

Breastfeeding After Gestational Diabetes Pregnancy

Subsequent obesity and type 2 diabetes in women and their offspring

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Breastfeeding provides important health benefits to both women and their offspring. Health benefits of lactation for women include a lower risk of breast and ovarian cancer (1) and possibly protection against type 2 diabetes (2). For the offspring, breastfeeding confers protection against both undernutrition and overnutrition during early childhood (3) and may lower risk of developing obesity, hypertension, cardiovascular disease, and diabetes later in life (4–7). Postnatal feeding is one of several critical or sensitive developmental periods (fetal life, adiposity rebound in childhood, and adolescence) hypothesized to result in “metabolic programming” of future chronic disease risk (8,9).

In developed countries, there is a robust association between breastfeeding and a lower risk of becoming overweight during childhood and adolescence, even after accounting for maternal obesity and family lifestyle behaviors (10–13). Moreover, greater protection against childhood overweight is associated with more prolonged exclusive breastfeeding. In the U.S., the association of breastfeeding and lower risk of childhood overweight has been observed in Caucasians, but not among low-income Hispanics or African-Americans.

Fetal life is another important developmental period influencing future health. Maternal gestational diabetes mellitus (GDM) alters the intrauterine milieu for fetal development that may affect risk factors for chronic disease later in life (14). In some (15–18), but not all (19)

studies, offspring of GDM mothers may be more likely to become overweight and to develop type 2 diabetes later in life. A combination of genetic, intrauterine, and postnatal factors contribute to development of childhood obesity and type 2 diabetes in the offspring of women with GDM.

Whether breastfeeding affects the future health of offspring of women with GDM is uncertain based on limited and conflicting findings from studies of Native Americans or women with diabetes during pregnancy. Furthermore, no studies that examined the relation of breastfeeding to development of obesity and diabetes in the offspring of women with GDM have controlled for the intrauterine metabolic environment.

Lactation may also confer health benefits to women with a history of GDM. Lactation improves glucose tolerance in the early postpartum period, but it is unclear whether future risk of type 2 diabetes is reduced.

Here, the evidence for the general population is critically examined for an association of breastfeeding with the risk of obesity and its biological plausibility. Next, evidence is examined among offspring of women with GDM that breastfeeding influences their risk of overweight and type 2 diabetes. Lastly, lactation's effect on maternal postpartum glucose tolerance and prevention of type 2 diabetes among women with and without previous GDM is examined. Given the equivocal findings for GDM women and their offspring, further research is recommended.

BREASTFEEDING AND DEVELOPMENT OF OVERWEIGHT IN OFFSPRING IN THE GENERAL POPULATION —

Breastfeeding is recommended as the preferred method of infant feeding for the first year of life or longer, and exclusive breastfeeding is recommended for the first 6 months of life (20). The Institute of Medicine defines exclusive breastfeeding as an infant's consumption of human milk with no supplementation of any type (no water, juice, nonhuman milk, or foods) except for vitamins, minerals, and medications (21). In the U.S., breastfeeding initiation rates have increased steadily since 1990, but exclusive breastfeeding rates have shown little or no increase over the same period (22). Exclusive breastfeeding at 6 months declined from 18 to 12% between 1981 and 1997 (22) and by 2003 had reached 17% (23). From 1988 to 1994, the prevalence of overweight (defined as BMI >95th percentile) in U.S. youth aged 6–17 years was 11% (24). By 1999–2002, the prevalence had increased to 16% of youth aged 6–19 years (25). Given that weight tracks from early life into adult life (26–28) and that childhood weight gain and obesity have been linked to chronic diseases later in life (29,30), breastfeeding may be an important contributor to prevention of obesity and its sequelae.

Breastfeeding and overweight in early childhood and adolescence

Breastfeeding protects against becoming overweight and obese during childhood and adolescence, as well as underweight during infancy and childhood (3). Because breastfeeding decreases the variability in BMI within a population, comparison of the means does not distinguish the effects of breastfeeding on infant growth (3). The prevalence of overweight or obesity is the outcome measure used to evaluate the effects of breastfeeding in the population.

Three reviews of published studies, one quantitative review, one meta-analysis, and one systematic review, all

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Received for publication 28 March 2006 and accepted in revised form 3 October 2006.

This article is based on a presentation at a symposium. The symposium and the publication of this article were made possible by an unrestricted educational grant from LifeScan, Inc., a Johnson & Johnson company.

Abbreviations: GDM, gestational diabetes mellitus.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

DOI: 10.2337/dc07-s210

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concluded that breastfeeding reduces the risk of overweight in children and adolescents (11–13). Of six additional studies not included in these reviews, four reported protective associations adjusted for covariates (31–34), one found that adjustment for paternal attributes abolished the association (35), and another had mixed findings (36). Overall, 21 studies that included 100 or more subjects per feeding group and examined overweight or obesity in children at least 3 years of age provide the most informative estimates (3,10,31–39). In 17 of these 21 studies, breastfeeding resulted in a 20–50% lower risk of overweight depending on duration of breastfeeding and degree of supplementation. Adjustment for maternal obesity, infant birth weight, and other confounders generally attenuated, but did not abolish, the association. In a meta-analysis of 17 studies, Harder et al. (13) found a strong dose-response relationship between increasing duration of months of breastfeeding and 4% reduction in risk of overweight per month of breastfeeding unadjusted for potential confounders.

A quantitative review of 61 studies focusing on infant feeding and obesity through the life course concluded that breastfeeding moderately reduced the risk of overweight (12). Among 28 studies reporting odds ratios (ORs), breastfeeding was associated with a lower risk of obesity, compared with formula feeding (OR 0.87, 95% CI 0.85–0.89). A stronger inverse association between breastfeeding and obesity was found in 11 studies with <500 subjects (OR 0.43, 95% CI 0.33–0.55). The consistency of the association across all age-groups, from infancy to adulthood, suggests that early breastfeeding may have lasting protective effects independent of dietary and physical activity patterns later in life (12).

The association of breastfeeding with child overweight may vary by race/ethnicity and maternal attributes such as smoking, pregravid obesity, and diabetes during pregnancy. In two studies of low-income U.S. children aged 4 years (73,000 in Ohio and 177,000 across the U.S.), breastfeeding was associated with a lower risk of child overweight and obesity in non-Hispanic white children, but no relationship was found among African-American or Hispanic children (3,31). In mothers who smoked during pregnancy, breastfeeding was not found to reduce risk of obesity in the offspring (35). This may be because maternal smoking dur-

ing pregnancy retards fetal growth, which then leads to rapid postnatal growth and higher risk of obesity in the offspring (31). Disparities by race/ethnicity group and maternal attributes (i.e., smoking) in the association of breastfeeding with child overweight warrant further investigation.

To our knowledge, maternal GDM during pregnancy was examined as a potential confounder in only one study of breastfeeding and risk of overweight in the general population (31). Maternal GDM was associated with a 30% higher risk of obesity in adolescent offspring after adjustment for duration of breastfeeding and other potential confounders, but no data were presented to determine whether breastfeeding influenced the risk of overweight specifically among the offspring of women with GDM (17).

Influence of maternal obesity on breastfeeding and overweight in offspring

Maternal obesity represents genetic and intrauterine and postnatal environmental influences on the development of offspring (14). Maternal pregravid obesity is correlated with fetal macrosomia and subsequent obesity in the offspring (40). In most studies, the reduction in risk of overweight in childhood with breastfeeding has remained after adjustment for or stratification by maternal or parental BMI (3,10,11,31–39). Maternal pregravid obesity has been found to be a significant effect modifier in the association between breastfeeding and child overweight (33). Longer duration of breastfeeding was associated with lower prevalence of offspring overweight across all levels of maternal body size, but risk of overweight remained higher among children of obese women within each category of infant feeding. Specifically, children of obese mothers who did not breastfeed had the highest prevalence of overweight at 2–14 years of age (31.5%) compared with the children of normal-weight women who breastfed for 4 months or longer (6.0%) (33). Breastfeeding appears to confer protection against overweight for children of obese mothers.

Limitations of studies on breastfeeding and growth in children

There is a strong association between prolonged exclusive breastfeeding and lower risk of overweight in childhood and adolescence for the general population. Residual confounding by parental attributes

and/or family environment is a potential limitation, because breastfeeding is a behavior that is self-selected and women are not randomized to breastfeeding or formula feeding. Sources of bias (41) include 1) confounding by higher socioeconomic status of women in developed countries who choose to breastfeed and who are less likely to overfeed their infants, independent of the feeding method; 2) reverse causality that “creates a bias in the opposite direction: slow-growing infants” may be deliberately supplemented or weaned to reverse this poor growth trend; and 3) selection bias may result because “fast-growing infants” have greater hunger demands that leads to supplementation to reduce crying, and only infants whose growth demands are met by their mother’s milk supply continue to breastfeed. Future studies should measure behavioral and feeding attributes of infants to quantify and estimate their impact on the risk estimates and whether biases exist.

One method to address these potential biases used a cluster-randomized design of breastfeeding support in the Republic of Belarus (41). Infants who received prolonged exclusive breastfeeding showed patterns of growth characterized by higher weight and length growth (*z* scores) through 3 months of age, with slower growth thereafter to 12 months of age compared with infants weaned at earlier ages. It is possible that breastfeeding may be a marker for more healthful behaviors in families rather than exerting a true biological effect. However, the robustness of the protective association in the general population, breastfeeding’s effects on infant growth patterns, and emerging evidence of physiological differences in metabolism support a causal relationship.

EFFECTS OF BREASTFEEDING AND MATERNAL DIABETES DURING PREGNANCY ON THE OFFSPRING

Maternal diabetes during pregnancy affects fetal growth and development through the altered intrauterine milieu. Relatively few studies have examined breastfeeding and subsequent obesity or diabetes in the offspring of women with GDM. Of seven studies, four included mixed samples of mothers with diabetes during pregnancy, women with pregestational diabetes, or women with GDM; two examined the offspring of Pima Indians and maternal diabetes status during pregnancy; and one

examined offspring of mothers with previous GDM only.

Breastfeeding and subsequent overweight and diabetes in offspring

Research on breastfeeding and subsequent diabetes in the offspring has been largely focused on women with type 1 diabetes. Less is known about breastfeeding and development of obesity and type 2 diabetes, specifically among the offspring of women with a history of GDM. Breastfeeding has been linked to lower rates of type 1 diabetes among genetically susceptible individuals (42). Early introduction of cow's milk or other foods are hypothesized to trigger autoimmune responses leading to type 1 diabetes, especially among children with high-risk HLA genotypes, but findings are inconclusive (43). Growth patterns among children of women with diabetes, including those with GDM, in general are slower after birth through the first 2 years of life, with rapid weight gain thereafter (44,45).

Differences in breast milk constituents between women with and without diabetes are hypothesized to affect infant growth and development of overweight. Whether breast milk from mothers with diabetes differentially influences early infant growth compared with banked donor breast milk has been evaluated in a non-randomized longitudinal study of German children born to mothers with diabetes during pregnancy. The cohort included 83 women with type 1 diabetes and 29 women with GDM (46,47). The highest tertile of breast milk intake from mothers with diabetes during the first week of life was associated with twice the risk of overweight, defined as relative body weight above 110% at 2 years of age, compared with the lowest tertile (OR 1.91, 95% CI 1.10–3.30) (46). The association was strengthened after adjusting for age, sex, type of maternal diabetes, and maternal BMI (OR 2.51, 95% CI 1.32–5.04), and a stratified analysis of GDM women showed a similar trend. Furthermore, an inverse association with overweight risk was found for the highest versus lowest tertile of banked donor breast milk intake. A subsequent analysis of the same cohort examined the association between later breastfeeding and total duration of breastfeeding and risk of overweight at age 2 years in the offspring. These factors were strongly associated with child overweight in minimally adjusted models but exhibited no independent relationship once early neonatal

breast milk from diabetic mothers was included in the model (47). Findings for impaired glucose tolerance during early or later neonatal periods were inconsistent. Limitations of the study include the following: lack of randomization to source of breast milk, no data on prenatal and postnatal maternal blood glucose control, no description of the specific indications for donor breast milk supplementation (e.g., poor infant feeding, neonatal hypoglycemia, and weight loss), and no adjustment for total volume of milk intake from all sources, which in 23 infants included artificial formula. Total volume of milk ingested tended to be higher among infants of mothers with GDM. Higher intake of breast milk from mothers with diabetes may merely be a marker for higher energy intake, leading to rapid growth that is driven by intrauterine “metabolic programming” rather than postnatal exposures.

In the Nurses' Health Study, risk of overweight (based on self-reported weight and height) at age 9–14 years among offspring of mothers who had diabetes during pregnancy (419 with GDM and 56 with pregestational diabetes) was inversely associated with having been breastfed during the first 6 months of life. This association was similar to that among offspring of normal-weight women ($n = 8,617$) and overweight women ($n = 6,190$) without diabetes during pregnancy (48). Another study of 324 offspring of mothers with GDM from Berlin, Germany, found that exclusive breastfeeding for >3 months was associated with a lower risk of overweight (>90th percentile) at ages 2–8 years (OR 0.55, 95% CI 0.33–0.91), but lower risk of overweight was limited to offspring of obese GDM mothers (49).

The first study to examine the relationship between breastfeeding and development of type 2 diabetes in the offspring was conducted in the Pima Indians, a population with a high prevalence of type 2 diabetes (7). Exclusive breastfeeding compared with exclusive bottle-feeding during infancy was associated with a lower prevalence of type 2 diabetes (OR 0.41, 95% CI 0.18–0.93) among individuals between the ages of 10 and 39 years adjusted for age, sex, parental diabetes, and birth weight (7). However, this study did not examine whether maternal diabetes during pregnancy altered the observed association with breastfeeding.

The only prospective study, to our

knowledge, that examined breastfeeding and the risk of type 2 diabetes in the offspring of women with GDM involved this same cohort of Pima Indians. Women were tested with a 75-g oral glucose tolerance test during their pregnancies and were classified as having diabetes during pregnancy according to World Health Organization criteria. Follow-up of the women and their children starting at 5 years of age was conducted through a biennial standardized examination and oral glucose tolerance tests. Among offspring 10–39 years of age whose mothers did not have diabetes during pregnancy ($n = 551$), the adjusted prevalence of type 2 diabetes was 6.9% for those exclusively breastfed for at least 2 months and 11.9% for those not breastfed (OR 0.56, 95% CI 0.41–0.76) (50). Among 21 offspring whose mothers had diabetes during pregnancy, the prevalence of type 2 diabetes was lower for those exclusively breastfed versus those not breastfed (30.1 vs. 43.5%), but statistical significance was not reached (50). The risk estimates were adjusted for age, sex, birth weight, birth date, and the presence of diabetes in either parent. However, other potential confounders including sibship status and severity of diabetes during pregnancy were not taken into account.

A case-control study examined breastfeeding and risk of type 2 diabetes in the offspring in 46 children below 18 years of age with type 2 diabetes and 92 age- and sex-matched control subjects from a clinic serving Native Canadians. Their mothers had preexisting type 1 diabetes, GDM, or no diabetes during pregnancy. The risk of type 2 diabetes was lower among offspring who were breastfed longer than 12 months versus none (OR 0.24, 95% CI 0.13–0.84) adjusted for type of maternal diabetes during pregnancy (51). Only 22 of 138 mothers had GDM during pregnancy. Limitations of the study were that case and control subjects were not matched by actual birth year, the association was absent at shorter duration of breastfeeding, and there was no adjustment for parental socioeconomic status and area of residence.

A limitation of all studies is that risk estimates were not adjusted for maternal blood glucose control during pregnancy. To date, evidence that breastfeeding protects the offspring of women with GDM from developing overweight and type 2 diabetes is inconclusive.

Lactogenesis in women with previous GDM

Lactation may be more difficult for women with GDM because both maternal diabetes and obesity can delay the onset of lactogenesis (52,53). Furthermore, medical management of their newborns that involves provision of supplemental milk feedings may interfere with maternal milk production. In obese women, lactogenesis may be impaired because of lower physiological levels of prolactin in response to suckling (52). Delayed milk production may lead to lower rates of breastfeeding and shorter duration among obese women (53). A small sample of women with GDM were observed to have no marked delays based on similar concentration of lactose in the colostrum of GDM women compared with control women at 40–50 h postpartum (54). However, GDM women had more difficulty expressing colostrum from their breasts during the first 2 days of lactation.

Biological plausibility for breastfeeding and lower risk of overweight and diabetes

Postnatal growth patterns have been linked to future risk of overweight, but whether breastfeeding may affect early weight gain is unclear. The average daily milk volume consumed by an infant increases from 50 ml on day 1 to 500 ml by day 5 of life (55). Behavioral mechanisms include infant self-regulation of breast milk intake. Macronutrient composition (i.e., protein, fat, lactose content) of breast milk may influence hormonal responses that influence metabolic programming of body fatness and rates of growth. Levels of insulin, leptin, and ghrelin that regulate energy homeostasis in early neonatal life may be affected by the mode of infant feeding.

Breastfeeding and early neonatal growth

Breastfeeding may influence neonatal fat deposition that affects adiposity in childhood and adolescence that later tracks into adulthood. Animal studies demonstrate that overfeeding during infancy leads to higher adiposity during adolescence (56). In humans, a greater decline in weight for length z score between 3 and 12 months was found for breastfed compared with formula-fed infants (57,58). Both groups exhibited increased fatness in the first 6 months; but thereafter fatness decreased in both groups and more in the breastfed group. Mean weight-for-

length was greater among formula-fed infants from 7–24 months and percent body fat was higher from 5–24 months. Lower energy intake among breastfed infants explained the difference between groups. Six other studies in North America and Europe showed similar findings, that is, infants who were breastfed for 12 months or longer tended to be leaner by 12–18 months of age (59). Others have reported slower growth during infancy for those breastfed compared with formula fed (60,61). Also, formula and other milk feedings compared with breast milk had “growth-accelerating effects on weight and length gain throughout infancy” as compared with breast milk (61). The dose-response gradient for this association was strongest at 3–6 months of age (61).

The early postnatal period has emerged as an important predictor of overweight in childhood (62–64) and adult life (65). In the U.S. Perinatal Collaborative Study of 19,937 infants born between 1959 and 1965, rapid weight gain during the first 4 months of life was associated with higher risk of overweight at age 7 years (63). The adjusted odds ratio for being overweight at age 7 years for every 100 g/month gained was 1.38 (95% CI 1.32–1.44). This association was attenuated (OR 1.17, 95% CI 1.11–1.24) but remained significant after adjustment for the weight attained at age 1 year. A limitation is that no data on method of infant feeding were available for this cohort, except initial type. In 653 healthy infants born in the region of Iowa City from 1965 to 1978 who were exclusively formula fed (65), rapid weight gain during the first week of life (>100 g/day) was associated with greater risk of becoming overweight as an adult, with a 28% increase in risk per 100 g gained (OR for each 100-g increase 1.28, 95% CI 1.08–1.52), as was weight gain during the first 112 days of life (OR 1.04, 95% CI 1.01–1.08). The influence of breastfeeding on growth rates during early neonatal life may be important to postnatal programming of adiposity.

Postulated mechanisms: constituents of breast milk and metabolic programming

Breastfeeding may exert protective biologic effects through behavioral and hormonal mechanisms that influence metabolic programming. Breast milk contains bioactive substances that may influence regulation of energy balance and fat

deposition and has less protein relative to formula milk. Higher protein levels in early life have been linked to higher BMI later in life in some (66,67) but not all (68) studies. Higher insulin levels have also been reported in formula-fed compared with breastfed babies (69). The hormones leptin and ghrelin are involved in regulating food intake, energy homeostasis, and body weight. Leptin levels have been reported to be higher for breastfed than formula-fed infants in one (70) but not another (71) study. The circulating leptin levels were not only related to adipose tissue production, but may be contributed from human milk (70). Because ghrelin stimulates insulin secretion and body fat accretion in animals (72), higher ghrelin levels in formula-fed than breastfed infants (73) may influence early weight gain (74). Regulation of energy homeostasis in infancy via hormone levels in human milk and metabolic responses may be especially important for metabolic programming of infants of women with diabetes or previous GDM.

LACTATION AND SUBSEQUENT OBESITY AND DIABETES IN WOMEN —

Lactation after pregnancy may have lasting effects on risk factors that influence future chronic disease risk for women. Evidence is conflicting about whether lactation promotes greater postpartum weight loss (75–85). Prospective studies in which maternal weights (not self-reported) were measured before or during early pregnancy have reported lower postpartum weight retention, more rapid return to pregravid weight, or greater weight loss within 1 year among lactating women (79,82,83,85–88). Prolonged breastfeeding (>6 months) compared with formula feeding was associated with a 2 kg greater maternal weight loss by 1 year postpartum (79,84), as well as a smaller waist girth after weaning (89). Total body fat mass loss at 1 year postpartum measured using dual X-ray absorptiometry was 2 kg greater for lactating women, but did not reach statistical significance possibly because of the small sample size (90). Longer duration of breastfeeding has also been associated with lower maternal weight gain 10–15 years later (91,92). Lactation may also influence long-term regulation of body weight as well as regional fat distribution in women.

Lactation: immediate and post-weaning effects on maternal metabolic parameters

Maternal postpartum glucose tolerance is enhanced in lactating women with recent GDM. Yet, it is uncertain whether lactation reduces risk of type 2 diabetes in women with previous GDM. Lactation markedly alters maternal fuel metabolism and increases energy expenditure by 15–25% (93,94). The 400–500 kcal/day required for milk production during the first 6 months by exclusively breastfeeding women is derived from maternal dietary intake, with an additional 170 kcal/day mobilized from fat stores, and/or decreased physical activity (55,94,95). About 50 g/day glucose is diverted for lactogenesis (the process of milk synthesis and secretion) via non-insulin-mediated pathways of uptake by the mammary gland (94). Thus, lactating women exhibit lower blood glucose and insulin concentrations along with higher rates of glucose production and lipolysis compared with nonlactating women (96).

In women with recent GDM, results of a frequently sampled intravenous glucose tolerance test showed that lactating ($n = 14$) versus nonlactating ($n = 12$) women had greater β -cell compensation for insulin resistance (97). Basal and glucose-stimulated β -cell secretory activity in response to a standardized glucose load was lower for lactating women than for nonlactating women (98). Greater non-insulin-mediated use of glucose for milk production may theoretically reduce the load on the β -cells and thereby delay or prevent the progression to type 2 diabetes. Whether prolonged exclusive breastfeeding by women with GDM has post-weaning effects on glucose tolerance and insulin sensitivity has not been examined.

Few studies have examined breastfeeding and postpartum glucose tolerance in women with previous GDM. Of 28 studies cited in a published review (99) and four subsequent studies (100–103) evaluating predictors of type 2 diabetes after GDM, only four specifically examined lactation (104–107). The definition of lactation in these studies was limited to “any” versus “none” at a single point in time (104–107), and few other postpartum behaviors were examined. Lactation has immediate beneficial effects on glucose tolerance, although evidence for lasting effects is more limited and inconclusive (104–107). In a cross-sectional study of Latinas with previous GDM attending family planning clinics, lactating

women had a lower total area under the glucose tolerance curve and lower fasting serum glucose after controlling for BMI, maternal age, and insulin use during pregnancy (104). In this study, prevalence of type 2 diabetes for lactating women at 4–12 weeks postpartum was half that of nonlactating women (104). Other studies in the same clinic population report inconsistent findings. In 122 Latinas with normal fasting glucose and no insulin use during GDM pregnancy, those diagnosed with diabetes within 6 months postpartum were less likely to have breastfed (42%) than those with normal glucose tolerance (71%) (106). The same investigators found that lactation status (yes versus no) at 11–26 months postpartum did not influence diagnosis of type 2 diabetes in 91 Latinas with recent GDM (107). Lastly, a retrospective study of Latinas attending family planning clinics and tested via an oral glucose tolerance test at variable intervals found no association between lactation status at 4–16 weeks postpartum (yes versus no) and subsequent development of type 2 diabetes within 5 years (105).

Two studies examined the cumulative effects of lactation on future glucose tolerance among women in the general population. In a sample of 67 Brazilian women, increasing duration of lactation (weighted score) was inversely associated with the area under the insulin curve at 12–18 months postpartum independent of body adiposity (108). The Nurses' Health Study reported that increasing duration of lactation was associated with reduced risk of type 2 diabetes, with each additional year decreasing the risk by 15% among women in general. These effects were independent of current BMI and other risk factors, and risk reductions were stronger with exclusive breastfeeding (2). The retrospective analysis stratified by GDM status showed no association between lactation and risk of type 2 diabetes (2). These findings are based on over 150,000 nurses with several years of follow-up, but limitations include the retrospective assessment of lactation, lack of standardized time intervals for screening of type 2 diabetes, classification of diabetes and GDM status by self-report, and differences in rates of GDM screening by age.

Studies have generally used cross-sectional measures of lactation (current status at screening, ever versus never) and variable timing for assessment of glucose tolerance. They also lack data on maternal

postpartum behaviors (dietary intake, physical activity). Whether breastfeeding delays or prevents the onset of type 2 diabetes in women with a history of GDM remains unknown, and prospective population-based studies are needed.

SUMMARY AND FUTURE RESEARCH DIRECTIONS

— Since 1986, the American Diabetes Association has recommended that women with GDM should be encouraged to breastfeed (109,110). Recommendations from the Fourth International Workshop-Conference on Gestational Diabetes Mellitus encouraged women to breastfeed, although data demonstrating efficacy were lacking (111). In the general population, breastfeeding is associated with a reduced risk of the offspring being overweight later in life by 20–50% across the age spectrum, from preschool children to adults. There is a dose-response gradient with increasing duration of breastfeeding and lowest risk with prolonged exclusive breastfeeding. This association may vary by maternal attributes such as pregravid obesity, smoking, diabetes during pregnancy, and race/ethnicity. Because randomization to breastfeeding versus formula is not desirable or ethical, the causal link is not definitive.

Among the offspring of women with GDM, evidence is inconclusive as to whether breastfeeding reduces their risk of overweight, obesity, and type 2 diabetes. Findings in Pima Indians suggest that lower rates of type 2 diabetes may occur in the offspring of both women with and without diabetes during pregnancy who were breastfed. Whether breastfeeding reduces risk of overweight in the offspring of GDM women is uncertain. Evidence that early neonatal intake of breast milk from women with diabetes during pregnancy adversely affects child growth requires confirmation as well as control for intrauterine influences on postnatal growth.

In women with a history of GDM, lactation has immediate favorable effects on glucose tolerance, but some data show that there are lasting post-weaning effects on maternal metabolic profiles (112). Maternal obesity, central adiposity, and weight gain subsequent to GDM pregnancy are strong predictors of type 2 diabetes in women several years later. Few data are available on the effects of lactation on these risk factors for type 2 diabetes among women with GDM and,

specifically, the effects of prolonged exclusive breastfeeding.

Prospective studies of women with GDM and their offspring are needed to evaluate whether breastfeeding 1) leads to metabolic “programming” in early infancy after accounting for intrauterine exposures, 2) prevents overweight and diabetes later in life among the offspring, 3) reduces postpartum weight retention and/or central adiposity in women, and 4) preserves maternal glucose tolerance to delay or prevent type 2 diabetes among women with previous GDM. More research is also needed to evaluate the influence of breast milk constituents as they relate to early infant growth patterns and future development of obesity and type 2 diabetes in the offspring.

Acknowledgments— This work was supported by Career Development Award Grant 2 K01 DK059944 from the National Institute of Diabetes, Digestive, and Kidney Diseases (NIDDK) and a Research Award from the American Diabetes Association.

Comments from Kathryn G. Dewey, PhD, Professor, University of California, Davis, were very helpful in preparing this manuscript.

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