Review Article

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Relationship Between Early Childhood Caries and Anemia: A Systematic Review

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Abstract

Background: Early childhood caries (ECC) is one of the important caries occuring in children under the age of 6. ECC is defined as possible risk factor for iron deficiency-related anemia. In this review study, the current evidence about the effect of ECC on the prevalence of anemia was studied.

Material and Methods: A systematic review on ECC and anemia was done based on published article in PubMed and Google scholar databases. The search profiles included ECC/risk factor, SECC/ risk factors, ECC/anemia, ECC/ferritin, and ECC/iron deficiency. Inclusion criteria comprised of all studies that focused on ECC and anemia or related fields.

Results: A total of 3546 articles on early childhood caries were identified in PubMed and google scholar databases. After screening the titles and abstracts as well as limitation the subjects to ECC and risk factors, 175 articles underwent further investigation, of which 12 articles on ECC and anemia were finalized. Other research efforts in this regard had been made through theses and reported in non-PubMed English journals; thus, Conducting further search by Google, 3 more relevant articles were discovered.

Conclusion: According to this literature review on ECC and anemia, it is suggested to consider ECC as one of the risk factors for iron deficiency and anemia in children. More studies are needed to examine lifestyle and socioeconomic risk factors that can be associated with the malnourished status of these children. Preventive strategies against ECC should be developed to reduce the risk of iron deficiency and its related anemia.

Key words: Anemia, Caries, Iron Deficiency, Risk Factor

Introduction

Early childhood caries (ECC) is one of the important caries occuring in children under the age of 6. A number of criteria are defined for ECC diagnosis (1). These criteria include one or more cavities, one or more missing teeth as a result of caries, one or more filled surfaces in primary maxillary teeth, etc. The prevalence of ECC is various among different regions of world, ranging from 4% to 50%. For example, the incidence of ECC was reported to be 4%, 6%, 20.2%, 48%, 20.2%, and 31.5% in England, Finland, the United States, Indonesia, Western China, and Hong Kong, respectively (2-5). In Iran, the prevalence of this disease, as dental disease, is high, ranging from 45% to59% (6). There are many reasons for ECC prevalence such as high consumption of carbohydrates and improper bottle- or breast-feeding practices. One of the important consequences induced by ECC is malnutrition, followed by anemia. ECC is defined as possible risk factor for iron deficiency-related anemia (1, 7). In this review study, the relationship between ECC and anemia was studied based on previous published articles in this regard.

Materials and Methods

All published articles were searched in PubMed and Google Scholar in the last 10 years using these key words: “childhood dental caries”, “pediatric”, “incidence”, “risk factors”, “serum iron”, “ferritin”, “anemia”, “iron deficiency”, “SECC”, “ECC”, “early childhood caries”, and

"severe early childhood caries ". The language of search was English. Inclusion criterion was: All studies that focus on ECC and anemia. The exclusion criteria were: articles in adult group and duplicate of previous publication. The lists of reviews and retrieved studies were manually searched. All suitable studies were selected and their results were extracted. Similar findings were deleted. For limiting the search effort, the search was proceeded using two keywords: "iron deficiency" and "anemia" with conjunction "and".

Results

Figure 1 graphically illustrates the trial flow chart. A total of 1079 articles regarding early childhood caries were found in PubMed database. In addition, a total of 4450 articles in this regard were identified in google scholar database. After removing similar article, 3564 article were remained. Approximarely, 94 studies were review and 127 case report. So, these article were deleted from review list. We limited the subjects to ECC and risk factors as well as its outcomes, especially iron deficiency and anemia. Examining article titles and subjects based on this limitations, 175 articles were chosen. Finally, 12 articles had addressed the ECC and anemia. Other research efforts in this regard had been made through theses and reported in non-ISI and non-PubMed English journals; thus, further search by Google gave us 3 more relevant articles. Finally, 15 articles were found that fulfilled our defined inclusion criteria (Table I).

Early childhood caries definition

The most important infectious disease of childhood is dental caries. This infection is caused by different bacteria such as streptococcus mutans sugary foods, etc. This term was coined by Disease Control and Prevention Centers on 1994. Severe early childhood caries (SECC) were applied for childhood caries in children younger than 3 years old with any sign of smooth-surface caries. ECC is recognized as a dull white demineralized enamel that quickly advances to obvious decay along the gingival margin. Labial or lingual surfaces of the teeth is affected by ECC. In some cases, both of labial and lingual surfaces get involved. The decayed hard tissue is clinically evident as a yellow or brown cavitated area. In older children, whose entire primary dentition is fully erupted, it is not unusual to see considerable advancement of the dental damage (8-11).

Incidence of ECC in Iran and other regions

Prevalence of ECC in European countries (England, Sweden, and Finland) is in the range of 1-32%. This disease is more prevalent in some eastern European countries. The prevalence of dental caries in children is 24-28% in US from 1988 to 2004. Approximately, 72% of decayed or filled tooth surfaces remain untreated. The prevalence of ECC children is less than 5% in the general population of Canada and 50–80% in the high-risk population (12). Published studies showed higher prevalence figures for 3-year-olds, which ranges from 36 to 85% in Asia and 44% in Indi (3, 13, 14). The published documents showed that ECC has epidemic proportions in the developing countries. Studies conducted in the Middle East indicated that the prevalence of dental caries is between 22% and 61% and it is between 38% and 45%in Africa. Iran as one of developing countries has high prevalence of ECC (15, 16). There are a few studies on children under age three in Iran. The countrywide report for Iran gives a prevalence of 47% for ECC in three-year-old children. As a probable future for these three-year olds, the prevalence of caries in the primary dentition increases to 86% by six years of age with a mean dmft of 4.8, which is much higher than the WHO goals for caries level in the primary dentition for the year 2000 (17-19). As Iran is one of the countries with the youngest populations in the world, 13%

under age six, this increase in caries experience should be considered as an alarming finding, regarding public health issues.

Risk factors

In this section, three main risk factors considered by almost all researchers are summarized and discussed.

Microbiological risk factors

Two important bacterial strains in ECC are streptococcus mutans and streptococcus sobrinus. On the other hand, lactobacilli have key role in the caries progression. This infection can be transmitted by vertical and horizontal transmission. Vertical transmission is carried between mother or father and child (20, 21).

Dietary risk factors

Diet with high-sugared drinks increase the risk of this disease in addition to infection. Streptococcus mutans and lactobacilli process the sugar to acid by glycolysis and fermentation. This produced acid lead to demineralization of tooth structure. Evidence recommends that both cow's and human milk are considered to be less cariogenic than sucrose, with cow's milk being the least cariogenic (22, 23).

Environmental risk factors

Several studies confirmed that when S streptococcus mutans M bacteria have been acquired at an early age, it will mostly lead to ECC, where other important factors, such as economic and financial situation, the use of fluoride and other related factors, can contribute to the development or prevention of ECC. Children with a background marked by dental caries, whose parents and siblings have serious dental caries, are viewed as being at high risk of having dental caries in their future. Additionally, kids involvement in financial burden influences grownup dental well-being (23-25).

ECC and anemia

In this section, we reviewed and compered all 15 related publications. All collected data from these studies are summarized in Table I. There were various factors that lead to anemia in children such as dietary factors, genetic (congenital) factors, environmental factors, and inflammatory processes. Children with SECC had higher rates of anemia and iron deficiency. According to these 15 studies, there are several theories association between iron deficiency anemia and ECC in children with dental caries:

1. Body's inflammatory response: inflammation in ECC can lead to the production of cytokines, which can inhibit erythropoiesis and so, reduction of hemoglobin level in the blood and then, level of iron. One important possible mechanism of severe caries on children health is that pulpitis and chronic dental abscesses affect growth by inducing chronic inflammation that affects metabolic pathways where cytokines influence erythropoiesis. For example, interleukin-1 (IL-1), which has a wide variety of actions in inflammation, can induce inhibition of erythropoiesis. This suppression of hemoglobin can lead to anemia of chronic disease, as a result of depressed erythrocyte production in the bone marrow.
2. Destruction of salivary gland function in children with iron deficiency and then, reduction of buffering capacity and dental caries.
3. Malnutrition due to ECC and difficulty in chewing and eating: This status lead to iron deficiency and its related anemia. Nutritional and Health Survey reported that the prevalence rate of iron deficiency in children between 4 and 6 years of age was 0.2–6.2%. Different studies reported higher incidence of iron deficiency and its related anemia in children with ECC.
4. Pain or discomfort in children: ECC lead to pain or discomfort in children. So, these children have problem in chewing iron-rich foods. Such problem may lead to nutritional deficiencies, including low iron levels.
5. Food habits or dietary factors: The dietary factors such as high consumption of carbohydrates, beverages, and low meat

intake reduce iron levels and develop the dental caries. Tang et al., and Shaoul et al., showed that iron deficiency anemia had high prevalence in children with severe childhood caries because of wrong eating habits. These groups claimed that change of food habits can be attributed to the relief from pain and improved eating habits after treatment for dental caries and so, reduction of iron deficiency anemia.

6. Chronic infections: Chronic infections are known to reduce Hb levels, which may contribute to anemia.

Comparison of the reasons cited in these articles was done. The results of this comparison are presented in Figure 2. As shown in this figure, inflammatory response and malnutrition due to ECC are two major reasons for iron deficiency and its related anemia.

The history of previous caries is known as one of the best predictors of future ecay. Children under the age of 5 with a history of dental caries should automatically be classified as being at high risk for future decay. However, the absence of caries is not a useful caries risk predictor for infants and toddlers because even if these children are at high risk, there may not have been enough time for carious lesion development. Since white spot lesions are the precursors to cavitated lesions, they will be apparent before cavitations. The main position of growth of these white lesions is near the gingiva and on the surface of enamel surfaces. Although only a few studies have examined staining of pits and fissures or white spot lesions as a caries risk variable, such lesions should be considered equivalent to caries when determining caries risk in young children. Schroth et al., investigated the relationship between S-ECC and nutritional iron status. This group compared the ferritin and hemoglobin levels between children undergoing rehabilitative dental surgery for S-ECC and cavity-free children recruited from the community. The results of this group showed that there is significant difference in the number of children exhibiting low ferritin levels. This study showed that children with S-ECC had lower ferritin level than cavity-free children. Schroth et al., also indicated that children with S-ECC had significantly lower hemoglobin levels than the caries free controls. According to these studies, Children with S-ECC had low ferritin status and low hemoglobin levels compared with caries-free children. Iron deficiency and iron deficiency anemia had more frequency in children with S-ECC in comparison with cavity-free children. Bansal et al., Pushpa Iranna et al., and Tang et al., showed that S-ECC strongly increased anemia due to iron deficiency. So, ECC is considered as one important reason for anemia and iron deficiency**.**

There are 2851 antimicrobial peptides from six kingdoms (303 bacteriocins/peptide antibiotics from bacteria, 4 from archaea, 8 from protists, 13 from fungi, 342 from plants, and 2181 from animals) with different activities in various recorded databases. These recorded peptides are divided to antibiofilm peptide, antiviral peptides, antifungal peptides, antiparasitic peptides, antimalarial peptides, anti-protist peptides, anticancer peptides, antioxidant peptides, chemotactic peptide, insecticidal peptide, protease inhibitor, spermicidal peptide, surface immobilized peptides, and wound healing peptides. Among all these recorded peptides, 210 ones have anticancer/antitumor activity. There are 123 human host defense peptides, 220 from mammals annotated, 1049 active peptides from amphibians, 117 fish peptides, 35 reptile peptides, 40 from birds, 509 from arthropods, 42 from molluscs, 6 peptides from protozoa, and more. In Figure 1, sources of antimicrobial peptides are shown. As seen in this Figure, the highest number of peptides was discovered from animal source (22-26).

Table I: The date of all published studies about ECC and anemia

	Title	Main Scope	Main Results	Ref
1	Evaluation and association of serum iron and ferritin levels in children with dental caries	association between dental caries and serum levels of iron and ferritin in children aged 3-12 years on 120 children	Inverse association between serum iron levels and dental caries and no association between serum ferritin levels and dental caries. Proposed reason: Body's inflammatory response, Malnutrition, Pain or discomfort in children	(58)
2	Influence of Full Mouth Rehabilitation on Iron Deficiency Anemia Status In Children With Severe Early Childhood Caries	assess the influence of full mouth rehabilitation on the status of iron deficiency anemia in children with severe early childhood caries on 30 children	positive correlation between SECC and low weight and presence of iron deficiency anemia Proposed reason: Body's inflammatory response, Malnutrition	(37)
3	The prevalence of iron deficiency anemia in children with severe early childhood caries undergoing dental surgery under general anesthesia	Investigate the IDA in children with severe caries on 160 children	no association between SECC and serum Hgb, Hct and MCV levels. Introduction od SECC as a risk marker for iron deficiency. Proposed reason: Body's inflammatory response, Malnutrition	(35)
4	Iron Deficiency in Young Children: A Risk Marker for Early Childhood Caries	Evaluation and comparison of the iron status of children with and without severe early childhood caries on 60 children	Iron deficiency is observed definitely in children having ECC Proposed reason: Malnutrition, Pain or discomfort in children	(32)
5	The association of childhood iron deficiency anemia with severe dental caries	investigating the Hb, iron and other anaemia indexes status before and 4–6 months after the dental SC restoration	Significant association between iron deficiency anaemia and severe dental caries. Proposed reason: Body's inflammatory response, Destruction of salivary gland function, Pain or discomfort in children	(59)
6	Is there an association between early childhood caries and serum iron and serum ferritin levels?	Investigation of a possible association between ECC with serum iron and serum ferritin levels on 240 children	significant association between ECC and with serum iron levels and no association between ECC experience and serum ferritin levels Proposed reason: Body's inflammatory response, Malnutrition	(60)
7	Association of severe early childhood caries with iron deficiency anemia.	Investigation of association between S-ECC with IDA on 60 children	strong association between S-ECC and anemia due to iron deficiency Proposed reason: Body's inflammatory response, Malnutrition	(61)
8	Relationship between dental caries status and anemia in children with severe early childhood caries.	Investigation of the nutritional status among preschool children with SECC on 101 children	Association between SECC and anemia (7.25-fold) Proposed reason: Body's inflammatory response,	(62)
9	Association between iron status, iron deficiency anemia, and severe early childhood caries: a case–	Comparison of ferritin and hemoglobin levels between preschoolers with S-ECC	lower ferritin and hemoglobin levels and higher iron deficiency anemia in children	(44)

	control study	and caries-free controls	with S-ECC Proposed reason: Body's inflammatory response, Malnutrition	
10	Malnourishment in a Population of Young Children With Severe Early Childhood Caries	Describe the nutritional status of children with severe early childhood caries	severe Early Childhood Caries as risk marker for iron deficiency anemia. Proposed reason: Body's inflammatory response, Malnutrition, Food habits or dietary factors	(29)
11	Evaluation of interrelationship of early childhood caries and iron deficiency Anemia	Relationship of severe early childhood caries and iron deficiency anemia on 102 children	forty four percent children suffered with Iron Deficiency Anemia. S-ECC and anemia are definitely interrelated, and S-ECC can be identified as a risk marker for under nutrition. Proposed reason: Body's inflammatory response,	(63)
12	Children with Severe Early Childhood Caries at risk for iron deficiency	Examination of serum ferritin and hemoglobin levels in children with S-ECC	Significant association among S-ECC with ferritin and iron deficiency anemia Proposed reason: Body's inflammatory response, Malnutrition	(64)
13	The association between dmft index and haemoglobin levels in 3e6 year-old Saudi children with anaemia: A cross sectional study	Assessmant of the association between the haemoglobin levels and the dmft index in a random sample of paediatric dental patients on 160 children	This study suggested the need for public health campaigns regarding oral hygiene and the prevention and treatment of anaemia Proposed reason: oral hygiene habits, Malnutrition	(65)
14	Estimation of ferritin levels in children with and without early childhood caries - A case–control study	Determination of the association between the ferritin level and the severity of ECC on 114 children	Lower ferritin levels in children with ECC. Consideration of S-ECC as a risk marker of anemia. Proposed reason: Body's inflammatory response, Food habits or dietary factors	(66)
15	The association between growth factors and blood factors with early childhood caries	association between growth factors, blood parameters, and ECC on 240 children.	No significant association between ECC and blood indices (MCV, hemoglobin and serum ferritin), but the mean height and weight in the caries-free group were significantly higher. Proposed reason: Destruction of salivary gland function, Malnutrition	(67)

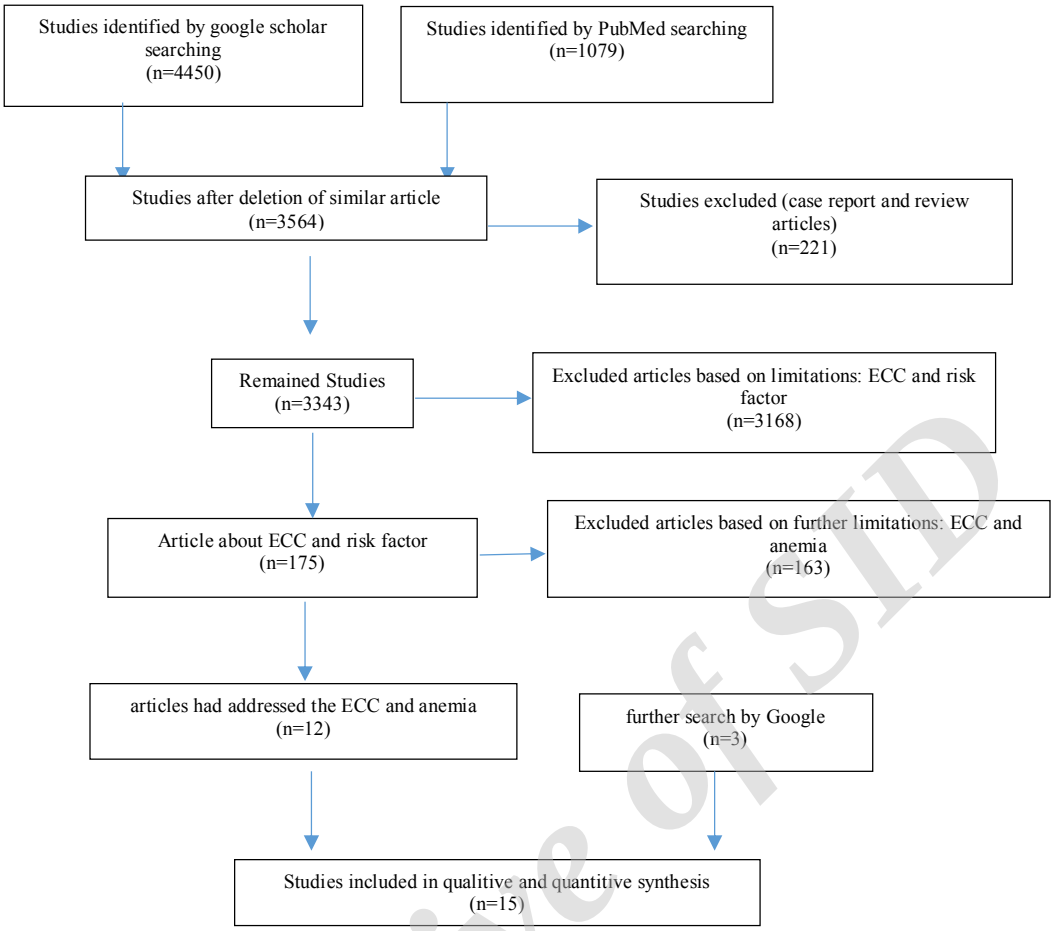

Figure 1. Flow chart displaying literature search and study selection.

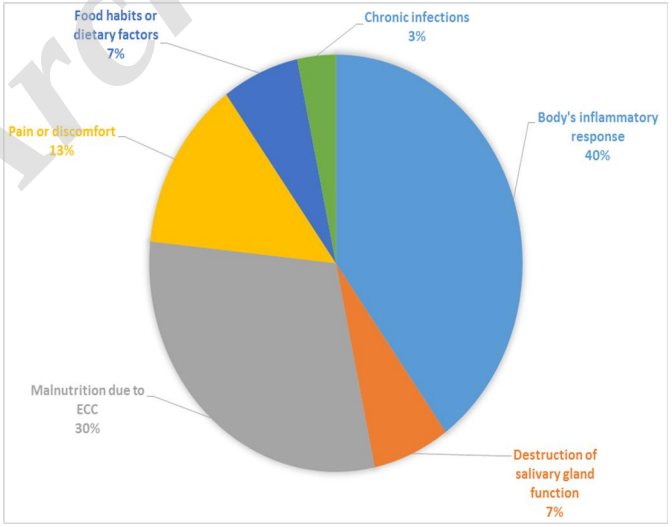

Figure 2. The main reasons of iron deficiency anemia due to ECC based on 15 related published studies.

Discussion

Early childhood caries (ECC) is a particular type of severe dental caries that affects infants and young children. These children have weight loss, growth retardation and iron deficiency due to pain, reduced ability to chew, and malnutrition (26-29). Impairment in sleep quality leads to insufficient growth by reducing the production of glucosteroids in these children (30). On the other hand, anemia can be occurred due to several factors such as: nutritional factors, genetic factors (congenital), inflammatory processes and environmental factors such as low socioeconomic status and dental caries (31-34). Nutrition-induced anemia is the most common form of malnutrition and includes nutritional deficiencies such as iron, folic acid, copper, and vitamins A, B, C, and E . Iron deficiency anemia is generally recognized by biochemical indices: hemoglobin, hematocrit, as well as MCV, and ferritin (35, 36). According to WHO, if at least 2 parameters of 3 parameters (Hb, MCV, and serum ferritin) are lower than normal, iron deficiency anemia is confirmed (37). Serum ferritin is an acute phase protein and its level is an indicator of body iron storage. However, ferritin may increase as an inflammatory phase protein during inflammatory, infectious and malignant infections, but this is not interpreted as a very high level of iron in the body (38). The iron status has a significant impact on the health of the baby. For example, a child who suffers from iron deficiency may not only show nerve symptoms such as reduced learning and memory deficits, reduced motor skills and increased anxiety, but also weakness, poor physical growth, and weakened immune systems that lead to injury. They also show infections (39-41). In this review, 15 articles about relationship between ECC and iron deficiency Anemia were assessed. Among the 15 studied articles, eight articles were cross-sectional studies, five articles were case-control articles, and two were longitudinal papers. In cross-sectional studies such as Babu's and Sadeghi studies (42, 43), there was a significant reverse correlation between DMFT index and serum iron level, suggesting a significant reverse relationship between serum iron and ECC levels. In case control studies of Schroth et al., (44), (12), Bansal et al., (45), and Koppal et al., (46), children with SECC had significantly lower hemoglobin levels than non-carious controls. In a cross-sectional study by Abdallah (31), significantly higher DMFT index was found in children with lower hemoglobin levels. In Sadegh's et al., (43) and Babu et al., (42) studies, serum ferritin levels did not show a significant difference with DMFT index. However, in Schroth's et al., (44) and Koppal et al., (32)studies, children with SECC had significantly lower serum ferritin levels than non-caries control group, suggesting that ferritin is an acute phase protein and its level is an indicator of body iron storage. However, in inflammatory diseases, the infection increases the amount of ferritin as an acute inflammatory phase protein and is not interpreted as a high level of iron in the body. Moreover, the cause of the difference can be due to a different methodology of studies (47). Tang found in his study that children suffering from severe ECC form had 46% iron deficiency . In Shaoul's study (48), children with IDA and SECC, treatment of dental caries improved self-paced IDA in most cases without the use of iron supplements, which is similar to Nagarajan's study (37), indicatind a direct correlation between SECC and lack of weight and IDA in these children. After full mouth rehabilitation in children with IDA, parameters related to this disease improved, which can be due to loss of pain and the improvement of children's nutritional habits in the treatment of caries. The relationship between iron levels and decay rates should be investigated in different ways. On the one hand, the long-term use of more than 2 years of milk and milk bottles for

nutrition, in addition to exposing the child to early childhood caries, can be exposed baby to malnutrition by not consuming enough food containing iron and other nutrients. As a result, the likelihood of early childhood caries and iron deficiency and other nutritional problems are higher in this group of children (49, 50). The presence of multiple dental caries in children causes difficulty in chewing and feeding, especially meat flesh and also decreases the absorption of nutrients in the intestine due to inappropriate chewing. In this situation, the child finds a tendency to drink sugary drinks in order to create a sense of satiety and to reduce the consumption of meat and iron containing substances (51, 52). It is reasonable to assume that diet factors that cause iron deficiency (high intake of beverages and low intake of meat) can also predict dental caries (53). Dietary diversity includes promoting a diet with a range of foods that naturally contain iron, in particular, red meat, chicken, and fish. (54). Iron in meat is found better than non-alcoholic iron found in dairy products, fruits, and vegetables, and it is absorbed into the body. Evidence showed that children who eat less meat and poultry and drink plenty of juice and milk, snacks, or candy are at high risk for iron deficiency because of high calories of these sources, the eating of other foods and Preventing nutritional needs (55). therefore, children with ECC should be evaluated for nutritional habits and iron levels (29). According to some animal studies, iron also affects the flow of saliva, in which iron deficiency has been associated with reduced salivation and reduced buffering ability, increasing the risk of caries (56). Untreated caries leads to acute and chronic inflammation such as pulpitis, periapical aphasia, and fistula, which release various inflammatory mediators, mainly interleukin I and cytokines (57). Second, nightly pulpal pain causes sleep disorder that results in decreased glycosteroids production. This reduction lead to suppress of the synthesis of hemoglobin in blood and anemia caused by chronic inflammation by suppressing erythropoiesis (48, 52).

Conclusion

This systematic review showed shortage of studies on the anemia caused by ECC. Based on this literature review, ECC must be considered as a risk factor for iron deficiency and anemia in children. More studies are needed to examine lifestyle and socioeconomic risk factors that may be associated with the malnourished status of these children. Preventive strategies of ECC should be developed to reduce the risk of iron deficiency and its related anemia. So, it is important that dentists and other specialists be aware about the relationship between ECC and its related. The findings of this review can help researchers to design future research.

Conflict of interest

The authors report no conflict of interest.

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