Relationship Between Exclusive Breastfeeding and Lower Risk of Childhood Obesity: A Narrative Review of Published Evidence

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ABSTRACT

BACKGROUND: The pattern of infant feeding during the first 1000-day period—from conception to the second birthday—has a significant influence on the child's growth trajectory. The relationship between exclusive breastfeeding and lower risk of childhood obesity has elicited much scientific interest, given the fact that this form of malnutrition is becoming a global epidemic.

AIM: This narrative review aims to examine the evidence in the literature linking exclusive breastfeeding with reduction in obesity in children.

LITERATURE SEARCH: Using appropriate search terms, PubMed database was searched for relevant articles that met the review objective.

RESULTS: Evidence for the protective effect of exclusive breastfeeding against childhood obesity have been provided by studies which explored 5 physiologic mechanisms and those that established the causality between breastfeeding and lower risk of obesity. The few studies that disputed this relationship highlighted the influence of confounding factors. A new insight on molecular mechanisms, however, points to a direct and indirect effect of human milk oligosaccharides on the prevention of overweight and obesity.

CONCLUSIONS: The preponderance of current evidence strongly suggests that exclusivity in breastfeeding can prevent the development of obesity in children.

KEYWORDS: exclusive breastfeeding, obesity risk, children, prevention

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Introduction

The first 1000 days of life spanning from conception to the second birthday is the most critical period in life because it has an extensive influence on the child's growth, learning, and survival potentials.[1] Thus, global attention is currently focused on this "window of opportunity" which has a lasting impact on the child's health. Nutrition during this extremely important period supplies the necessary macromolecules for cerebral maturation, healthy growth, and sturdy immunity.[2]

The foundations of a child's lifelong health are largely established during this 1000-day period: a time increasingly recognized as crucial to curtail the onset and progression of obesity, as well as its repercussions.[3] Exclusive breastfeeding for the first 6 months of life is the current recommendation for infant feeding based on a paradigm shift by the World Health Organization (WHO) in 2001.[4] Prior to this guideline, exclusive breastfeeding was proposed for 4 to 6 months. The evidence from a systematic review shows that infants exclusively breastfed for 6 months were less likely to suffer from gastrointestinal infections and deficits in growth.[5] For instance, a recent cross-sectional study by Marques Rde et al,[6] which aimed to assess the growth of infants who were exclusively breastfed for the first 6 months of life as well as compare the distributions of weight and length based on reference curves, indicates that exclusive breastfeeding provides adequate physical growth, leading to height and weight gain curves that are similar to or greater than the National Center for Health Statistics (1977) and WHO (2006) curves. Apart from these benefits, appropriate breastfeeding practices have other advantages, such as a lower risk of acute otitis media,[7-9] respiratory infections,[10] atopic dermatitis,[11] necrotizing enterocolitis,[12] sudden infant death syndrome,[13,14] and maternal type 2 diabetes mellitus (T2DM) following gestational diabetes,[15] as well as T2DM in the breastfed infant later in life.[16]

Prevention of childhood obesity is now seen as a prerequisite for reducing the prevalence of some noncommunicable diseases later in life. Thus, the relationship between exclusive breastfeeding and lower risk of childhood obesity has elicited much scientific interest, given the fact that this form of malnutrition is becoming a global epidemic. The present narrative review aims to examine the evidence in the literature linking exclusive breastfeeding with reduction in obesity in children.

Literature search: strategy and outcome

Using a combination of search terms that included "exclusive breastfeeding," "overweight/obesity," "risk factors," "children,"

"protective effect," and "prevention," literature search was conducted on the PubMed database. The search yielded 64 scientific and medical abstracts/citations in PubMed and 1898 full-text journal articles in PubMed Central. Evidence synthesis based on the review objective, however, narrowed down the number of selected articles which consisted of original studies, systematic reviews/meta-analyses, and information from textbooks.

Childhood overweight/obesity: risk factors, determinants, and health sequelae

From a historical perspective, the protective effect of breastfeeding against childhood obesity was first reported by Kramer[17] in 1981; subsequently, several studies have documented the link between breastfeeding and lower risk of childhood overweight/obesity,[5,18–31] although few other reports have disputed this relationship.[32–35]

Obesity in children currently poses a health challenge worldwide and is part of the "double burden" of malnutrition which afflicts children in developing countries.[36,37] It is associated with health risks and complications such as T2DM, malignancy, dyslipidemia, and hypertension, as well as carotid artery atherosclerosis.[38,39]

Obesity refers to an abnormal adiposity in the body which may negatively affect health,[40] and it is difficult to measure directly. Hence, obesity is usually evaluated by the relationship between weight and height, which gives an estimate of adiposity that is accurate enough for clinical purposes. The body mass index (BMI) is the accepted standard measure of overweight and obesity for children 2 years of age and older and adolescents.[41] Growth charts are used for these pediatric age groups to determine the matching BMI for age and gender percentile. According to the Centers for Disease Control and Prevention, overweight children have a BMI for age and gender above the 85th percentile and below the 95th percentile, whereas obese children have a BMI for age and gender above the 95th percentile.[42–44]

Over the past several years, the prevalence of pediatric obesity has increased sharply, emerging as one of the most critical public health challenges of contemporary times.[45] For instance, in 2010, more than 40 million under-5 children were estimated to be obese worldwide.[46] Prevalence estimates in developed countries, such as the United States, indicate a rising trend with preponderance of cases among the low socioeconomic class[47] and a decreasing and stabilizing trend in some European countries.[48] Conversely, the pattern in developing countries appears different as the rising cases of obesity are associated with affluence, "westernized" diets, and sedentary lifestyle.[49–51]

Obesity is a multifactorial disease, but the details of the nexus involving the gene, dietary habits, and the environment are still unclear.[45] The risk factors for childhood overweight and obesity are well documented and can be identified in the antenatal period or during infancy.[52,53] One systematic review reports prepregnancy overweight, smoking during pregnancy, high infant birth weight, and rapid weight gain as potential risk factors.[52] Specifically, prenatal tobacco exposure, maternal excess gestational weight gain, and gestational diabetes were noted as factors that could affect the fetus in the intrauterine environment and subsequently result in childhood obesity.[53] Interestingly, several important determinants of pediatric obesity in developing countries have also been identified; these include dietary imbalance with excessive caloric intake, sedentary habits, high socioeconomic status (SES), urbanization and residence in metropolitan cities, sociocultural factors, age, and female gender, as well as school meal programs.[51] For instance, dietary imbalance specifically implies practices such as unrestricted access to energy-dense fast foods in school eating outlets and overfeeding of low-birth-weight babies; sedentary habits entail the shift from outdoor sporting activities to indoor leisure activities and paucity of open spaces and playgrounds in schools; and urbanization and residence in metropolitan cities involve nutrition transition to "westernized" dietary habits, including multiplicity of fast-food outlets.[51]

There are myriads of health sequelae related to childhood obesity; they are broadly classified into medical and psychosocial consequences. The list of medical consequences (some of which have been previously mentioned) includes the metabolic syndrome, T2DM, insulin resistance, adult obesity, hypertension, dyslipidemia, obstructive sleep apnea syndrome, eating disorders, early puberty and menarche, and orthopedic disorders, whereas psychosocial consequences encompass discrimination, social stigmatization, depression, anxiety, low self-esteem and self-confidence, poor learning, stress, poor body image, and exposure to bullying.[51]

Consequently, a number of recommendations have been proposed to reduce childhood obesity. These partly consist of targeting balanced nutrition to pregnant mothers and encouraging breastfeeding; periodic monitoring of nutritional and obesity status of children; initiating school-based programs with emphasis on promoting physical activity, healthy foods in cafeteria, and ban on sweetened beverages and energy-dense junk food; as well as restriction of TV-viewing time and parental supervision of a mandatory period of physical activity.[51] As the foundation of infant feeding, encouraging exclusive breastfeeding as a strategy for reducing childhood obesity should not only be evidence based but should also be a priority for mothers worldwide

Exclusive breastfeeding and reduction in obesity: evidence based on physiologic mechanisms

Despite the non-unanimity of findings indicating the link between exclusive breastfeeding and reduction in childhood obesity risk, 5 physiologic mechanisms have been hypothesized. These mechanisms include the concepts of differential appetite regulation between breastfed and bottle-fed infants, early protein hypothesis, comparatively lower growth-accelerating

influence of breast milk, role of leptin, and link of obesity risk with differences in the composition of the intestinal flora.[45]

First, concerning the feeding behavior hypothesis characterized by differential appetite regulation, one study noted that breastfed infants display a greater influence over their food intake, thereby developing a self-control of caloric ingestion.[54] Driven by their feeling of hunger and satiety, these infants specifically regulate the amount, time frame, and how often their feeds are offered. To support this observation, Disantis et al[55] reported that early breastfeeding is also linked with greater appetite control later in life unlike what is obtainable in formula-fed infants. However, the tendency of formula-fed infants to consume larger quantities of meals than their breastfed counterparts has been documented by other researchers.[56,57] Thus, this disparity in meal consumption would presumably reduce obesity risk among the breastfed infants later in childhood.

Second, in the early protein hypothesis, it is believed that high protein ingestion from formula feeding is related to the tendency to be obese via increased lipogenesis and development of fat cells; it also possibly reduces the elaboration of human growth hormone and breakdown of fat.[58] In a multicenter randomized study,[59] formula-fed infants were assigned to be fed with lower or higher protein formula for 12 months and were compared with exclusively breastfed infants. Infants fed with lower protein formula had lower weight-for-length *z* score than their counterparts fed with higher protein formula but similar weight-for-length *z* score with the breastfed infants.[59] Findings from other studies supporting this hypothesis include the positive relationship between early high protein ingestion and higher BMI later in life,[60] observation of lower weight gain in breastfed infants than in the formula-fed counterparts,[61] higher postprandial insulin levels with prolonged insulin response seen in formula-fed infants on sixth day of life compared with breastfed infants, and related to high protein intake,[62] as well as demonstration of a higher serum insulin-like growth factor (IGF-I) in formula feeding than in breastfeeding.[63] Interestingly, hyperinsulinemia promotes fat deposition with the risk of obesity,[64] whereas high IGF-I levels in infancy were linked with obesity in childhood.[65]

Another proposed mechanism is the relatively lower growth-accelerating effect of breast milk. Some investigators were able to demonstrate that formula feeding compared with breastfeeding accelerated growth in infancy.[66] At 1 year of life, it is estimated that the difference in body weight is about 0.4 and 0.6 to 0.65 kg when infants are breastfed for 9 and 12 months, respectively.[67]

Furthermore, leptin apparently contributes to the protective influence of breastfeeding against obesity as it suppresses the craving for food and regulates calorie metabolism.[45]

Unlike formula milk, breast milk contains leptin; its level is directly related to maternal plasma level and maternal BMI. Miralles et al have reported that leptin level in breast milk within the first month of life may influence the infant's weight at the first and second year of life, among mothers with normal weight.[68] Similarly, it has also been shown that early breastfeeding of preterm infants is linked to leptin levels at 13 to 16 years of age, as greater ingestion of breast milk during infancy led to significantly lower leptin levels relative to fat mass in adolescence, highlighting the fact that early feeding style may influence later obesity.[69]

Finally, another proposed mechanism is the differential composition of gut microflora in breastfed and formula-fed infants which is linked with an increased risk of obesity.[70] Although the association of these differences with certain diseases, including obesity, needs further validation, some researchers have concluded that the presumed relationship between breastfeeding and weight trajectory is the presence or absence of *bifidobacteria*.[71] For instance, they observed that 7-year-olds with weight appropriate for age harbored more population of *bifidobacteria* than their overweight colleagues. Notably, breast milk contains *bifidobacteria* which is a reflection of the characteristic intestinal microflora of healthy breastfed infants.[71]

Exclusive breastfeeding and reduction in obesity: evidence based on causality

Several reports indicate that exclusive breastfeeding significantly protects against the risk of overweight/obesity in children.[5,17–31,72–75] Some of these studies were systematic reviews and meta-analyses,[5,18,72–75] whereas others were prospective and longitudinal,[21,23,29–31] as well as cross-sectional[17,19,20,24–26,28,31] and retrospective.[22,24]

In one of the systematic reviews and meta-analyses, the authors examined published epidemiologic studies which included cohort, case-control, or cross-sectional studies, comparing early feeding mode and adjusting for potential confounders.[5] Out of the 28 studies the authors reviewed, 9 studies with more than 69 000 subjects met their inclusion criteria. Their meta-analysis showed that breastfeeding reduced the risk of childhood obesity significantly. Moreover, 4 of the reviewed studies reportedly showed that the prevalence of obesity was influenced by both the amount and duration of breastfeeding.[5] Weighing all the evidence from the analyzed studies, the authors concluded that breastfeeding possibly exerts a minimal but consistent protective effect against childhood obesity.[5] In a related review, Harder et al[74] performed a thorough meta-analysis of the existing studies on the subject, in which 17 studies fulfilled the eligibility criteria. By meta-regression, the more the period of breastfeeding lasted, the less the risk of overweight while a categorical analysis underscored this dose-response relationship. Specifically, 1 month of breastfeeding was associated with a 4% reduction in risk. Their findings strongly supported a dose-dependent relationship between longer duration of breastfeeding and reduction in risk of overweight.[74]

Owen et al[76] conducted a meta-analysis based on probability ratios of obesity among initially breastfed infants in

comparison with their formula-fed counterparts. A total of 61 reports on the association of infant feeding with obesity risk in childhood were noted; of these, 28 (n = 298 900) provided odds ratio (OR) estimates. They confirmed that breastfeeding was related to a reduced tendency of being obese in comparison with formula feeding (OR: 0.87; 95% confidence interval [CI]: 0.85-0.89). This relationship was especially pronounced in 11 studies with small sample size (n < 500), but was still apparent in studies with large sample size (n ⩾ 500). In 6 studies which adjusted for 3 main confounders related to the parents (parental obesity, maternal smoking, and socioeconomic class), the relationship was minimized substantially but not nullified.[76] Finally, a recent updated meta-analysis by Horta and Victora[77] noted only a modest effect on overweight/obesity, in which the prevalence was reduced by approximately 10% in children exposed to longer duration of breastfeeding. These findings are nonetheless consistent with those of previous systematic reviews and meta-analyses which confirmed a causal relationship between breastfeeding and reduced risk of childhood overweight/obesity.[5,18,72-75]

One of the longitudinal studies examined the effect of feeding patterns in infancy on pediatric obesity, including the identification of processes linking social class with obesity, based on a national early childhood survey.[21] The researchers found that infants predominantly exposed to formula feeding for the first 6 months were about 2.5 times more likely to be obese at 1 year of age compared with infants on predominant breastfeeding. Furthermore, complementary feeding before 4 months and the use of pacifiers increased the likelihood for obesity; thus, early introduction of formula feeding and premature complementary feeding in infancy were the basic mechanisms which mediated this link between social class and obesity.[21]

In a cross-sectional study of a population-based sample of 32 200 Scottish under-5 children who were evaluated over a 1-year period, Armstrong and Reilly[20] found that the prevalence of obesity was significantly lower in breastfed children. The adjusted OR for obesity was 0.70 (95% CI: 0.61-0.80). This relationship between obesity and breastfeeding persisted even after the adjustment for confounders, such as social class, birth weight, and gender.[20] Another cross-sectional study conducted in Hawai'i set out to determine the characteristics of early childhood overweight/obesity and to evaluate the impact of breastfeeding.[19] Data from Hawai'i's Special Supplemental Nutrition Program for Women, Infants, and Children were analyzed for children (aged 2 years) and their mothers. Significant differences in childhood overweight/obesity were observed between breastfeeding duration and other sociodemographic groups. Remarkably, children who were breastfed for 6 months or more had a lower risk of obesity at the age of 2 years relative to those who were never breastfed, after adjustment for child-related variables, such as race/ethnicity and birth weight, and maternal variables, such as age, trimester of prenatal care entry, and smoking status.[19] In addition, the researchers found that the prevalence of early childhood overweight/obesity was associated with shorter duration of breastfeeding (duration less than 6 months).

Elsewhere in the United States, Metzger and McDade[25] evaluated the relationship between feeding chronicle in infancy and BMI in late childhood or adolescence. In the enrolled sibling dyads, the breastfed sibling had an adolescent BMI that was 0.39 SDs lower than his or her paired, non-breastfed sibling, controlling for variables which might have affected parental feeding choices.[25] In addition, logistic regression models predicting obesity revealed that breastfed siblings would less probably attain those BMI thresholds. The authors concluded not only that breastfed infants were less prone to developing obesity in the country but also, more importantly, that the use of a sibling fixed-effects model provided convincing evidence of a causal link than in previously reported studies.[25] In a recent longitudinal study of a cohort of Chinese children, Zheng et al[29] reported that longer duration of exclusive breastfeeding was associated with lower risk of becoming overweight. For instance, compared with children exclusively breastfed for less than a month, their counterparts who were exclusively breastfed for 3-5 months and ⩾6 months had 13% (relative risk [RR] = 0.87; 95% CI: 0.77-0.99) and 27% (RR = 0.73; 95% CI: 0.56-0.95) lower risk of becoming overweight, respectively.[29]

The summary of the major findings reported by these studies, which show causality between exclusive breastfeeding and lower risk of childhood obesity, is displayed in Table 1.

Studies disputing the protective role of breastfeeding against obesity

In a prospective study conducted in Hong Kong, a group of researchers evaluated the prospective adjusted associations of breastfeeding with BMI, height, and weight *z* scores at 7 years of age.[32] Interestingly, they did not find any relationship between breastfeeding and BMI, height, or weight after adjusting for sex, birth weight, gestational age, social class, exposure to passive smoking, parity, maternal age at birth, and location of birth, as well as critical infant morbidity. The authors then concluded that breastfeeding was not related to pediatric obesity in their clime, insisting that the previously observed protective effects may be as a result of socially determined confounders such as social class, maternal obesity, and maternal smoking.[32]

Other investigators in Belarus conducted a longitudinal study in which they assessed whether an intervention designed to promote exclusive and prolonged breastfeeding influenced children's anthropometrics such as height and weight, adiposity, as well as blood pressure at the age of 6.5 years.[33] A total of 17 046 healthy breastfed infants were enrolled from 31 maternity hospitals and their affiliated clinics; of those infants, 13 889 (81.5%) were followed up at 6.5 years with duplicate estimations of the anthropometric variables and blood pressure. Remarkably, the authors did not observe any significant intervention-related effects on

Table 1. Studies reporting causality between exclusive breastfeeding and lower risk of childhood obesity.

AUTHORS (YEAR), COUNTRY OF ORIGIN	STUDY DESIGN	OBESITY RISK REDUCTION	ODDS RATIO (95% CONFIDENCE INTERVAL [CI])
Zheng et al (2014),[29] China	Longitudinal	13% (breastfeeding duration: 3–5 months) 27% (breastfeeding duration: ⩾6 months)	0.87 (0.77–0.99) 0.73 (0.56–0.95)
Anderson et al (2013),[19] USA	Cross-sectional	Not provided (breastfeeding duration: ⩾6 months)	0.79 (CI: 0.69–0.91)[a]
Armstrong and Reilly (2002),[20] UK	Cross-sectional	Not provided	0.70 (0.61–0.80)[b]
Horta et al (2007),[73] Brazil and Switzerland	Systematic review/ meta-analysis	Not provided	0.78 (0.72–0.84)
Yan et al (2014),[75] China	Meta-analysis	Not provided	0.78 (0.74–0.81)
Owen et al (2005),[76] UK	Systematic review	Not provided	0.43 (0.33–0.55)[c] 0.88 (0.85–0.90)[d]
Harder et al (2005),[74] Germany	Meta-analysis	4% (breastfeeding duration: 1–3 months)	0.81 (0.74–0.88)

[a]Adjusted for child's race/ethnicity, maternal age, maternal smoking, and child's birth weight.
[b]Adjusted for socioeconomic status, birth weight, and sex.
[c]Small sample size (n < 500).
[d]Large sample size (n ⩾ 500).

the anthropometrics, measures of adiposity, and systolic or diastolic blood pressure, despite the greater prevalence of exclusive breastfeeding at 3 months in the subjects than in the controls.[33] Again, it was concluded that even with marked increases in the duration and exclusivity of breastfeeding, the intervention did not reduce the measures of adiposity at the age of 6.5 years in the subjects, controverting previously reported beneficial effects on adiposity which were attributed to uncontrolled confounding and selection bias.[33]

In Sweden, Huus and colleagues[35] examined the association between exclusive breastfeeding and obesity after taking into consideration potential confounders such as socioeconomic factors. Short-term exclusive breastfeeding (defined as <4 months of exclusive breastfeeding) was found to be associated with obesity in 5-year-old children, a finding which did not attain statistical significance when other independent factors were considered in the analysis. They concluded that even though the possible influence of exclusive breastfeeding on weight trajectory could not be excluded, yet it did not appear to protect against obesity at 5 years of age.[35]

Despite the conflicting findings from studies that support or dispute the protective effect of breastfeeding against overweight/obesity, new clinical insights reveal that the differences may not just be explained by confounders and selection bias alone, but by the differences in breast milk constituents, such as macronutrients, micronutrients, and a host of other novel bioactive compounds under study, which change among women and over time.[78] Notably, the conclusion from one meta-analysis is that sample size (publication bias) and residual confounding by SES are important issues that should be considered in the evaluation of causality because the protective effect of breastfeeding may be overestimated by these variables.[77] The authors of this meta-analytical study further observed that studies with more painstaking control of confounding variables, such as socioeconomic factors, birth weight or gestational age, and parental anthropometry, reported smaller benefits of breastfeeding.[77]

Concerning the influence of breast milk constituents on causality, breast milk has been found to contain high levels of human milk oligosaccharides (HMOs); more than 150 structurally distinct HMOs have been identified so far, and many of their biological effects are highly structure specific.[79] Human milk oligosaccharide and their fucosylated components promote increased *bifidobacteria*, which dominate the microbiota of breastfed infants.[80,81] Given the established link between the gut microbiome and overweight/obesity,[70,82] it is now being speculated that specific HMOs might affect the development of overweight/obesity indirectly by altering the structure or function of the gut microbiome.[83,84]

Conclusions

Despite the few contradictory reports, preponderance of evidence from this review strongly supports the relationship between exclusivity of breastfeeding and lower risk of obesity. The underlying physiologic and causal mechanisms have been advanced by several of the reviewed studies. Obviously, analysis of the literature favors the causal relationship, but this finding is not as robust in the meta-analytical studies compared with evaluating the individual studies. The recent insight on the molecular mechanism for this relationship, however, raises a fundamental research question: namely, whether the influence of race and dietary patterns on HMO composition of maternal breast milk could have accounted for the disparity in study findings from different regions of the globe. Interestingly, a recent study has attempted to answer this question by reporting that the protective effect of breastfeeding against early

childhood overweight and obesity may differ by race and ethnicity.[85] Perhaps, more research on the subject may in future resolve the disparate reports on the causal relationship. Presently, it is still correct to conclude that published evidence substantially show that exclusive breastfeeding lowers the risk of overweight/obesity later in life.

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Author Contributions

SNU conceived the topic, conducted the literature search, and wrote the first draft. CIE and IKN made contributions to the manuscript in the initial form. All the authors read and approved the final manuscript.

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