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Breast-Feeding and Diabetes: Long-Term Impact on Mothers and Their Infants

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Abstract

In the general population, breast-feeding is associated with a reduced risk of the offspring being overweight later in life by 22% to 24% across the age spectrum, from preschool children to adults. There is a dose-response gradient with increasing duration of breast-feeding, and lowest risk with prolonged, exclusive breast-feeding. Breast-feeding has been shown to slow infant growth up to 2 years of age. By contrast, the scientific evidence is inconclusive about whether breast-feeding protects against the onset of overweight and subsequent development of type 2 diabetes among offspring whose mothers had diabetes during pregnancy. Moreover, evidence is insufficient to determine if lactation protects against development of type 2 diabetes later in life in women with a diabetes history during pregnancy. Given the paucity of the evidence and equivocal findings about the long-term effects of breast-feeding on future health of women with diabetes during pregnancy and their infants, further research is recommended.

Introduction

Breast-feeding has beneficial effects on long-term health, for mothers and their children. Mothers who lactate may reduce their risk of developing type 2 diabetes and receive protection against onset of breast and ovarian cancer later in life [1]. Moreover, infants who breast-feed are less likely to become overweight or to develop chronic diseases of childhood and adolescence [2]. Yet, whether breast-feeding has beneficial effects on future disease risk among mothers with diabetes during pregnancy (ie, gestational diabetes mellitus; GDM) and their offspring is less certain based on the paucity of existing scientific evidence.

In the general population, a substantial body of scientific evidence supports the association of infant breast-feeding with a 22% to 24% lower subsequent risk of childhood and adolescent overweight [3••,4]. For the mother, lactation may have immediate and long-term favorable effects on metabolic and cardiovascular risk factors [5,6,7••]. Evidence of lasting effects is less available, but suggests a lower risk of future type 2 diabetes in women, despite inconsistent findings related to postpartum weight retention. Whether breast-feeding confers the same benefits to mothers with diabetes during pregnancy and their infants is uncertain based on the limited and conflicting evidence. It is important to determine the impact of breast-feeding on the future health of these high-risk individuals because they are more likely than the general population to become overweight, and to develop impaired glucose tolerance, the metabolic syndrome, and type 2 diabetes [8-13].

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Furthermore, breast-feeding is a modifiable risk factor in early life that may have lasting effects on the development of obesity and type 2 diabetes later in life. Herein, findings on breast-feeding and overweight for the general population are summarized, as well as the constituents of breast milk that may be responsible for slower growth in breast-fed infants. Given this context, we critically examine the available data for breast-feeding's effects on the development of overweight and diabetes among mothers with diabetes and their infants. We also make recommendations for future research.

Breast-Feeding and Development of Overweight

The general population

In developed countries, a wealth of evidence supports a robust association between breast-feeding and a lower risk of becoming overweight during childhood and adolescence, even after accounting for maternal obesity and family lifestyle behaviors [14-16]. Consensus expert panels in 2007 concluded that breast-feeding reduces the risk of overweight by 22% to 24% in children and adolescents [3••,4]. The World Health Organization conducted a meta-analysis that included 39 studies published during the past 40 years and concluded that breast-fed individuals were less likely to be classified as overweight/obese (pooled OR 0.78; 95% CI, 0.72–0.84). Adjustment for parental anthropometry, socioeconomic status, and birth weight did not abolish the association [3••]. The Evidence Report from the Agency for Healthcare Research and Quality found a 24% (95% CI, 14–33) reduction in risk of overweight and obesity associated with breast-feeding, taking into account potential confounders [4]. These data also support a greater protection against overweight with more prolonged, exclusive breast-feeding. Another meta-analysis of 17 studies showed a strong dose-response relationship between increasing duration of months of breast-feeding— 4% per month reduction in risk of overweight [17]. The consistency of these associations throughout the life cycle (infancy to adulthood) suggests that breast-feeding may have lasting protective effects independent of dietary and physical activity patterns later in life [15]. Because studies have been conducted primarily in European and white populations, there is less certainty that breast-feeding protects against overweight in childhood and adolescence among minority groups.

The overall reduction in overweight among breastfed infants is consistent with the observation that breast-fed infants grow more slowly and are leaner at 1 to 2 years of age than non–breast-fed infants [18-20]. The slower rate of growth persists at least 2 years, and the protective effects continue through childhood and adolescence [14,15,21]. Because randomization to breast-feeding versus formula feeding is not desirable or ethical, the causal link is not definitive. The robustness of the protective association, slower growth patterns in breast-fed infants, and emerging evidence of differences in metabolic markers support a possible causal relationship in the general population.

Breast-feeding's protection against future overweight may stem from breast milk's unique biochemical constituents and nutrient composition that favorably affect infant growth and regulate energy balance. Breast milk contains bioactive substances that may affect regulation of energy balance, fat deposition, and metabolic responses. For example, relative to formula feeds, breast milk contains lower protein levels. Higher protein levels in early life have been linked to higher body mass index (BMI) later in life in some [22,23], but not all, studies [24]. Higher insulin levels have also been reported in formula-fed compared with breast-fed babies [25]. Behavioral aspects may also contribute to the favorable effects of breast-feeding on optimal growth and development of energy balance.

Breast-Feeding and Impact on Development of Overweight

Infants of mothers with diabetes during pregnancy

The protective effects of breast-feeding found in the general population may not be apparent in women with diabetes during pregnancy and their offspring based on very limited evidence. Since 1986 the American Diabetes Association has recommended that women with previous GDM should be encouraged to breast-feed [26,27]. The Fourth International Workshop-Conference on Gestational Diabetes Mellitus recommended that women with previous GDM breast-feed, although it was acknowledged that data to demonstrate efficacy were lacking. More recently, conflicting findings have raised questions about whether breast-feeding confers the same health benefits for the offspring of women with diabetes during pregnancy as for the general population. In 2007, the Fifth International Workshop-Conference made the same recommendation and identified the need for research on breast-feeding's effects on health of their offspring based on the conflicting findings [28••].

Offspring whose mothers had pregestational diabetes or GDM during pregnancy are more likely to become overweight and develop metabolic abnormalities [29]. However, breast-feeding's impact by mothers with diabetes during pregnancy on the future health of their offspring remains uncertain. Studies have reported conflicting findings (Table 1), including higher risk [30,31], no significant difference [32], or lower risk [33] of childhood or adolescent overweight associated with breast-feeding among offspring whose mothers had diabetes during pregnancy [34]. Specifically, a nonrandomized, longitudinal study compared early intake of breast milk from diabetic mothers (83 type 1 diabetes, 29 GDM) with banked donor breast milk during the first week of life [30] and during the second to fourth week of life, controlling for the first week [31]. Higher intakes of breast milk from diabetic mothers during the first week of life were associated with a twofold higher (OR = 1.91; 95% CI, 1.10–3.30) risk of overweight at age 2, defined as relative body weight above 110%, compared with the lowest tertile. The association was strengthened (OR = 2.59; 95% CI, 1.32–5.04) after adjusting for age, sex, type of maternal diabetes, and maternal BMI [30]. The prevalence of impaired glucose tolerance was lower among 2-year-olds who were fed highest versus lowest amounts of banked donor breast milk in the first week of life (OR = 0.19; 95% CI, 0.05–0.70) [30]. In the same cohort, breast milk intake during the second to fourth week of life (OR = 1.61; 95% CI, 0.76–3.42) and total duration of breast-feeding were not associated with risk of overweight or with impaired glucose tolerance at 2 years of age adjusted for early neonatal breast milk intake and other covariates [31]. The findings are limited in that subjects were not randomized to donor-banked breast milk, which may have introduced selection bias and residual confounding. Also, total volume of diabetic breast milk in the first week of life was not reported in one study, and neither study assessed the severity of maternal gestational and postpartum hyperglycemia.

Two other larger studies reported that breast-feeding was protective against offspring overweight during childhood and adolescence. The Nurses' Health Study of Offspring examined risk of overweight among youth 9 to 14 years of age whose mothers had diabetes during pregnancy (417 GDM, 56 pregestational diabetes). The study found a lower but nonsignificant association for ever versus never breast-fed with odds of overweight (OR = 0.62; 95% CI, 0.24–1.60) [32]. Another study of German mothers with GDM and their offspring (n = 324, 2 to 8 years of age) found that exclusive breast-feeding for 3 months or longer was associated with a lower risk of overweight (OR = 0.55; 95% CI, 0.33–0.91), but only among offspring of obese mothers [33].

These conflicting findings may originate from the early age (2 to 3 years) that overweight was ascertained for subjects, which is less predictive of overweight status at older ages. Other limitations of these studies include the heterogeneity of maternal type of diabetes during

pregnancy, and residual confounding from severity of maternal gestational diabetes and glycemic control during the prenatal and postnatal periods.

Breast-Feeding and Impact on Development of Type 2 Diabetes

Infants of mothers with diabetes during pregnancy

Much less is known about breast-feeding's impact on future development of type 2 diabetes in offspring whose mothers had diabetes during pregnancy (Table 2). Breast-feeding and risk of type 2 diabetes in the offspring have been examined in indigenous North American populations with a high prevalence of type 2 diabetes [35-37]. In Pima Indians, exclusive breastfeeding compared with exclusive bottle-feeding was associated with a lower prevalence of type 2 diabetes (OR = 0.41; 95% CI, 0.18–0.93) among offspring 10 to 39 years of age adjusted for age, sex, parental diabetes, and birth weight [35]; however, the study did not examine maternal diabetes during pregnancy. Among offspring of Pima mothers without diabetes during pregnancy (n = 551), exclusive breast-feeding (> 2 months) was associated with a lower prevalence of type 2 diabetes versus not breast-fed (OR = 0.56; 95% CI, 0.41–0.76) [36]. No association of breast-feeding was observed with prevalence of type 2 diabetes among 21 offspring of Pima mothers with diabetes during pregnancy; prevalence for exclusively breast-fed and not breast-fed was 30.1% versus 43.5%, adjusted for age, sex, birth weight, birth date, and the presence of diabetes mellitus in either parent [36]. A case-control study of 46 Native Canadian children diagnosed with diabetes before 18 years of age and 92 age-matched and sex-matched controls found a lower odds of type 2 diabetes among offspring who were breast-fed 12 months or more versus none (OR = 0.24; 95% CI, 0.13–0.84) adjusted for type of maternal diabetes during pregnancy (type 1 diabetes, GDM, or none) [37]. A recent US case-control study of African American, Hispanic, and non-Hispanic white youth with type 2 diabetes (n = 80) and 167 controls 10 to 21 years of age (SEARCH for Diabetes in Youth) found a protective association between longer duration of breast-feeding and incidence of type 2 diabetes (OR = 0.43; 95% CI, 0.19–0.99) adjusted for 12 covariates [38].

It is biologically plausible that constituents in breast milk of diabetic mothers may adversely affect their offspring's growth. For example, glucose levels in breast milk from moderately controlled diabetic women were found to be higher and more variable than levels for nondiabetic women [39]. Based on these limited data, the evidence is insufficient to determine if breast-feeding prevents type 2 diabetes in the offspring of women with diabetes during pregnancy, or if breast milk from diabetic mothers has beneficial or detrimental effects on the growth and health of their infants [34].

Lactation and Impact on Future Health of Women

The general population

In the general population, prolonged, exclusive lactation may lead to lower postpartum weight retention in some, but not all, studies, and more favorable lipid profiles [7••] and lower prevalence of the metabolic syndrome in women [40]. Prospective studies in which maternal weights were measured before or during early pregnancy have consistently reported lower postpartum weight retention, more rapid return to pregravid weight, or greater weight losses within 6 months to 1 year among lactating women [41,42]. Greater frequency of lactation and higher breast milk energy output are associated with greater weight loss from 3 to 6 months. Exclusive breast-feeding from 2.5 to 6 months postpartum [42,43] and for the first year [44] resulted in 2-kg greater average maternal weight loss. Another study reported 2-kg greater losses in total body fat for lactating versus non-lactating women [45] that did not reach statistical significance. Longer duration of breast-feeding has also been associated with lower maternal weight gain 10 to 15 years later [46,47].

Lactation has immediate beneficial effects on maternal cardiometabolic risk factors but whether these effects persist postweaning has been rarely studied. Lactating women exhibit lower blood glucose and insulin concentrations along with higher rates of glucose production and lipolysis compared with non-lactating women [6]. Lactating women also exhibit more favorable lipid profiles. Among the 34 exclusively lactating women, plasma triglyceride (TG), low-density lipoprotein cholesterol (LDL-C), and total cholesterol (TC) levels declined between delivery and 6 months postpartum [48], but TC levels after 2 months postweaning returned to delivery levels [48]. However, preconception lipid levels, postpartum weight loss, and other lifestyle behaviors were not examined in this study.

Longitudinal studies of preconception to postpartum changes in blood lipid profiles found that lactating versus non-lactating women (6 weeks to 6 months postpartum) had higher high-density lipoprotein cholesterol (HDL-C) levels [49] but no differences in LDL-TG, LDL-C, or TC levels [50]. Others reported significantly lower fasting serum TG levels at 6 months postpartum [51], and more rapid declines in plasma TC and TG levels from delivery to 3 to 4 months postpartum in lactating women [52]. From preconception to 40 weeks postpartum, lactation was an important factor in reversing gestational hyperlipidemia. TG levels declined significantly more rapidly in lactating (n = 22) than non-lactating (n = 12) women within 20 weeks postpartum and stabilized thereafter; TC levels declined earlier, although not significantly [53]. However, none of these studies examined lipid profiles postweaning.

Gunderson et al. [7••] examined changes in maternal lipid profiles and other cardiometabolic risk factors from preconception to postweaning (average, 13 months postweaning; range, 2–24 months). Lactation was not associated with reduced pregnancy-related gains in weight and waist girth, but changes in other metabolic risk factors (ie, plasma LDL-C and fasting insulin) were more favorable for women who had lactated compared with those who did not. Lactation for at least 3 months was associated with a more favorable lipid profile—in particular, a 6-mg/dL smaller decrement in HDL-C levels [7••]. Lactation's beneficial effects on plasma HDL-C levels are important because of the strong inverse association between plasma HCL-C and onset of type 2 diabetes, particularly in women.

In the Nurses' Health Study cohort, higher cumulative duration of lifetime lactation was associated with a 25% lower incidence of diabetes in women several years later [54]. The association was independent of current BMI and other risk factors, and risk reductions were stronger with exclusive breast-feeding [54].

Mothers with diabetes during pregnancy

Although some evidence suggests that lactating women in general exhibit more favorable cardiometabolic profiles, less is known about lactation's long-term effects on the health of mothers with a diabetes history during pregnancy. Some studies report that GDM mothers who lactate have more favorable lipid profiles and glucose tolerance in the early postpartum period. Among women with previous GDM [5], lactating (n = 14) versus nonlactating women (n = 12) had higher insulin sensitivity, glucose effectiveness, and first-phase insulin response to glucose (AIRg) assessed by Bergman's minimal model, but statistical significance was not reached given the small sample size. However, the disposition index (insulin sensitivity multiplied by AIRg) was 2.5 times higher (129.9 ± 26.0 vs $53.4 \pm 18.0 \times 10^{(-4)}/\text{min}^{(-1)}$; $P < 0.05$) in lactating compared with non-lactating women matched for age, weight, postpartum weight loss, and exercise habits [5]. These data suggest improved insulin sensitivity and β-cell function in women who breast-feed.

A series of cross-sectional and follow-up studies of Latinas with previous GDM that assessed lactation at a single time point show inconsistent findings about a link to type 2 diabetes mellitus after GDM pregnancy [55-58]. Among women with previous GDM, current lactation had

immediate favorable effects on glucose tolerance at 4 to 12 weeks postpartum with a lower total area under the curve (AUC) (17.0 ± 4.2 vs 17.9 ± 5.0 g/min/dL), lower fasting serum glucose (93 ± 13 vs 98 ± 17 mg/dL), and 2-hour oral glucose tolerance test glucose levels (124 ± 41 vs 134 ± 49 mg/dL) after controlling for BMI, maternal age, and insulin use during pregnancy [55]. The same study found that lactating women had half the prevalence of type 2 diabetes as non-lactating women with previous GDM [55]. Yet, it is unclear if these favorable effects persist to influence disease onset years after delivery.

Few studies have examined lactation's impact on development of diabetes among women with a diabetes history during pregnancy. One study of Latina women attending a family planning clinic assessed lactation status (yes vs no) at 4 to 16 weeks postpartum and found no association with subsequent development of type 2 diabetes within 5 years [56]. Buchanan et al. [57] examined 122 Latinas with normal fasting glucose and no insulin use during GDM pregnancy. They found that those diagnosed with diabetes within 6 months postpartum were less likely to have breast-fed (42%) than those with normal glucose tolerance (71%). However, among 91 Latinas receiving oral glucose tolerance test screening at 15-month intervals, lactation status (yes vs no) at 11 to 26 months postpartum did not influence the onset of type 2 diabetes [58]. Similarly, a large, retrospective study of women with a GDM history found no association of lactation duration among women with GDM with lower risk of self-reported type 2 diabetes later in life [54]. Thus, evidence that lactation confers long-term protection against type 2 diabetes later in life is unclear given the limited number of prospective studies and lack of population-based studies.

Conclusions

The American Academy of Pediatrics recommends that all infants should be exclusively breast-fed through 6 months of age and that breast-feeding should continue until the infant is 1 year of age [59]. Although 80% of US women initiate lactation, 45% percent report "any" breast-feeding at 6 months and less than 20% report "exclusively" breast-feeding their infants at 6 months. Thus, increasing lactation rates among women has substantial potential for positive effects on infant and maternal health in the general population.

Abundant evidence for the general population of developed countries supports a robust association between breast-feeding and lower risk of becoming overweight during childhood and adolescence, even after accounting for maternal obesity and family lifestyle behaviors. However, evidence is inconclusive that breast-feeding confers the same protection against obesity for offspring of women with diabetes during pregnancy as for the general population. Findings are mixed, with higher, lower, or no difference in risk of overweight for breast-fed compared with non–breast-fed infants whose mothers had diabetes during pregnancy. Prospective studies of these infants of diabetic mothers are needed to examine the effect of breast-feeding on infant growth and development of overweight in childhood controlling for parental attributes, intrauterine metabolic milieu, maternal postpartum glucose tolerance, and postnatal behavioral traits.

For the mother, clinical and epidemiologic evidence support the hypothesis that lactation has immediate favorable effects on maternal glucose tolerance for the general population and for those with a diabetes history during pregnancy. In the Nurses' Health Study, women who lactated for 4 months or more had a 25% reduction in risk of type 2 diabetes, and exclusive lactation was associated with a 35% to 40% reduction in diabetes risk. In this same study, among women with a GDM history, findings were inconclusive. To determine if breast-feeding delays or prevents the onset of type 2 diabetes in women with a diabetes history during pregnancy and their offspring, prospective, populationbased studies that control for intrauterine and postnatal exposures are needed.

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Table 1

Association of breast-feeding with risk of overweight among offspring of mothers with diabetes during pregnancy

Study	Study design	Mothers′ type of DM during pregnancy, *n*	Study population	Breast-feeding measure	Obesity definition	Offspring age range	OR (95% CI)	Adjusted covariates
Mayer-Davis et al. [32]	Retrospective cohort, 1996	GDM 417, PG 56 (self-reported)	Nurses′ Health Study, GUTS	Exclusive breast-feeding vs exclusive formula-feeding	BMI ≥ 25 kg/m^2 (self-reported weight and height)	9–14 y in 1996	0.62 (0.24–1.60)	Age, sex, race, Tanner stage, maternal BMI, smoking , income, birth order, diet, physical activity, gestational age
Schaefer-Graf et al. [33]	Prospective cohort, 1995–2000	GDM 324	Berlin, Germany	Retrospective duration > 3 mo vs ≤ 3 mo	BMI ≥ 90th percentile in cohort	2–8 y (mean, 5.4 y)	0.55 (0.33–0.91) in offspring of obese mothers	Parental obesity, birth weight percentile
Rodekamp et al. [31]	Longitudinal, 1980–1989	T1DM 83, GDM 26	Berlin, Germany	2nd–4th wk of life, highest tertile of donor-banked breast milk	RW > 110%	2 y	1.61 (0.76–3.42)	Diabetic breast milk volume 1–7 d life and other covariates from Plagemann et al. [30]
Plagemann et al. [30]	Longitudinal, 1980–1989	T1DM 83, GDM 26	Berlin, Germany	1–7 d of life, highest tertile of donor-banked breast milk	RW > 110%	2 y	2.59 (1.32–5.04)	Birth weight, gestational age, sex, maternal BMI, type of maternal diabetes

BMI—body mass index; DM—diabetes mellitus; GDM—gestational diabetes mellitus; GUTS—Growing Up Today Study; OR—odds ratio; PG—pregestational; RW—relative weight; T1DM— type 1 diabetes mellitus.

Table 2

Association of breast-feeding with risk of T2DM or IGT among offspring of mothers with diabetes during pregnancy

Study	Study design	Mother's type of DM during pregnancy,*n*	Study population	Breast-feeding measure	T2DM outcome definition	Offspring age range	OR (95%CI), or % with DM*	Adjusted covariates
Mayer-Davis et al. [38]	Case-control	Any DM: cases 16, controls 8	SEARCH Diabetes in youth	Ever vs never BF	Provider diagnosed, T2DM 80, control 167	10–21 y	0.43 (0.19–0.99)	Sex, age, race, family DM history, maternal attributes, child BMI z-score
Young et al. [37]	Case-control, 2000–2001	T1DM 14, GDM 22, none 102	Native Canadian, Manitoba	Duration > 12 mo vs none	T2DM 46, control 92; diagnosis < 18 y, FPG ≥ 126 mg/dL	< 18 y	0.24 (0.13–0.99)	Age, sex-matched, type of maternal diabetes
Pettitt et al. [36]	Longitudinal, 1978	75-g OGTT during pregnancy, GDM 21, none 551	Pima Indians	Exclusive BF for ≥ 2 mo vs none	75-g OGTT WHO criteria, child every 2 years since age 5 y	10–39 y	30.1% vs 43.5%*	None
Pettitt et al. [35]	Longitudinal, 1978	Not measured during pregnancy (*n* = 720)	Pima Indians	Exclusive BF for > 2 mo vs none	75-g OGTT WHO criteria, prevalent T2DM	10–39 y	0.41 (0.18–0.93)	Age, sex, birth year, parental diabetes, relative weight, birth weight
Plagemann et al. [30]	Longitudinal, nonrandomized, 1980–1989	T1DM 83, GDM 29	Berlin, Germany	1st–7th d of life donor-banked breast milk vs diabetic breast milk	IGT based on 2-h OGTT, 1.75-g glucose/kg of body weight	2 y	0.19 (0.05–0.70)	Birth weight, sex, age, gestational age, relative birth weight, maternal BMI, type of maternal DM
Rodekamp et al. [31]	Longitudinal, nonrandomized, 1980–1989	T1DM 83, GDM 29	Berlin, Germany	2nd–4th wk of life donor-banked breast milk	IGT based on 2-h OGTT, 1.75-g glucose/kg of body weight	2 y	0.66 (0.22–2.02)	Volume of diabetic breast milk in 1st wk of life and others

BF—breast-fed; BMI—body mass index; DM—diabetes mellitus; FPG—fasting plasma glucose; GDM—gestational diabetes mellitus; IGT—impaired glucose tolerance; OGTT—oral glucose tolerance test; T1DM—type 1 diabetes mellitus; T2DM—type 2 diabetes mellitus; WHO—World Health Organization.