncbi.nlm.nih.gov/17208642/)].
57. National Center for Health Statistics . Healthy people 2010: Final review. Hyattsville: US Government Printing Office; 2012.
58. Kawashita Y, Kitamura M, Saito T. Early childhood caries. *Int J Dent.* 2011;**2011**:725320. doi: [10.1155/2011/725320](https://doi.org/10.1155/2011/725320). [PubMed: [22007218](https://pubmed.ncbi.nlm.nih.gov/22007218/)].
59. Grodzka K, Augustyniak L, Budny J, Czarnocka K, Janicha J, Mlosek K, et al. Caries increment in primary teeth after application of Duraphat fluoride varnish. *Community Dent Oral Epidemiol.* 1982;**10**(2):55-9. [PubMed: [6952970](https://pubmed.ncbi.nlm.nih.gov/6952970/)].
60. Autio-Gold JT, Courts F. Assessing the effect of fluoride varnish on early enamel carious lesions in the primary dentition. *J Am Dent Assoc.* 2001;**132**(9):1247-53. [PubMed: [11665349](https://pubmed.ncbi.nlm.nih.gov/11665349/)] quiz 1317-8.
61. Zhan L, Cheng J, Chang P, Ngo M, Denbesten PK, Hoover CI, et al. Effects of xylitol wipes on cariogenic bacteria and caries in young children. *J Dent Res.* 2012;**91**(7 Suppl):85S-90S. doi: [10.1177/0022034511434354](https://doi.org/10.1177/0022034511434354). [PubMed: [22699675](https://pubmed.ncbi.nlm.nih.gov/22699675/)].
62. Kovari H, Pienihakkinen K, Alanen P. Use of xylitol chewing gum in daycare centers: a follow-up study in Savonlinna, Finland. *Acta Odontol Scand.* 2003;**61**(6):367-70. [PubMed: [14960009](https://pubmed.ncbi.nlm.nih.gov/14960009/)].
63. Milgrom P, Ly KA, Tut OK, Mancl L, Roberts MC, Briand K, et al. Xylitol pediatric topical oral syrup to prevent dental caries: a double-blind randomized clinical trial of efficacy. *Arch Pediatr Adolesc Med.* 2009;**163**(7):601-7. doi: [10.1001/archpediatrics.2009.77](https://doi.org/10.1001/archpediatrics.2009.77). [PubMed: [19581542](https://pubmed.ncbi.nlm.nih.gov/19581542/)].
64. Weinstein P, Spiekerman C, Milgrom P. Randomized equivalence trial of intensive and semiannual applications of fluoride varnish in the primary dentition. *Caries Res.* 2009;**43**(6):484-90. doi: [10.1159/000264686](https://doi.org/10.1159/000264686). [PubMed: [20016179](https://pubmed.ncbi.nlm.nih.gov/20016179/)].
65. Lopez L, Berkowitz R, Spiekerman C, Weinstein P. Topical antimicrobial therapy in the prevention of early childhood caries: a follow-up report. *Pediatr Dent.* 2002;**24**(3):204-6. [PubMed: [12064491](https://pubmed.ncbi.nlm.nih.gov/12064491/)].
66. Fahy C, Costi D, Cyna A. Invasive 'placebo' controls: have we lost sight of whom we are blinding?. *Paediatr Anaesth.* 2011;**21**(11):1089-91. doi: [10.1111/j.1460-9592.2011.03650.x](https://doi.org/10.1111/j.1460-9592.2011.03650.x). [PubMed: [21966959](https://pubmed.ncbi.nlm.nih.gov/21966959/)].
67. Braga MM, Mendes FM, De Benedetto MS, Imparato JC. Effect of silver diammine fluoride on incipient caries lesions in erupting permanent first molars: a pilot study. *J Dent Child (Chic).* 2009;**76**(1):28-33.

- [PubMed: [19341576](#)].
68. Rosenblatt A, Stamford TC, Niederman R. Silver diamine fluoride: a caries "silver-fluoride bullet". *J Dent Res.* 2009;**88**(2):116–25. doi: [10.1177/0022034508329406](#). [PubMed: [19278981](#)].
69. Cummins D. Dental caries: a disease which remains a public health concern in the 21st century—the exploration of a breakthrough technology for caries prevention. *J Clin Dent.* 2013;**24 Spec no A**:A1–14. [PubMed: [24156135](#)].
70. Cantore R, Petrou I, Lavender S, Santarpia P, Liu Z, Gittins E, et al. In situ clinical effects of new dentifrices containing 1.5% arginine and fluoride on enamel de- and remineralization and plaque metabolism. *J Clin Dent.* 2013;**24 Spec no A**:A32–44. [PubMed: [24156138](#)].
71. Michalek SM, Katz J, Childers NK. A vaccine against dental caries: an overview. *BioDrugs.* 2001;**15**(8):501–8. [PubMed: [11543691](#)].