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Impact of Breastfeeding on Maternal Metabolism: Implications for Women with Gestational Diabetes

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Abstract

Lactating compared with nonlactating women display more favorable metabolic parameters, including less atherogenic blood lipids, lower fasting and postprandial blood glucose as well as insulin, and greater insulin sensitivity in the first 4 months postpartum. However, direct evidence demonstrating that these metabolic changes persist from delivery to postweaning is much less available. Studies have reported that longer lactation duration may reduce long-term risk of cardiometabolic disease, including type 2 diabetes, but findings from most studies are limited by self-report of disease outcomes, absence of longitudinal biochemical data, or no assessment of maternal lifestyle behaviors. Studies of women with a history gestational diabetes mellitus (GDM) also reported associations between lactation duration and lower the incidence of type 2 diabetes and the metabolic syndrome. The mechanisms are not understood, but hormonal regulation of pancreatic β-cell proliferation and function or other metabolic pathways may mediate the lactation association with cardiometabolic disease in women.

Keywords

Maternal metabolism; Diabetes; Cardiometabolic disease; Women's health; Lactation; Diabetes; Breastfeeding; Gestational diabetes mellitus; Cardiovascular disease; Prospective cohort studies; Epidemiology; Pregnancy; Women

Introduction

Lactation confers important short- and long-term benefits to women's health. Short-term effects include uterine involution, mobilization of energy stores, and reversal of the metabolic adaptations of pregnancy involving less atherogenic blood lipid profiles. Long-term benefits of lactation for women's health include reduction in risk of breast and ovarian

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Compliance with Ethics Guidelines

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cancer [1], the metabolic syndrome [2••], cardiovascular disease (CVD) [3, 4], and possibly lower risk of type 2 diabetes during mid to late life [5]. Lactation appear to have lasting favorable effects on cardiometabolic risk factors for postpartum women, including better glucose tolerance and increased insulin sensitivity during the early postpartum period. With regard to long-term effects on risk factors, findings from prospective studies are mixed, and very few provide direct evidence for lactation's lasting effects on biochemical risk factors (eg, glucose, lipids, insulin, adipokines, endothelial function) that determine subsequent development of cardiometabolic diseases in women.

The lasting effects of lactation on maternal metabolism are of particular importance for prevention of type 2 diabetes and cardiovascular disease in women with previous gestational diabetes mellitus (GDM). GDM is defined as glucose intolerance of variable severity with first onset during pregnancy [6], and occurs in ~7 % of all US pregnancies with over 200,000 women affected per year [7]. A history of GDM confers a 4- to 7-fold higher risk of diabetes and 3-fold higher risk of the metabolic syndrome [8], depending on whether hyperglycemia is present before conception [9, 10]. Almost 50 % of women with GDM will be diagnosed with type 2 diabetes mellitus within 5–8 years after pregnancy [10–12]. Risk factors influencing onset of type 2 diabetes and the metabolic syndrome after GDM pregnancy include obesity, pancreatic β-cell dysfunction, and glucose intolerance in the early postpartum period [11, 13–18]. Much less is known about postpartum behaviors, including lactation, as influencing progression to type 2 diabetes after GDM pregnancy. The Diabetes Prevention Program (DPP) randomized women with impaired glucose tolerance to lifestyle intervention and found a lower diabetes risk among those with a history of GDM, but could not evaluate the impact of lactation and postpartum behaviors because women had delivered pregnancies more than a decade earlier [19]. Thus, evidence is inconclusive as to whether lactation prevents onset of type 2 diabetes, or glucose intolerance in women later in life, as most studies rely on self-report of diabetes, lack data on GDM status, or have not taken into account reverse causation due to the more healthful lifestyle behaviors practiced by women who choose to breastfeed. Herein, we critically examine the evidence for both immediate and lasting effects of lactation on maternal metabolism and disease risk, as well as the implications for women with a history of GDM.

Lactation and Adaptations of Maternal Metabolism

Pregnancy is characterized by 200 %–300 % higher fasting triglycerides and marked insulin resistance by mid gestation [20, 21]. The metabolic adaptations during lactation can reverse some of the atherogenic and diabetogenic effects of gestation. The favorable effects of lactation on maternal cardiometabolic risk factors during the first year postpartum include decreased blood lipids, increased insulin sensitivity, greater weight loss, and fat store mobilization. Overall maternal adaptations during lactation include increased basal metabolic rates and mobilization of fat stores [22–24]. Maternal fuel metabolism is altered markedly, with a 15 %–25 % increase in energy expenditure for milk production [24, 25]. For exclusively lactating women, an additional 400–500 kcal per 24 hours is required for milk production during the first 6 months after delivery. The increased nutrient needs to support lactogenesis (the process of milk synthesis and secretion) are obtained from

maternal dietary intake, as well as about 170 kcal per 24 hours that is mobilized from fat stores and/or decreased physical activity [22, 24, 26].

Blood Glucose and Insulin Sensitivity

The metabolic adaptations to lactogenesis are pronounced to meet the greater need for lipids and glucose metabolites required for milk production. About 50 g of glucose per 24 hours is diverted for lactogenesis via noninsulin mediated pathways for uptake by the mammary gland [24]. The diversion of metabolic fuels result in lower maternal blood glucose, insulin, and lipid concentrations despite the higher rates of glucose production and lipolysis observed in lactating women [27]. Lactation is also characterized by elevations in the respiratory quotient and higher carbohydrate utilization, which is consistent with the preferential use of glucose by the mammary gland [24].

Increased insulin sensitivity has also been reported in lactating women during the early postpartum period [27]. Tigas et al found that in the fasting state, lactating compared with nonlactating women had a 33 % higher glucose production rate that was attributed to the 50 % higher rates of glycogenolysis to meet the increased glucose demand for milk production [27]. Ingestion of a 30 % higher glucose load by lactating women resulted in similar plasma glucose despite lower insulin concentrations in lactating women [27]. Other studies have reported lower fasting plasma glucose and insulin concentrations in [28], as well as lower plasma insulin concentrations in the postabsorptive state for lactating women [29]. Hubinont et al [30] administered frequently sampled oral glucose tolerance tests (OGTT) with blood samples drawn every 15 minutes for 120 minutes. The corrected insulin response at 30 minutes was significantly higher in nonlactating ($1.24\pm0.26\ \mu U\cdot mg^{-2}\cdot 10^{2}$) than in lactating women ($0.67\pm0.11\ \mu U\cdot mg^{-2}\cdot 10^{2}$). These findings show that basal and glucose-stimulated β-cell secretory activity for a standardized glucose load is lower for lactating than nonlactating women [30]. Lactation influence future disease risk by substantially reducing the load on the pancreatic β-cells through reduced demand for insulin secretion for transport of metabolic substrates to the mammary gland for milk synthesis. Little is known about biological pathways through which lactation may have a lasting impact on pancreatic β-cell function or cell mass. These short-term favorable effects on cardiometabolic risk factors may have lasting effects that influence future progression to glucose intolerance and metabolic diseases in women during mid to late life.

Blood Lipids and Lipoproteins

Lactation may play an important role in reversal of the atherogenic lipid profile of normal pregnancy. Close to parturition, induction of lipoprotein lipase activity in the mammary glands leads to greater utilization of circulating triglycerides in preparation for lactogenesis [31]. In lactating women, blood triglyceride concentrations decline more rapidly from delivery through 3–6 months postdelivery [24, 32, 33] and these levels stabilize thereafter [33]. Others studies reported that lactating women had higher plasma high density lipoprotein cholesterol (HDL-C) from 6 weeks to 6 months postpartum [34] but found no differences in plasma LDL-triglyceride, LDL-C, or total cholesterol [35], although another study reported more rapid declines in plasma total cholesterol up to 3–4 months postpartum

[32]. In summary, lactating compared with nonlactating women consistently exhibit lower plasma triglycerides [32, 33] and higher plasma HDL-C and HDL-C: total cholesterol ratios at 3–6 months postpartum [34–36].

A 3-year longitudinal study in the Coronary Risk Development in Young Adults (CARDIA) Study assessed changes in cardiometabolic risk factors from prepregnancy through postweaning, and reported significantly higher plasma HDL-C on average 7 mg/dl up to 2 years postweaning in women who had lactated for >3 months vs≤3 months, adjusted for preconception parameters and weight gain [37]. In summary, these studies support the hypothesis that lactation has favorable and lasting effects on maternal blood lipids that reflect a less atherogenic risk profile. Yet, long-term studies that link these risk factors changes to future disease risk are important to establish the lasting effects. Moreover, residual confounding by BMI differences or other lifestyle attributes among nonlactating women may influence these findings as many studies did not account for changes in maternal physical activity levels, or dietary habits during the interval postpartum.

Lactation and Body Weight and Composition

Lactation may improve cardiometabolic profiles, including glucose tolerance by promoting postpartum weight loss and mobilization of regional fat depots. Milk production increases maternal total energy expenditure by 15 %–25 % [24, 25], yet the association between lactation and greater weight loss is equivocal [38]. Prospective studies that measured maternal weights (not self-reported) from before or during early pregnancy have generally reported lower weight retention at 1 year postpartum [39], more rapid weight loss approaching pregravid weight [40], or 1–2 kg greater average weight loss within 3–6 months postpartum among lactating women [41]. Prolonged, exclusive lactation is associated with lower postpartum weight retention in some [39, 41], but not all studies [42] and decreased risk of becoming overweight [43, 44]. Higher lactation intensity and breast milk energy output resulted in a 2 kg greater weight loss within 3–6 months [41, 45, 46], and up to 12 months postpartum [39].

In studies employing the body imaging methodologies, lactation may also alter maternal body composition and regional fat distribution given the preferential mobilization of fat stores from certain tissue depots. Well-nourished lactating women lose about 2 kg in total fat mass by 6 months postpartum [23, 47]. Regional changes in adiposity in lactating women include enhanced fat mass mobilization from the trunk and thighs in some [47, 48], but not all studies [49], as well as from suprailiac and subscapular sites measured by skinfold thickness [50, 51]. One study using dual-energy X-ray absorptiometry (DXA) to serially assess body composition and regional fat distribution in postpartum women reported greater decrements in total fat mass (2 kg) at 1 year postpartum in lactating vs nonlactating women with the largest decline between 3 and 6 months [52]. However, fat mobilization from leg, arm, and trunk regions did not differ by lactation groups [52, 53]. Lactation history has been associated smaller visceral fat area in women, but only for the group who reported that they lactated for at least 3 months across all prior births [54]. Lactation history may influence future metabolic disease risk in women, although it is unclear whether mechanisms involve greater weight loss or reduction in specific fat depots.

Lactation and Future Cardiometabolic Disease Risk

Several studies have examined women during mid to late life without knowledge of their prior history of GDM in relation to disease prevalence. These studies reported protective associations with longer lactation duration, including a 20 %–30 % lower prevalence of the metabolic syndrome [55, 56], or prevalence of type 2 diabetes [4, 57]. One prospective study, the Shanghai Women's Study, reported a 10 % lower incidence of self-reported diabetes associated with 3 years of lactation, but lacked data on prior history of GDM [58]. A second prospective study, the Nurses' Health Study (NHS), assessed lactation and incidence of type 2 diabetes among women who reported no history of GDM, and found a 14 %–15 % lower incidence of self-reported diabetes per year of lactation [5]. Both studies reported a null association for lactation and diabetes among older women (40–65 years) or postmenopausal women. Limitations of the previous studies that assessed diabetes incidence include: (1) diabetes cases by self-report only, (2) inclusion of White women or Asian women only, and (3) limited data on history of GDM.

Finally, a third prospective study of Black and White women of reproductive age evaluated lactation duration and incidence of the metabolic syndrome during the 20-year study period. Lactation for longer than 1 month to >9 months vs <1 month was associated with a 3- to 7-fold lower relative hazards of incident metabolic syndrome on average of 8 years after their last delivery adjusted for prepregnancy biochemical parameters, parity, sociodemographics, follow-up lifestyle behaviors, and weight gain [2••].

This study provides the first evidence that biochemical changes were associated with disease onset several years after lactation cessation, independent of prepregnancy metabolic risk factors, and lifestyle behavior changes during the same time period.

Implications for Women with Diabetes

Women with a history of GDM comprise a high-risk group for future development of type 2 diabetes. About 5 %–10 % of women with previous GDM will be diagnosed with type 2 diabetes within 6 months and another 10 %–15 % will develop type 2 diabetes within subsequent 1–2 years postpartum [11, 16, 18, 59–62]. Lifestyle behaviors may also influence the future development of metabolic diseases following GDM delivery, however, only 2 published studies have evaluated the impact of lactation and long-term risk of type 2 diabetes after GDM pregnancy. Postpartum women with overt diabetes, especially type 1 diabetes, are likely to have lower insulin requirements when lactating [63], and may experience more frequent episodes of hypoglycemia. Frequent glucose monitoring and adjustment of dietary intake and insulin and oral hypoglycemic medication dosage may occur [63].

Lactation and Maternal Metabolism for Women with GDM

Studies of Latinas with recent GDM reported more favorable glucose tolerance and lipid metabolism during 1–4 months postpartum for lactating compared with nonlactating women [64]. Specifically, lactating women displayed a lower total area under the glucose tolerance curve (AUC) (17.0±4.2 vs 17.9± 5.0 g/minute/dL) lower fasting serum glucose (93±13 vs

98± 17 mg/dL) and 2-hour OGTT glucose levels (124±41 vs 134± 49 mg/dL) after controlling for BMI, maternal age, and insulin use during pregnancy, as well as a lower prevalence of type 2 diabetes mellitus [64]. Another study administered a frequently sampled intravenous glucose tolerance test (FSIGT) at 3 months postpartum to 14 lactating and 12 nonlactating women with previous GDM matched for age, weight, postpartum weight loss, and exercise habits. In lactating women, insulin sensitivity, glucose effectiveness and first phase insulin response to glucose (AIRg) assessed by Bergman's Minimal Model were higher, but statistical significance was not reached given the small sample size. However, the disposition index (DI=insulin sensitivity multiplied by AIRg) was 2.5 times higher (129.9±26.0 vs 53.4±18.0×$10^{(-4)}$ $min^{(-1)}$; $P<0.05$) in lactating vs nonlactating women [65]. The higher DI supports the hypothesis that lactation promotes much better beta cell compensation for insulin resistance, which may help maintain β-cell function in the long-term. In 122 Latinas with normal fasting glucose and no insulin use during GDM pregnancy, those later diagnosed with diabetes within 6 months postpartum were less likely to have breastfed [66].

Prospective epidemiologic studies have also assessed lactation measures and glucose and insulin metabolism in women with recent GDM. In the Atlantic Diabetes and Pregnancy Study of 300 Irish women with recent GDM, lactating vs nonlactating women were 58 % less likely to have dysglycemia at 12 weeks postpartum (defined by the World Health Organization criteria) adjusted for maternal BMI, age, ancestry, insulin treatment during pregnancy, and family history of diabetes [67]. However, lifestyle behaviors and lactation duration and intensity were not assessed in this study.

The Study of Women, Infant Feeding and Type 2 Diabetes after GDM pregnancy (SWIFT) is the first study to evaluate lactation intensity in relation to postpartum glucose tolerance among women with recent GDM [68]. SWIFT reported a graded monotonic inverse association between higher lactation intensity (prospectively assessed formula supplementation) from birth at 6–9 weeks postpartum (baseline) and lower fasting plasma glucose and insulin obtained from the 2-hour 75 g OGTT at 6–9 weeks postpartum [69••]. Specifically, compared with exclusively or mostly formula feeding groups (>17 oz formula per 24 hours), the exclusively lactating and the mostly lactating (≤ 6 oz formula per 24 hours) groups had lower adjusted mean (95 % CI) fasting plasma glucose (mg/dL) of −4.3 (−7.4, −1.3) and −5.0 (−8.5, −1.4), fasting insulin (uU/ml); −6.3 (−10.1, −2.4) and −7.5 (−11.9, −3.0), and 2-hour insulin; −21.4 (−41.0, −1.7) and −36.5 (−59.3, −13.7), respectively. Higher lactation intensity was associated with lower prevalence of prediabetes among obese women as well as nonobese women [69••]. Although lactating women were advised to bring expressed breast milk to feed their babies during the OGTT, about 25 % breastfed during the 2-hour OGTT at 6–9 weeks postpartum and our results were controlled for this potential confounder of biochemical measures [70]. The SWIFT study was designed to prospectively assess lactation intensity and duration in relation to the 2-year incidence of type 2 diabetes mellitus in 1035 women with recent GDM [68]. Standardized postpartum annual screening for glucose tolerance is underway in the SWIFT cohort of racially and ethnically diverse women (75 % minority). The SWIFT study will evaluate the effects of

lactation measures on diabetes risk independent of lifestyle behaviors and obtain direct biochemical evidence for risk factors changes post-weaning.

Blood Lipids and Previous GDM

Similar to the effects on blood lipids in healthy women, Kjos et al reported that postpartum Latinas (*n*=809) with recent GDM, HDL-C was 4 mg/dl higher among women who were lactating after adjusting for maternal age, BMI, and pregnancy insulin use, but blood total cholesterol, LDL-C, and triglycerides did not differ by lactation group [64]. Because blood glucose and lipids are diverted for milk production, lower plasma glucose, and lipids may "unload" the β-cells such that β-cell function is preserved and insulin response is improved. It is biologically plausible that these physiological changes related to lactation may have lasting effects that sustain glucose tolerance and protect against β-cell exhaustion leading to progression to prediabetes and type 2 diabetes.

Body Weight and Composition After GDM

Higher total body fat and central obesity (ie, waist girth) are strong risk factors for type 2 diabetes in women with prior GDM. A 23-year follow-up study of women with a history of GDM reported that 61 % of women who were obese or had gained weight had developed diabetes vs 28 % who were not obese or lost weight [71]. One study of 26 women with recent GDM measured visceral fat mass via computed tomography at 3 months postpartum, and reported no differences for lactating compared with nonlactating women [65]. Longitudinal studies are needed to examine postpartum visceral fat changes in larger samples. Weight loss and changes in overall and regional body composition are plausible mechanisms through which lactation improves glucose tolerance.

Lactation and Disease Risk in Women with GDM

Biochemical evidence that lactation has long-term effects on future glucose tolerance is largely unavailable. Early cross-sectional and follow-up studies of Latinas attending family planning clinics after GDM pregnancy suggest short-term favorable effects, but provide no conclusive evidence for long-term effects [14, 62, 64, 66, 72, 73], or have not assessed lactation duration or intensity. For example, a retrospective cohort study of Latinas with prior GDM with variable follow-up reported that lactation status (yes or no) at 4–16 weeks postpartum was not associated with 5-year incidence of diabetes [14]. Studies that assessed lactation and glucose tolerance during the early postpartum period support the hypothesis that lactation may lower risk of type 2 diabetes in women with GDM, but do not provide evidence for long-term effects of lactation on future disease risk. Studies of long-term effects in the high-risk women with a history of GDM are discussed below.

Incidence of Type 2 Diabetes and the Metabolic Syndrome in Women with GDM

Three studies that evaluated lactation duration and subsequent incidence of cardiometabolic disease in women with previous GDM are displayed in Table 1. Two of 3 published studies assessed lactation duration in relation to incidence of type 2 diabetes after GDM pregnancy

[5, 74•]. A retrospective study of women from the Nurses' Health Study (NHS) cohort of White women found no association between lifetime lactation or other lifestyle behaviors (ie, diet, exercise habits) and incidence of type 2 diabetes several years after GDM delivery [5]. This study did not conduct standardized screening for diabetes, but relied on diabetes ascertainment by self-report. A prospective study of 264 German women with previous GDM followed up to 19 years after delivery reported a 45 % reduction in incident type 2 diabetes among White women who lactated for longer than 3 months independent of insulin therapy and maternal BMI [74•]. However, this study did not control for postpartum lifestyle behaviors, breastfeeding during the 2-hour OGTT, lactation intensity, or other confounders that may influence the lactation duration and diabetes risk. This study cannot rule out whether the strong protective association stems from reverse causation (more healthful lifestyle leading to increased lactation duration and lower diabetes risk). Moreover, biochemical data was not available to provide evidence that metabolic effects due to lactation persisted post-weaning. Limitations of these studies include (1) incident diabetes by self-report only, (2) no measurement of glycemia before or after pregnancy, postweaning, or later, (3) data available only for White women or Asian women, and (4) retrospective data in women with GDM. Studies within racially and ethnically diverse cohorts of women with GDM are also needed to determine whether lactation can eliminate disparities in future diabetes onset.

The third study assessed lactation duration and incidence of the metabolic syndrome by GDM status in Black women and White women of childbearing age during a 20-year follow-up period. CARDIA prospectively measured cardiometabolic risk factors, both before and after pregnancies in 702 nulliparous women who were free of the metabolic syndrome and gave birth during subsequently. Increasing months of lactation was associated with lower incidence of the metabolic syndrome; 44 %–86 % lower among women with a history of GDM and 39 %–56 % lower among women with no history of GDM several years postweaning adjusted for prepregnancy metabolic syndrome components measured, obesity, and lifestyle behaviors and weight gain during the 20-year follow-up [2••]. These findings support the hypothesis that lactation has persistent favorable effects on women's cardiometabolic health, and that effects may be stronger among women with a history of GDM (Fig. 1) [2••]. The findings provide the first direct biochemical evidence that link lactation duration protective against cardiometabolic disease and that women with a history of GDM may also benefit [2••].

Conclusions

Evidence for favorable effects of lactation on maternal metabolism improved insulin sensitivity is based primarily on cross-sectional studies comparing lactating vs nonlactating women during the early postpartum period. Almost all longitudinal studies measured metabolic indices at a single point in time and were unable to distinguish effects of lactation from confounding factors. Future longitudinal studies should determine whether women are currently lactating at the time of blood samples collection, or whether women breastfed their child during the postpartum OGTT, as variation in metabolic indices occurs due to these factors [70]. Collection of postweaning blood samples is required for inferences about biochemical changes that persist postweaning.

Lactating compared with nonlactating women display more favorable metabolic parameters, including less atherogenic blood lipids [34], lower fasting and postprandial blood glucose and insulin [27, 28], and greater insulin sensitivity [27]. Exclusive lactation is associated with greater weight loss in some studies, and with the most favorable metabolic profiles [69]. Women with previous GDM manifest similar improvements in metabolic profiles, as well as enhanced pancreatic β-cell compensation for a glucose load, [65], and lower prevalence of diabetes during 1–4 months postpartum [64]. Women with pregestational diabetes, particularly type 1 diabetes, may experience reduced insulin needs during the lactation period.

Evidence is more limited regarding the persistence of beneficial effects postweaning or several years later. Very few studies have measured biochemical parameters longitudinally, including postweaning. Thus, although lactation has been linked with lower incidence or prevalence of diabetes, and the metabolic syndrome in women, a direct link between biochemical changes and future disease risk has not been established. Furthermore, little is known about the biological mechanisms for lactation's effects on cardiometabolic risk factors. A limitation of studies evaluating lactation duration and type 2 diabetes is that the protective association may be due to reverse causation, because women who choose to breastfeed may practice more healthful lifestyle behaviors before and after pregnancy, which lower their risk of type 2 diabetes. Prospective studies are needed that engage in standardized screening methods for diabetes at regular intervals, assess both lactation duration and intensity, and control for potential confounders including severity of gestational glucose tolerance, maternal postpartum lifestyle behaviors, and sociodemographics. Biochemical evidence is also needed to determine whether effects of lactation persist postweaning, as well as identify metabolic pathways influenced by lactation.

In summary, lactation has favorable effects on maternal glucose tolerance during the postpartum period after GDM pregnancy, but evidence is insufficient to conclude that these effects endure postweaning, or lactation influences development of type 2 diabetes in women years later. Biochemical evidence for lasting effects of lactation on long-term risk of type 2 diabetes and the metabolic syndrome is less available, but lactation appears to have lasting effects on HDL-C and other risk factors. For women with a history of GDM, well-controlled, prospective studies with more detailed measures of lactation intensity and lifestyle behaviors, as well as standardized screening for glucose intolerance are needed to conclusively determine whether lactation may reduce risk of type 2 diabetes. In particular, longitudinal biochemical measurements are needed to substantiate the epidemiologic evidence that lactation influences diabetogenesis beyond the childbearing years. Lactation is a modifiable health behavior that may play an important role in future disease risk not only for women with a history of GDM, but for their offspring as well.

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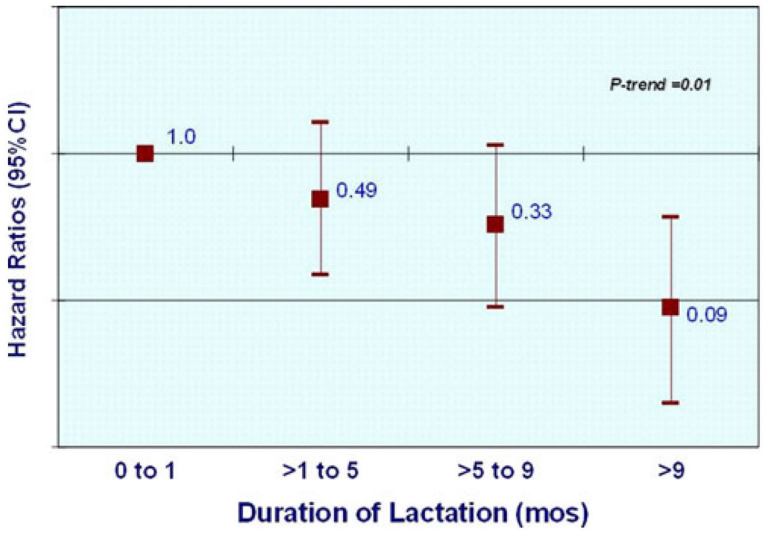

Fig 1.

Adjusted relative hazard ratio (95 % CI) for incident metabolic syndrome associated with lactation duration in CARDIA women with gestational diabetes mellitus (GDM) adjusted for prepregnancy risk factors, BMI, race, sociodemographics, parity, lifestyle behaviors, and weight gain during the 20-year study follow-up. (From: Gunderson EP, Jacobs DR Jr, Chiang V, Lewis CE, Feng J, Quesenberry CP Jr, et al. Duration of lactation and incidence of the metabolic syndrome in women of reproductive age according to gestational diabetes mellitus status: a 20-Year prospective study in CARDIA (Coronary Artery Risk Development in Young Adults). Diabetes. 2010;59:495–504.) [2••]

Table 1

Lactation duration and incidence of type 2 diabetes or incidence of the metabolic syndrome among women with previous GDM

Reference	Study design, y	n, GDM pregnancy	Study population	Lactation measure	Type 2[a] diabetes incidence	Time postpartum	Outcome	Conclusion
Stuebe, 2005 [5]	Retrospective cohort 1989–2003	n, not reported	The Nurses' Health Study USA, White; Aged 24–43 y in 1989 (baseline)	Duration: months of lactation for all pregnancies;	Self-report of diabetes chart confirmation	Variable up to 14 y	Diabetes; incidence rate: 6.24 cases per 1000 person-y	Null, association; adjusted for lifestyle behaviors
Gunderson, 2010 [2••]	Prospective cohort 1985–2006	702 Non-GDM 84 GDM; (women nulliparous at baseline)	CARDIA, multicenter 50 % White; 50 % Black; and Aged 18–30 in 1985–1986 (baseline)	Duration: months of lactation for all post-baseline births;	Fasting glucose, 2-h 75 g OGTT; and metabolic syndrome components[a] (before and after pregnancies; up to 6 exams)	Average follow up of 8 y postpartum and up to 19 y after delivery; 72 % retention at 20 y	Metabolic syndrome incidence rate[a]: 22.1 cases per 1000 person-y	44 %–86 % lower incidence; P=0.03; for >1 to >9 mos of lactation vs 0–1 mo; Relative Hazards adjusted for parity, race, age, smoking, prepregnancy BMI, biochemical and lifestyle behaviors, education and changes in physical activity
Ziegler 2012 [74•]	Prospective cohort 1989–1999	264 GDM	Germany, White,	Duration ≤3 mo vs >3 mo	Fasting glucose, 2-h OGTT; (up to 8 exams)	Follow up from 2 mo up to 19 y after delivery	Diabetes Incidence; on average 12 y to diabetes	45 % lower >3 mo vs ≤3 mos of lactation Hazard ratio: 0.55, (95 % CI:0.35–0.85) Antibodies, BMI, Age, smoking, family history of diabetes

CARDIA Coronary Risk Development in Young Adults, *GDM* gestational diabetes mellitus

[a]Diabetes and the metabolic syndrome