

REVIEW ARTICLE

Influence of Breastfeeding Pattern on Cardiovascular Disease Risks During Adulthood: A Review

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ABSTRACT

Infant feeding is thought to modulate cardiovascular risk factors such as obesity, hypertension, hyperglycemia, and dyslipidemia. This possible association between patterns of feeding with development of cardiovascular disease later in life provides the opportunity for early intervention and prevention strategies. Among all the feeding methods applied, breastfeeding is thought to be the best method and is said to be attributable to future health benefits. However, current evidence from the literature is weak and inconsistent to advocate risk factors management. Therefore, this narrative review aims to provide current findings in assessing the association of breastfeeding pattern and risk of developing cardiovascular diseases later in life. We searched three databases (MEDLINE, PubMed and Google Scholar) from year 2000 to 11 July 2018. Findings on the association between breastfeeding and cardiovascular risk factors are equivocal, although positive trend of beneficial effects of breastfeeding in reducing risk of cardiovascular diseases in adulthood was reported in majority of the studies. Future research should address all limitations that were identified by previous studies such as bias of study design and heterogeneity of samples to establish the association between breastfeeding pattern and cardiovascular disease in later life.

Keywords: Infant feeding, Breastfeeding, Cardiovascular diseases

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of the behavioral determinants that may have significant effects onto risk of CVD is pattern of feeding during infancy.

INTRODUCTION

Infant feeding is defined as mode of feeding during infancy, which includes exclusive breastfeeding, mixed-feeding of breastfeeding and formula-feeding, exclusive formula feeding, and/or inclusion of complementary food. Infant feeding is thought to modulate cardiovascular risk factors such as obesity, hypertension, hyperglycemia, and dyslipidemia. During this period of infancy, feeding practice has been shown to influence, in part, later development of cardiovascular disease (CVD) (1). Among all the feeding methods applied, breastfeeding is thought to be the best method and is said to be attributable to future health benefits. The pathophysiological pathway of CVD involves interaction of multiple factors from genetic predisposition, as well as environmental and behavioral determinants (2). One

Current evidence demonstrates that breastfeeding pattern especially exclusive breastfeeding reduces risk of CVD development in adulthood (3). It is hypothesized that during this sensitive period, pattern of feeding will result in programming of infant's physiological and metabolic functions, which later during adolescent and adulthood, increases risk of cardiovascular disease (4, 5). This possible association between patterns of breastfeeding, that constitute types, duration and introduction of complementary food, provides opportunity for implementing early intervention and prevention strategies. However, current evidence from the literature is weak and inconsistent to advocate risk factors management (6, 7). Therefore, this narrative review aims to provide current available findings in assessing the association of breastfeeding pattern and risk of developing four common cardiovascular diseases (obesity, hypertension, hyperglycemia and hyperlipidemia) later in life.

MATERIALS AND METHODS

We searched three databases (MEDLINE, PubMed and Google Scholar) from year 2000 to 11 July 2018, using Boolean operators and searched terms around breastfeeding or infant feeding and adulthood and cardiovascular disease risk (obesity or diabetes or hyperglycemia or hyperlipidemia or cholesterol or blood pressure or hypertension). Only publications in English, and journals, reviews, experimental and observational study designsources were included. Articles involving animal studies, assessing maternal health outcomes to breastfeeding, and health policies studies were excluded in this narrative review. We identified 170 titles for examination using the search terms. After removing duplicates and irrelevant studies, 27 papers were included in this review (Figure 1).

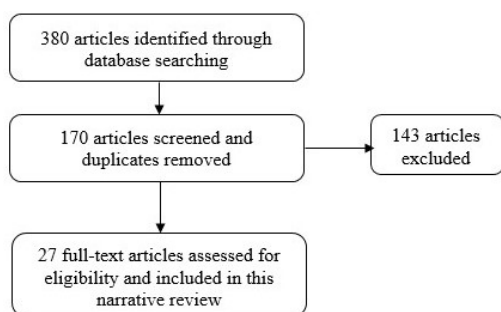


Figure 1: Flow of articles reviewed

RESULTS AND DISCUSSION

Obesity

Obesity is classified as having a weight-for-height index, also known as body mass index (BMI) equal to or greater than 30 kg.m⁻² (8). For Asian populations, the cut-off point for obesity is lower compared to international standard, that is equal to or greater than 27.5 kg.m⁻² (9). Obesity is not only an independent risk factor for cardiovascular disease, but also a predisposing factor for developing other cardiovascular risk factors such as diabetes mellitus and hypertension (10). Individuals who are obese are at higher risk for death due to cardiovascular disease compared to individuals with normal BMI. Increments in BMI is positively correlated with risk of death. (11). The global burden of obesity increases yearly with more children, adolescents, and adults, from both developed and developing countries. (12). In Malaysia specifically, it is reported that 37.3% and 12.9% of the population are overweight and obese, respectively, with similar increasing prevalence in both groups (13).

Breastfeeding is thought to be associated with reduced prevalence of obesity in later life. A recent systematic review and meta-analysis of 75 studies, conducted until September 2011, reported a weak protective effect from overweight or obesity among subjects who were

breastfed compared to not breastfed (OR 0.76; CI 0.71, 0.81). However, a large number of the studies included had a large heterogeneity as well as publication bias and residual confounding factors which may have overestimated the protective effect of breastfeeding. This was proved by the reduced protective effect found when only 16 studies of large sample size, and adjusted to socioeconomic status, weight at birth or gestational age, and parental BMI, were meta-regressed (OR 0.88; CI 0.83, 0.93).

Similarly, this association was inconclusive because other confounding factors such as level of education and income were not included which may result in an overestimation of protective effect of breastfeeding from overweight or obesity (14). Similar protective effect was previously reported in a quantitative review of 28 studies, conducted until September 2003, which showed a weak protective effect of breastfeeding from obesity, compared to formula-feeding. Meta-regression and adjustment of confounders, including socioeconomic status, parental BMI, and maternal smoking, of only 6 studies attenuated the protective effect of breastfeeding from obesity (OR 0.93; CI 0.88, 0.99) (15). These findings explain that prevalence of overweight and obesity in adolescents and adults is not solely associated with pattern of infant feeding.

In addition, longer duration of breastfeeding is thought to be associated with lower obesity prevalence in later life. A prospective study reported that early cessation of exclusive breastfeeding and introduction of formula-feeding before 6 months resulted in increased overweight and obesity prevalence at the age of 20 years old (OR 1.47; CI 1.12, 1.93). The study design, large sample size, and multivariate predictive model used to calculate the odd ratio provided strong evidence on the effect of continuing breastfeeding to more than 6 months (16). This finding is in line with breastfeeding recommendations by the World Health Organization for mothers to maintain exclusive breastfeeding for 6 months (17). This is in contrast to a previous study which reported no association between longer duration of breastfeeding of more than 6 months with reduced risk of being obese (OR 0.98; CI 0.43, 2.24), even after adjusting for confounders including socioeconomic status, parents' characteristics, birth order and weight, presence of chronic disease in family, and sedentary lifestyle (OR 1.29; CI 0.41, 4.10) (18,19). Another similar finding was also reported where there was no association between duration of breastfeeding and obesity risk (OR 1.03; CI 0.99, 1.07) in adults from five low- to middle-income countries, after adjusting to maternal socioeconomic status, smoking, education, and birth weight (OR 1.04; CI 1.00, 1.09) (20). These inconsistent findings as well as heterogeneity in study design, types of exposure and outcomes, populations being studied, result in difficulty to advocate breastfeeding duration of 6 months as a strategy to prevent obesity in later life.

Breastfeeding is also thought to be associated with lower adiposity in later life as indicated by lower mean BMI and waist-to-hip ratio (WHR). It was reported in a quantitative review of 36 observational studies and meta-analysis that was adjusted to mother's BMI, socioeconomic, and smoking status, resulted in reduced mean BMI difference, compared to formula-feeding (21,22). Furthermore, breastfeeding was reported to result in greater reduction in waist-to-hip ratio in adult life among subjects who were breastfed for more than 1 month compared to being breastfed less than a month after adjusted to socioeconomic status, smoking, maternal characteristics, birth weight, and other confounders (23). In contrast, several studies reported no association between breastfeeding and lower adiposity in adolescence and adulthood even after adjusted to socioeconomic status, birth weight, gestational age, and parental BMI (24).

Hypertension

Increase in blood pressure levels is a well-known indicator of premature cardiovascular disease. There are several evidence shown that blood pressure levels affected by early nutritional exposures and can lead to cardiovascular diseases (25). In view of breastfeeding and hypertension, breastmilk is said to contain high amounts of Long-Chain Polyunsaturated Fatty Acids (LCPUFAs) such as Decosahexanoic acid (DHA) and Arachidonic acid(AA); which are important structural components of tissue membrane systems, including the vascular endothelium. There is also evidence that show that LCPUFA supplementation reduces blood pressure among adult with hypertension. Thus, levels of LCPUFA through breast feeding could be a potential mechanism for in reducing blood pressure long term (26).

A systematic review was conducted to estimate the mean differences in systolic and diastolic blood pressure among breastfed and bottle-fed subjects. Based on the observation from eight studies, the results showed that the mean systolic blood pressure of breast-fed infants was lower compared to bottle-fed infants. Meanwhile, seven observations from six studies showed that there is no or only little difference in systolic blood pressure among breastfed and formula-fed infants. Besides, according to random effects model, there was also lower mean systolic blood pressure among breast-fed infants (mean difference: -1.4 mmHg, 95 percent confidence interval (CI): $-2.2, -0.6$; $p = 0.001$). The mean differences of diastolic blood pressure in breast-fed infants was also lower compared to bottle-fed infants based on the nine observations from eight studies. The pooled mean diastolic blood pressure was also lowered among breastfed infants which was (difference: -0.5 mmHg, 95 percent CI: $-0.9, -0.04$; $p = 0.03$) (27).

Findings from this systematic review was found to be in line with work done by Lawlor and Smith (2005) which concluded that children from poorer socioeconomic

positions, those whose mothers experience pregnancy-induced hypertension, those whose mothers smoke throughout pregnancy, those with low birthweight, who are not breast-fed, who have high sodium diets in infancy and who are obese in childhood or adolescence, tend to have higher blood pressure in adulthood (28). However, the definitive mechanisms linking these early life factors to later blood pressure and the most appropriate means of preventing adult hypertension by intervening in early life are unclear. Few mechanisms were speculated in linking variation in blood pressure in adulthood and breastfeeding pattern in infancy. Among others are reducing sodium intake in infancy, increasing intake of long-chain polyunsaturated fatty acids, protecting against hyperinsulinemia in infancy, insulin resistance in early life and it may program both growth rate and the formation of blood pressure control mechanisms which later leads to lower blood pressure in adulthood (7).

On the other hand, promising findings that correlated breast feeding in infancy and arterial function and structure in adulthood were seen in a population-based cohort of Finnish adults by Jarvisalo et al. (2009) (29). This study found that adult men who have been breast fed have better brachial endothelial function compared to men who have been formula fed. However, this hypothesis was not true in adult women. In conclusion, breastfeeding showed an inverse association with blood pressure. However, some other factors such as socioeconomic status, family educational level and health care status also affect cardiovascular disease risk factor.

Hyperglycemia

While most researchers found a correlation between infant feeding and several chronic diseases, some of the findings claimed that breast feeding influences risk of type 2 diabetes in later life. Studies during the Dutch Famine from 1943 to 1947, on Pima Indians and adults have shown that those initially breast-fed have less insulin resistance and glucose intolerance in later life compared with those with formula-fed (30,31). Similar findings were also demonstrated by many other studies with various observational study designs (30,32,33). A study was conducted to examine the association between the method of infant feeding in the first week after birth and glucose tolerance, plasma lipid profile, blood pressure, and body mass in adults aged 48 to 53 years old. Results from their findings suggested that subjects who were bottle fed had a higher concentration and a higher prevalence of impaired glucose tolerance than those who were exclusively breast fed. They suggested that there is some degree of insulin resistance as fasting insulin and split proinsulin concentrations appeared to be high. Therefore, they concluded that babies who were exclusively breast fed during the first few days of their life had lower prevalence of cardiovascular disease with respect to glucose and lipid metabolism (34).

Findings by Davis (2007) was found to be in line with

previous study which looked at the differential effects of ethnicity (African-American, Hispanic, and non-Hispanic white youth) on breast-feeding and development of type 2 diabetes, mediated in part by current weight status. From the study they found breast-feeding appears to be protective against development of type 2 diabetes in youth regardless of their ethnicity (35). Efforts to determine the effect of breastfeeding onto the risk of developing diabetes was then continued by Al Mamun et al. (2015) in their longitudinal study that involves 3,595 young adults in Australia. This study found that offspring who were breastfed for at least 4 months are protected from diabetes later in their life compared offspring who had never been breastfed. Adjusting for potential confounding and mediating factors including maternal age, education, pre-pregnancy body mass index (BMI), smoking, offspring sports, TV and their BMI at 21 years did not substantially alter this association (36).

Hyperlipidemia

Lipid is mainly produced by our liver. Liver manufactures almost 80% of the cholesterol endogenously from Acetyl Co-A from the pathway that connects both carbohydrates and lipids (37). There are so many classifications of lipids including the plasma membrane layer which is made up from phospholipid bilayer. The main parts of lipids include try-acyl-glyceride (TAG) or triglyceride, or often called as fatty acid, and cholesterol; which include high-density lipoprotein (HDL) and low-density lipoprotein (LDL). These groups regulate the condition of the blood vessels indirectly. For the distribution of lipids, liver secrete the very-low-density lipoprotein (VLDL) and transports fatty acid and cholesterol to adipose tissue for storage or to other tissues for immediate use, systemically (through the blood vessel). HDL is the counter balance to LDL, where HDL will scavenge the excess cholesterol and triglycerides from the tissues and the blood vessel, transporting them back to the liver.

Hyperlipidemia is one of the cardiovascular diseases (CVD) risk factors, where the lipids in the body is in excess amount or the total cholesterol amount is high. It can also be defined as dyslipidemia, the imbalance the amount of HDL and LDL in the blood vessel (38). This imbalance and excessive amount of lipid will result in atherosclerosis, the building of plaques at the wall of the blood vessels. If it becomes severe, it can increase the risk of getting CVD and other comorbidities. In this article, we saw the pattern of some studies that investigated the relationship of infant feeding and the occurrence of getting hyperlipidemia during adolescence or adulthood. Breastmilk has a high content of cholesterol; thus, it might affect the blood cholesterol levels as early as infancy. Keleshadi and Farajian (2014) in their reviews had proposed a mechanism that may explained the beneficial effects of cholesterol in breastmilk and lower cholesterol level later in adulthood. High intake of cholesterol from breastfeeding may have long-term effects on cholesterol endogenesis, this may be mediated through diminishing the regulation of hydroxymethyl glutaryl liver coenzyme

A. The enzyme of hydroxymethyl glutaryl coenzyme A is a restrictive enzyme in cholesterol biosynthetic pathway from acetate; its inhibitors have a blood cholesterol reducing effect. This mechanism was proposed based on observations in animal studies that high cholesterol level in infancy is associated with low cholesterol level in older ages (39). Yet, this mechanism is less to be tested in human studies. One longitudinal study known as The Hertfordshire study was among the earliest effort to test the idea. Interestingly, this study suggested that prolonged breastfeeding (>1 year) was associated with increased LDL-C and mortality. However, the result of this study was not consistent with many studies that were conducted later (40).

According from Khan et al. (2009), there was no association between mean total cholesterol with the presence of breast feeding during infancy. The mean of total cholesterol between those groups that had breast feeding and those who were not breastfed are similar, with the mean being 4.05 mmol/L and 4.01 mmol/L respectively (41). Similar to Holmes (2010), from his findings there was no significance relationship between blood cholesterol and breastfeeding (42). In terms of feeding duration, Rudnicka (23) found that breastfeeding more than a month would not affect the cholesterol amount during adolescence and adulthood.

Furthermore, there was a cohort-retrospective study by Gunnarsdottir (43) in Iceland that recorded that there was no association between breast feeding and total cholesterol. Another Iranian study (44) also had similar results, where the duration of breast-feeding had no significant relationship with CVD risk factors. The inconsistency in findings related to breastfeeding in infancy and hyperlipidemia in adulthood may happen due to limited information on the confounding factors such as mothers' educational level and family socioeconomic status which may indirectly affect the breast feeding pattern.

CONCLUSION

In conclusion, the findings on the association between infant feeding and cardiovascular risk factors are equivocal, although positive trend of beneficial effects of breastfeeding in reducing risk of cardiovascular diseases in adulthood was reported in majority of the studies. The association is still inconclusive because publication bias such as retrospective study design and small sample size, and residual confounding factors may result in overestimation or underestimation of the outcome. However, infant feeding may play a role in the pathophysiological pathway in cardiovascular disease and its risk factors. Although breastfeeding as a prevention strategy for obesity cannot be advocated, its practice should be continued as recommended by the World Health Organization. We need more prospective studies with sounds methodology to establish the

association between infant feeding and cardiovascular disease in later life.

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