Breastfeeding and its Association with Early Childhood Caries – An Umbrella Review

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Objective: *To systematically assess systematic reviews and meta-analyses investigating the association of breastfeeding with ECC.* ***Study Design:*** *A systematic search was carried out from MEDLINE® (PubMed), EMBASE, the Cochrane Central Database, OVID, Joanna Briggs Institute Database of Systematic Reviews and Implementation Reports and Epistemonikos Databases up to November 2019. Data extraction was carried out by two investigators. ROBIS tool was used for quality assessment of included systematic reviews.*

Results: *Four systematic reviews were found assessing the correlation of breastfeeding with ECC. Findings were grouped into four categories, according to the duration, frequency, pattern, and comparison of feeding habits. Two systematic reviews assessing duration of breastfeeding above the age of 12 months had odds ratios of 1.86 and 1.99, showing positive correlation with ECC while nocturnal breastfeeding showed highest odds ratio of 7.14. Of the four included reviews, three had low risk of bias and one had unclear risk of bias.*

Conclusions: *Breastfeeding beyond the age of 12 months, accompanied by nocturnal feeding, had a positive association with ECC. Further research is warranted for assessment of diurnal and nocturnal sleep-time breastfeeding habits, together with the role of enamel defects (hypoplasia), and the risk of ECC.*

Keywords: *Breastfeeding*, *Early Childhood Caries*, *Risk factor*

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INTRODUCTION

Early Childhood Caries (ECC) is defined as the presence of one or more decayed (non-cavitated or cavitated lesions), missing (due to caries), or filled surfaces in any primary tooth of a child under age six.[1] ECC continues to be the most common infective disease chronically affecting young children.[2] Breastfeeding is considered the recommended source of nutrition for infants.[3] The World Health Organization (WHO) recommends exclusive breastfeeding for infants for six months, followed by complementary breastfeeding up to the age of two years or beyond.[4]

One of the first reports, published by Pitts in 1927, observed that breastfeeding can be one of the causes for ECC.[5] A 2015 study by Nakayama *et al* concluded with the understanding that nocturnal breastfeeding is positively correlated to ECC, while a 2016 study by Neves et al. analyzed that breastfeeding does not cause a decrease in the pH of the biofilm and hence is not cariogenic.[6,7] While the findings are inconsistent and inconclusive, a number of systematic reviews also exist in this particular domain.[2,8,9]

The number of systematic reviews in this field illustrate the need for an umbrella review, which would combine the results of the available systematic reviews to arrive at a conclusion. Umbrella reviews are overviews of systematic reviews designed to answer a broad question with the data available from the existing systematic reviews. Therefore, the aim of this umbrella review was to systematically assess the systematic reviews and meta-analyses investigating the association of breastfeeding with ECC.

METHODS

The protocol for the umbrella review was registered in PROSPERO in October 2019 (Registration ID – CRD42020150644).

Search Strategy

The identification of included studies was completed in November 2019. Search was performed in six electronic databases namely: MEDLINE® (PubMed), EMBASE, Cochrane Central Database, OVID, Joanna Briggs Institute Database of Systematic Reviews and Implementation Reports and Epistemonikos Database. Two groups of key words were applied: (1) Type of exposure — breastfeeding, breast milk, human milk, milk; (2) Types of outcome measures — caries, ECC, nursing bottle caries, tooth decay. Filter of Systematic Reviews and Meta-analysis was added. Search strategy used in MEDLINE (PubMed) is described in Table 1. Comparable search strategies were applied in other databases.

Table 1 : MEDLINE (PubMed) Search Strategy

((((((((((breastfe*[Title/Abstract]) OR "human milk"[Title/Abstract]) OR "breast milk"[Title/Abstract]) OR lactati*[Title/Abstract]) OR nursing*[Title/Abstract]) OR "infant nutrition*"[Title/Abstract]) OR breastfeeding[MeSH Terms]) OR exclusive breastfeeding[MeSH Terms]) OR human milk[MeSH Terms]) OR breast milk[MeSH Terms]) OR lactation[MeSH Terms])) AND (((((“dental caries”[Title/Abstract]) OR “nursing bottle caries”[Title/Abstract]) OR “early childhood caries”[Title/Abstract]) OR “tooth decay”[Title/Abstract]) OR dental caries[MeSH Terms]).

Selection Criteria

This umbrella review included systematic reviews, with or without meta-analysis, that assessed the correlation of breastfeeding and ECC. No time restriction was applied and all systematic reviews published in English up to November 2019 were taken into consideration. RevMan 5.3 (Review Manager 5.3, The Cochrane Collaboration) software was used to generate graphs for this review.

Participants

The review considered systematic reviews with or without meta-analyses that included studies of infants and children, aged 0 – 71 months, without any systemic disorder.

Interventions/Comparator

All systematic reviews assessing the correlation of breastfeeding pattern, duration, or frequency alone or in comparison with bottle feeding or any other means of nutrition were included in the study.

Outcomes

Systematic reviews that included studies assessing ECC in the form of dmft (decayed, missing, filled teeth), dmfs (decayed, missing, filled surfaces), ICDAS (International Caries Detection and Assessment System), WHO (World Health Organization), microbial profile and decrease in plaque or biofilm pH were considered in the review.

Exclusion Criteria

Primary studies, narrative reviews or reviews that did not meet the definition of systematic reviews or did not follow a defined methodological approach, conference proceedings, and letters to editors were excluded.

Selection of Studies

The publications were retrieved from the searches and combined into one database with duplicates removed. Screening of the titles and abstracts was carried out independently and in duplicate by two trained authors (N.P. and A.S.). Full texts of studies assessed as potentially eligible were retrieved, and two investigators (N.P. and A.S.) screened them independently and in duplicate to assess eligibility. Where there were discrepancies, a third investigator (M.S.M.) was consulted. Data extraction was carried out by two investigators and was entered into the pre-piloted data extraction form. To determine the overlap of primary studies across the included systematic reviews, citation matrix was generated and Corrected Covered Areas (CCA) were calculated wherein CCA of 0-5 indicated slight, 6-10; moderate, 11-15; high and >15 indicated very high overlap amongst primary studies.[10]

Risk-of-bias (quality) Assessment

Quality assessment of the included systematic reviews and generation of figures was done with ROBIS (Risk of Bias in Systematic Reviews) tool developed by University of Bristol.[11] This tool assesses the review in 3 phases: Phase 1 assesses the relevance of the included review as ‘yes’, ‘no’, or ‘unclear’. Phase 2 identifies the concerns for the review process, divided into four domains. Phase 3 summarizes the concerns in the domains, and final risk-of-bias for the review is determined as low, high, or unclear. Risk-of-bias assessment was independently carried out by two investigators (N.P. and P.J.). Scoring discrepancies were resolved through discussion until consensus was reached.

RESULTS

An initial search of electronic databases yielded 424 relevant reviews. One additional review was included after a hand search of bibliographies from the potentially eligible reviews. After duplicates were removed, 397 records were screened by their titles/abstracts. After exclusion of 383 articles, 14 full-text articles were obtained. Ten articles were excluded (Table 2), since they did not adhere to the inclusion criteria and four systematic reviews remained for inclusion in our umbrella review (Figure 1).

Characteristics of Included Systematic Reviews (Table 3)

The time frame of the studies included in the systematic reviews ranged from 1980 to December 2015. Most of the primary studies were observational studies, including mainly cohort, case-control, or cross-sectional studies. Two randomized controlled trials were included in the review by Tham *et al.*[9] Only English language studies were taken into consideration, and the most-searched database was PubMed. The total number of unique primary studies included were 92, out of which six studies were included thrice, 29 studies were included twice and 57 studies were included once. CCA was calculated to be 0.14 (14% overlap).(Table 4)

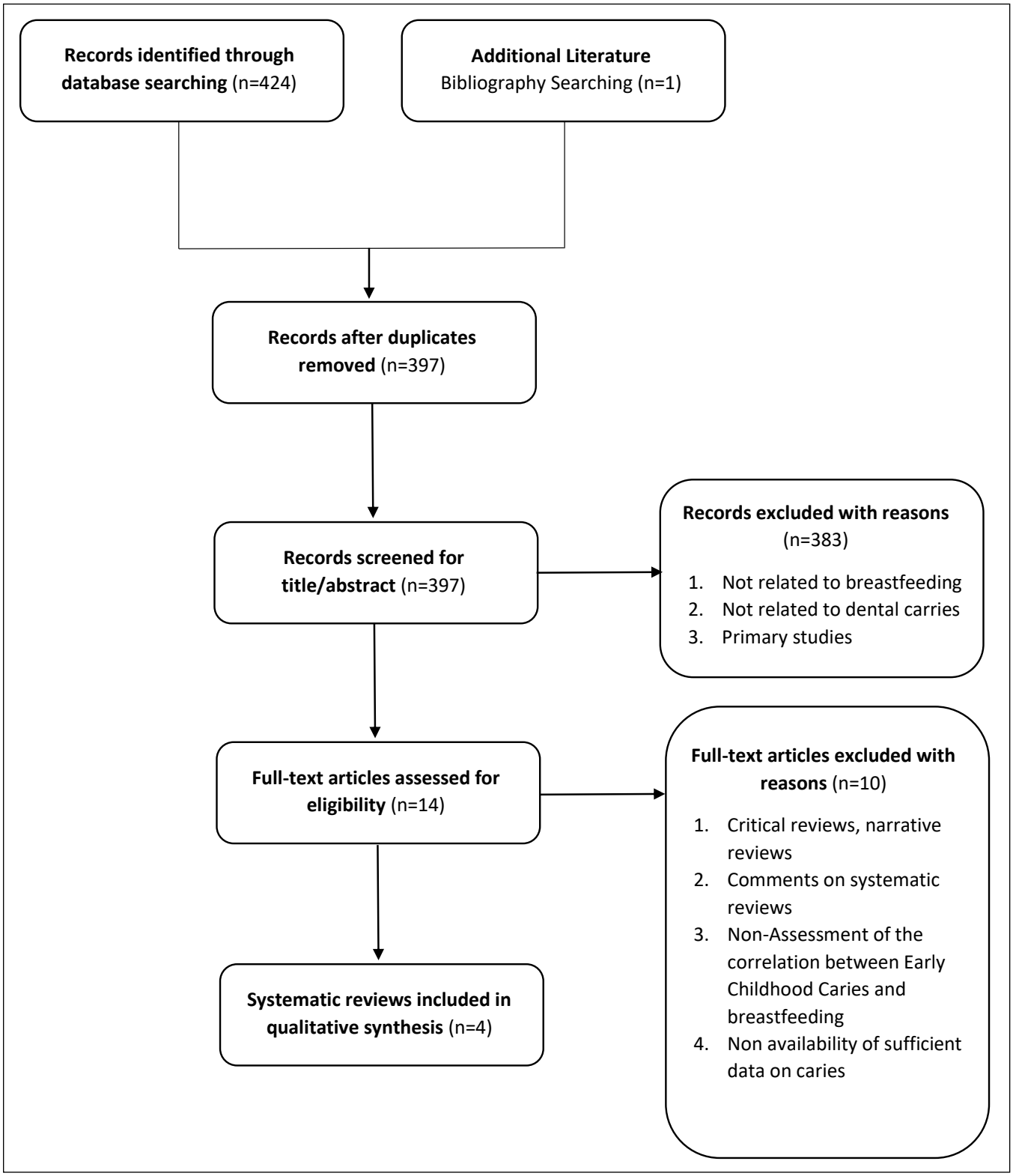

Figure 1: Flow chart of identification and selection of systematic reviews, with reasons for exclusion at every stage

Table 2 : Characteristics of excluded full text articles

S.No	Title	Reference	Reason for Exclusion
1.	Breastfeeding up to 12 months of age not associated with increased risk of caries: Question: Is breastfeeding associated with dental caries?	Richards D, 2016	Comment on a systematic review
2.	Role of Infant Feeding Practices on the Dental Health of Children.	Nainar SMH, 2004	Editorial
3.	Breastfeeding and Oral Health: Evidence and Methodological Challenges.	Peres KG, 2018	Narrative Review
4.	Breastfeeding – An overview of Oral and General Health Benefits.	Salone LR, 2013	Narrative review
5.	Optimal duration of exclusive breastfeeding.	Kramer MS, 2012	Dental caries is not considered as a direct outcome
6.	Breastfeeding in the 21st century: epidemiology, mechanisms, and lifelong effect.	Victora CG, 2016	Narrative review
7.	Breast and Bottle Feeding as Risk Factors for Dental Caries-Review.	Rezvi FB AR, 2016	Narrative review
8.	Breastfeeding and the risk of early childhood caries.	White V, 2008	Narrative review
9.	Parental Factors Influencing the Development of Early Childhood Caries in Developing Nations: A Systematic Review.	Rai NK, 2018	Dental caries is not considered as a direct outcome
10.	A Systematic Review of Clinical Diagnostic Criteria of Early Childhood Caries.	Ismail AI, 1999	Breastfeeding – not an intervention

Table 3: Data extraction form–Characteristics of included studies

S. No	Author/ year	Objectives	Participants	Intervention	Number of studies included	Types of studies included	Method of analysis	Conclusions
1.	R. Tham, 2015	To summarize current evidence for association between breastfeeding and dental caries with specific reference to exposure windows and breastfeeding practices	Children, adolescents from general and high-risk populations	Breastfeeding compared to formula or other feeding	63 (63,392 participants)	Randomised Controlled trials, Cohort, case-control, cross-sectional	OR, RR, PR	1. Qualitative assessment – up to 12 months – more duration of breastfeeding – protected from Dental caries than less (shorter duration). 2. Above 12 months of age – breastfeeding – not protective 3. Breastfeeding nocturnally – increased caries
2.	W. M. Avila, 2015	To systematically review the scientific evidence relating to the association between feeding practice (breastfeeding vs bottle feeding) and dental caries in childhood.	Children with exclusive primary dentition under the age of 71 months	Bottle feeding in comparison to breast feeding	7 (5,572 participants)	Observational, cross-sectional, case-control, cohort, clinical trials (not found)	OR, RR, PR, or absolute number of events/ total no. of individuals	1. Meta-analysis – Breastfed children less affected than bottle fed children

S. No	Author/ year	Objectives	Participants	Intervention	Number of studies included	Types of studies included	Method of analysis	Conclusions
3.	L. Cui, 2017	To comprehensively summarize the current evidence for the association between breastfeeding and ECC – meta-analysis on infant feeding patterns and duration of breast feeding	Children aged – 0-71 months	Infant feeding practices – breastfeeding, bottle feeding , mixed feeding or duration of feeding	35 (73,401 participants)	Birth cohort, case-control, cross-sectional	OR	1. Children ever breast fed (exclusive + mixed) – lower caries risk than children never breastfed 2. Exclusive breast-feeding did not significantly decrease the risk of ECC relative to bottle feeding 3. Breast fed more than or equal to 12 months – increased risk of ECC 4. Breastfed more than 6 months – NO significant ECC than less than 6 months
4.	R. Valaitis, 2000	To investigate the relationship between breast feeding and early childhood caries – duration	Children 0 – 4 years of age or a subset (2-6 years)	Breastfeeding duration, demand breastfeeding, nocturnal breastfeeding, solid food, sweetened pacifier, formula use	28 (Number of participants not described)	Cohort, Cross-sectional, case-control, case series	Not done	1. Breastfeeding of prolonged duration (6 months or 1 year) – positively associated with ECC 2. At will, night time, nap time breastfeeding – ECC

OR – Odds Ratio. PR – Prevalence Ratio RR – Relative Risk

Quality Assessment of Systematic Reviews

Three of the four included reviews showed low risk-of-bias[2,8,9]. Among individual domains, domain 2 indicated a particularly high risk-of-bias for three of the four included systematic reviews. This was primarily due to non-availability of an *a priori* protocol, language restriction to English, or lack of clear information on the methods of data extraction. A summary of concerns from the ROBIS tool, Phases 2 and 3, is given in Figure 2, Table 5.

Synthesis of Results

Of the four systematic reviews retrieved, three provided quantitative synthesis of the findings, while one did not. [12] Overall, the qualitative analysis was based on the following factors:

A. Duration of breastfeeding

1. More than 12 months or less than 12 months

2. More than six months or less than six months

B. Frequency of breastfeeding

1. More breastfeeding (longer duration) or less breastfeeding (shorter duration)

C. Pattern of breastfeeding

1. Ever breastfeeding or never breastfeeding

2. Nocturnal breastfeeding

D. Comparison of feeding habits

1. Breastfeeding or bottle feeding

Duration of breastfeeding

Breastfeeding duration and its correlation with the acquisition of ECC were assessed in 2 systematic reviews (Figure 3A). The time periods of 12-month and six-month breastfeeding were considered. It was found that breastfeeding for more than 12 months was positively associated with the acquisition of ECC. These results were consistent in both the systematic reviews that assessed this correlation.

Frequency of breastfeeding

Figure 3B presents the association between the frequency of breastfeeding and the acquisition of ECC. Assessment of frequency of breastfeeding and ECC in infants under the age of 12 months, revealed that there was no significant association of more or less breastfeeding (including never breastfeeding) and ECC, with an odds ratio of 0.50 (0.25-1.00).

Table 4: Citation Matrix of included systematic review

Overlap of Studies					
S.No	Primary studies	Systematic reviews			
		Avila et al	Tham et al	Cui et al	Valaitis et al
1	Al-Dashti et al, 1995	X	X		X
2	Du et al, 2000	X	X	X	
3	Du et al, 2007	X			
4	Quadri et al, 2012	X	X	X	
5	Perera et al, 2014	X	X	X	
6	Roberts et al, 1994	X	X		X
7	Majorana et al, 2014	X	X	X	
8	Feldens et al, 2007		X		
9	Feldens et al, 2010		X		
10	Chaffee et al, 2014		X	X	
11	Feldens et al, 2010		X	X	
12	Hong et al, 2014		X	X	
13	Kramer et al, 2007		X		
14	Kramer et al, 2009		X		
15	Ollila and Larmas, 2007		X		
16	Silver, 1987		X		X
17	Tada et al, 1999		X		
18	Tanaka et al, 2013		X	X	
19	Thitasomakul et al, 2009		X		
20	van Palestein Helderman et al, 2006		X	X	
21	Yonezu et al, 2006		X	X	
22	Bahuhuna et al, 2013		X		
23	Matee et al, 1994		X		X
24	Alaluusua et al, 1990		X		
25	Azevedo et al, 2005		X	X	
26	Campus et al, 2009		X	X	
27	Carino et al, 2003		X		
28	Dini et al, 2000		X	X	
29	Dye et al, 2004		X	X	
30	Folayan et al, 2010		X		
31	Folayan et al, 2008		X		
32	Forsman et al, 1974		X		
33	Hallett et al, 2003		X		
34	Hallonsten et al, 1995		X		
35	Haq et al, 1985		X		X
36	Hardy, 1978		X		
37	Harrison et al, 1997		X		
38	Holt et al, 1982		X		X
39	Hong et al, 2014		X		
40	Iida et al, 2007		X	X	
41	Johansson et al, 2010		X		

Calculation of Corrected Covered Area (CCA):

$$CCA = \frac{N-r}{rc-r}$$

N = Number of included publications (Number of X in the citation matrix)

r = Number of rows (Number of index publications)

c= Number of columns (Included systematic reviews)

Table 4: Citation Matrix of included systematic review (continued)

Overlap of Studies					
S.No	Primary studies	Systematic reviews			
		Avila et al	Tham et al	Cui et al	Valaitis et al
42	Linvy et al, 2007		X	X	
43	Masumo et al, 2013		X		
44	Maltos-Graner et al, 1998		X		
45	Nobile et al, 2014		X	X	
46	Nunes et al, 2014		X	X	
47	Prakash et al, 2012		X	X	
48	Prakasha Shrutha et al, 2013		X	X	
49	Retnakumari et al, 2012		X	X	
50	Rosenblatt et al, 2004		X	X	
51	Sankeshwari et al, 2012		X	X	
52	Santos, 2002		X		
53	Sayegh et al, 2002		X		
54	Sayegh et al, 2005		X	X	
55	Serwint et al, 1993		X		
56	Slabsinskiene et al, 2010		X	X	
57	Songo et al, 2013		X		
58	Tanaka et al, 2012		X	X	
59	Tiano et al, 2009		X	X	
60	Tyagi et al, 2008		X	X	
61	Vachirarojpisan et al, 2004		X		
62	Vazquez-Nava et al, 2008		X		
63	Wendt and Birkhed, 1995		X		X
64	Yonezu et al, 2007		X		
65	Kato et al, 2015			X	
66	Peltzer and Mongkolchati, 2015			X	
67	Seow, 2009			X	
68	Werneck et al, 2008			X	
69	Qin et al, 2008			X	
70	Mohebbi et al, 2008			X	
71	Olmez et al, 2003			X	
72	Derkson and Ponti, 1982				X
73	Johnsen, 1982				X
74	Vignarajah and Williams, 1992				X
75	Albert et al, 1988				X
76	Babeely et al, 1989				X
77	Eronat and Eden, 1992				X
78	Marino et al, 1989				X
79	Matee et al, 1992a				X
80	Matee et al, 1992b				X
81	Richardson et al, 1981				X
82	Roberts et al, 1993				X
83	Salako, 1985				X
84	Silver, 1992				X
85	Tee, 1987				X
86	Todd et al, 1994				X
87	Tsubouchi et al, 1994				X
88	Walton and Messer, 1981				X
89	Williams and Hargreaves, 1990				X
90	Adenubi, 1982				X
91	Dilley et al, 1980				X
92	Holt et al, 1988				X

X = Inclusion of primary study in individual systematic review

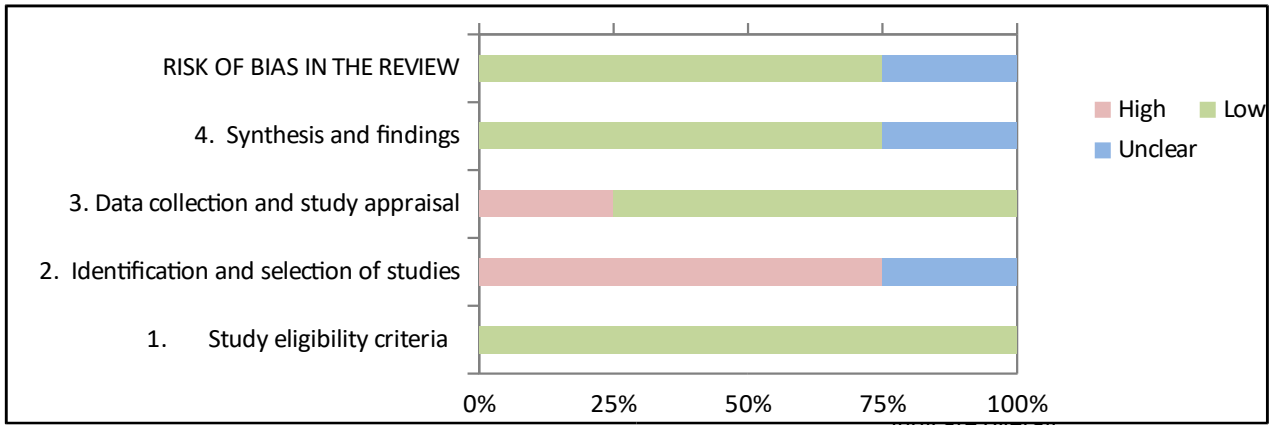

Figure 2: Overall Graphical Representation of ROBIS Domains

Darker colours indicate overall ROB rating; lighter colours concern judgments

Table 5: Quality Assessment of Studies

Study No.	Review	Phase 2				Phase 3
		1. Study eligibility criteria	2. Identification and selection of studies	3. Data collection and study appraisal	4. Synthesis and findings	Risk-of-bias in the review
1	Tham et al.	☺	☹	☺	☺	☺
2	Avila et al.	☺	☹	☺	☺	☺
3	Cui et al.	☺	☹	☺	☺	☺
4	Valaitis et al.	☺	?	☹	?	?

☺ = low risk; ☹ = high risk; ? = unclear risk.

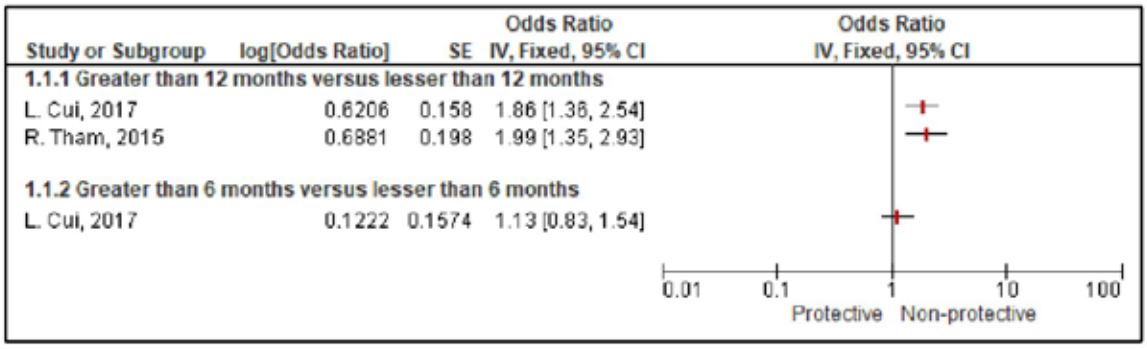

Figure 3A: Graphical Representation of Correlation between the Duration of Breastfeeding and the Acquisition of Early Childhood Caries

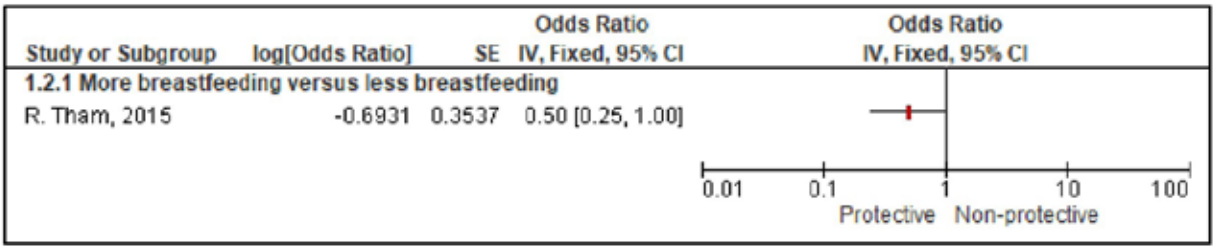

Figure 3B: Graphical Representation of Correlation between the Frequency of Breastfeeding and the Acquisition of Early Childhood Caries

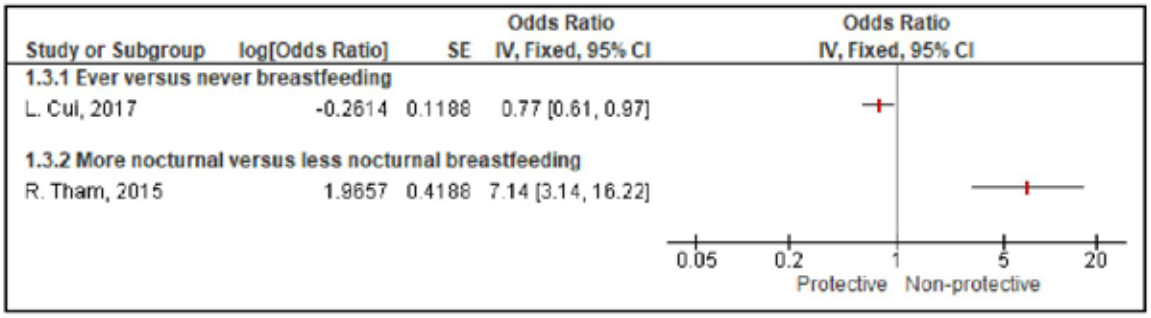

Figure 3C: Graphical Representation of Correlation between the Pattern of Breastfeeding and Acquisition of Early Childhood Caries

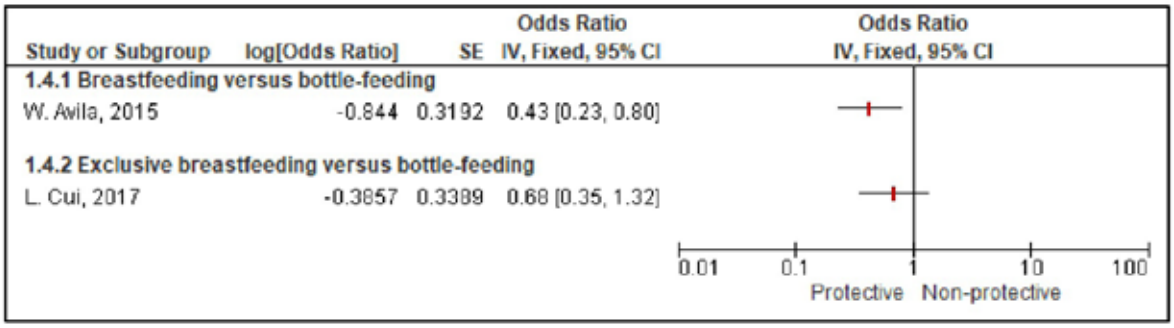

Figure 3D: Graphical Representation of Correlation of Comparison of Feeding Habits with the Acquisition of Early Childhood Caries

Pattern of breastfeeding

Assessment between patterns of breastfeeding and ECC revealed that 'ever breastfeeding' was negatively associated with the acquisition of caries. In contrast, nocturnal breastfeeding was positively correlated with the association of ECC, with an odds ratio of 7.14 (3.14-16.22) (Figure 3C).

Comparison of feeding habits

Comparison of breastfeeding with bottle feeding and its association with ECC, as determined by two systematic reviews, is presented in Figure 3D. While one systematic review[8] reported that breastfeeding had a protective role for ECC when compared with bottle feeding, findings from the other systematic review[2] suggested that there was no significant difference seen in the acquisition of ECC when exclusive breastfeeding was compared with bottle feeding.

DISCUSSION

Human breast milk is usually the first food offered to infants.[13] Several animal studies on the cariogenicity of human breast milk have suggested that human breast milk has greater cariogenicity as compared with cow's milk but less than that of infant milk formulae.[14,15] We identified four systematic reviews that assessed the direct correlation of breastfeeding with ECC, based on several parameters, including duration of breastfeeding, frequency of breastfeeding, pattern of breastfeeding, and comparison of breastfeeding and bottle feeding and their association with ECC. No single review assessed the association of breastfeeding with ECC based upon all these parameters combined. Thus, the purpose of this umbrella review was to narratively combine the results of the included systematic reviews to assess the correlation of breastfeeding and ECC based upon the above mentioned parameters.

Duration of Breastfeeding and Its Association with Early Childhood Caries

Duration of breastfeeding and its association with ECC was assessed by two included systematic reviews. [2,9] When a window of 12 months was taken into consideration, both reviews concluded that breastfeeding of 12 months or beyond had a positive correlation with ECC. These findings proved that the chances of acquiring ECC were more when the child was breastfed for more than 12 months of age. Possible reasons for these findings could be the presence of enamel defects, deleterious habits like sleep-time feeding, consumption of cariogenic complementary foodstuffs, pH of saliva, and oral hygiene practices. When a window of six months was taken into consideration, Cui et al. concluded that no significant association with ECC was present when a child was breastfed for more than six months or less than six months. [2] The possible reason for this particular correlation can be the eruption of primary teeth after the age of six months, beyond which the microbiome of the child's oral cavity changes and thus the chances of acquiring ECC at this young age is minimal.[9]

Frequency of Breastfeeding and Its Association with Early Childhood Caries

Frequency of breastfeeding, as assessed by the systematic review by Tham *et al*, was classified as more breastfeeding, i.e., breastfeeding for a longer duration, and less breastfeeding, i.e., breastfeeding for a shorter duration.[9] This systematic review did not clearly define the terms 'more or less breastfeeding', making the results of this systematic review questionable. The assessment of more or less breastfeeding was done for children under 12 months of age. No significant difference was found when more or less breastfeeding was compared with the acquisition of ECC. No systematic

review presented data related to the frequency of breastfeeding or *ad libitum* feeding after the age of 12 months.

Frequency of intake of dietary substances as well as oral clearance have a correlation with each other. Dietary substances given during the day time are usually cleared through oral clearance because of saliva.[16] This leads to prevention of prolonged accumulation of substances on enamel, thereby preventing demineralization of enamel. The possibility of prolonged accumulation increases, as the frequency of intake of dietary substances increases, leading to increased demineralization of enamel. Also, in the sleep time this oral clearance does not happen leading to prolonged demineralization of enamel without any remineralization happening in between.[17]

Pattern of Breastfeeding and Its Association with Early Childhood Caries

Pattern of breastfeeding is determined by whether the child was fed nocturnally, was ever breastfed in his/her lifetime (ever breastfeeding), or was never breastfed in his/her lifetime. 'Ever' versus 'never' breastfeeding and its association with ECC was assessed by Cui et al., who concluded that 'ever breastfeeding' was protective, with an adjusted odds ratio of 0.77.[2] Tham *et al* reviewed the studies assessing nocturnal breastfeeding as a risk factor for ECC.[9] The possible explanation for this association can be that the child goes to sleep while feeding. Lack of salivary production, non-movement of the tongue, and the accumulation of milk in the child's mouth are the predisposing factors for the acquisition of caries at an early age.

Though meta-analysis is not available, Valaitis *et al*, in her systematic review postulated that nocturnal breastfeeding and breastfeeding beyond the age of one year may be associated with ECC.[12] Further research was suggested due to the lack of good-quality methodological studies in the same domain.

Comparison of Feeding Habits and Their Association with Early Childhood Caries

Comparison of feeding habits and the risk for ECC was assessed by Avila *et al*, who observed that breastfeeding was protective compared with bottle feeding.[8] In contrast, the systematic review by Cui *et al* concluded that there was no significant difference pertaining to the acquisition of ECC when the child was exclusively breastfed or fed with the bottle. The difference in the results of these two reviews could be because of the variation in the inclusion criteria of the individual reviews. Cui *et al* compared only exclusive breastfeeding with bottle feeding, while no such criteria were applied to the inclusion of studies in the systematic review performed by Avila *et al*.[2,8] The limitation of this particular parameter lies in the content of the bottle. None of the systematic reviews discussed formula milk, bovine milk, or sweetened milk, which might have led to the various results.

Quality assessment of the systematic reviews was done with ROBIS. ROBIS categorizes the overall risk of bias of systematic reviews as either low, high or unclear based on multiple domains and phases. The overall risk of bias of the reviews by Tham *et al*, Avila *et al*, Cui *et al*, was low. However, systematic review by Tham *et al* did not mention any sources of unpublished information.[9] In the review by Cui, number of reviewers involved in the inclusion of studies was not mentioned, indicating the chances of reporting bias, nor was a proper search strategy pertaining to the databases given, making the risk-of-bias high in that particular domain.[2] Since no information on quantitative synthesis was available for the systematic review by Valaitis *et al*, the risk-of-bias of this review was noted as unclear.[12]

Limitations in understanding association of breastfeeding and ECC

We are proposing two hypotheses below which needs further research. Firstly, the studies related to the pattern of breastfeeding/bottle-feeding and its association with ECC have primarily taken into consideration the nocturnal feeding practices.[6,18-22] However, during infancy possibility of infant sleeping with the nipple or bottle in the mouth during early morning hours, day time naps in the morning and in the evenings must be taken into consideration. Specifically, targeted questionnaires about the sleep time feeding practices rather than only nocturnal should be circulated amongst new mothers to understand the pattern of breastfeeding/bottle-feeding and its correlation to ECC. Sleep time feeding practices in general rather than only nocturnal will give us information about the overall duration of accumulation of milk on the enamel surface through the day and night.

Secondly the nature of the tooth enamel on which the milk is getting accumulated should be assessed or known. Various studies have shown that enamel hypoplasia of primary teeth is one of the major risk factors for ECC.[23-25] If milk in any form is getting in contact with a strong, healthy, well mineralized smooth enamel surface, the chances of milk getting adhered to it for longer duration are minimal. This could be the reason for infants remaining without ECC, despite of prolonged nocturnal and sleep time breast feeding or bottle-feeding practices. However, if the enamel surface is rough and weak (hypoplastic) or poorly mineralized, prolonged contact of milk on this enamel surface, might lead to prolonged accumulation, longer duration of acid production, and prolonged demineralization phase without any remineralization in between, for days and months, leading to a breach in continuity of enamel and enamel breakdown. The higher porous, permeable nature of ECC affected enamel has been reported in the literature.[26,27] Two possibilities why milk is considered as a major risk factor is because, milk remains the most common sleep time substance that is given by the mothers or caretakers to the infants and toddlers. Moreover, the possibility of other dietary substances remaining on the enamel surface for prolonged duration is not possible as they are not given during sleep time. However, further specific research to delineate these complex interactions is needed. Relationship of sleep time feeding habits and enamel with and without hypoplasia must be assessed further to arrive at a concrete answer for these questions.

We deviated from the protocol by searching additional databases of OVID and Epistemonikos Database till November 2019, which was not planned at the protocol stage. Also, the inclusion criteria for this umbrella review included only systematic reviews with or without meta-analyses assessing direct correlation of breastfeeding with ECC. Quality appraisal of primary study level data was beyond the scope of this umbrella review. The authors had to rely on the findings presented in the published reviews. The overall findings of this study conclude that breastfeeding beyond the age of 12 months, accompanied by nocturnal feeding, has deleterious effects on child's oral health. Though breastfeeding

tends to be an important risk factor for ECC, multifactorial etiology involves around 123 risk factors. [23,25] Among these, the presence of enamel defects, difficulty in cleaning a child's teeth, the presence of *S. mutans*, the consumption of sweetened drinks, and maternal anxiety were found to be the most common risk indicators for ECC. [24, 25] Further trials are required to assess the correlation of these risk factors, breastfeeding, and enamel defects before an understanding of this global infectious disease can be achieved. Possibility of breastfeeding while the infant or toddler is awake rather than while sleeping should be explored. Benefit of the prolonged breastfeeding will remain the same irrespective of whether the infant or toddler is fed while sleeping or awake. Further research in this direction is warranted.

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