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Breastfeeding and growth during infancy among offspring of mothers with gestational diabetes mellitus: a prospective cohort study

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Summary

Background—Breastfeeding (BF) may protect against obesity and type 2 diabetes mellitus in children exposed to maternal diabetes in utero, but its effects on infant growth among this high-risk group have rarely been evaluated.

Objectives—The objective of this study was to evaluate BF intensity and duration in relation to infant growth from birth through 12 months among offspring of mothers with gestational diabetes mellitus (GDM).

Methods—Prospective cohort of 464 GDM mother-infant dyads (28% White, 36% Hispanic, 26% Asian, 8% Black, 2% other). Weight and length measured at birth, 6–9 weeks, 6 months and 12 months. Categorized as intensive BF or formula feeding (FF) groups at 6–9 weeks (study baseline), and intensity from birth through 12 months as Group 1: consistent exclusive/mostly FF,

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Conflict of interest statement

The authors have no potential conflicts of interest to disclose, except that Dr. Quesenberry has received research funding, unrelated to the current study, from pharmaceutical companies (Takeda, Merck & Company, Inc., Sanofi-Aventis, Lilly, Genentech, Valeant and Pfizer), and Dr. Gunderson receives funding unrelated to the current study from Janssen Pharmaceuticals, Inc. (June 2017).

Authors' contributions

Erica P. Gunderson: Dr. Gunderson is the study's principal investigator and conceived the study design, assembled the prospective cohort, directed all scientific aspects of the SWIFT Offspring Study and prepared the manuscript. Shanta R. Hurston: Ms. Hurston participated in the study coordination and recruitment of participants, data collection and management. Louise Greenspan: Dr. Greenspan provided critical review of the manuscript and technical expertise. Myles Faith: Dr. Faith provided critical review of the manuscript and technical expertise. Charles Quesenberry: Dr. Quesenberry performed sample size calculations, developed the statistical analysis plan in collaboration with Dr. Gunderson and provided consultation on the analysis. All authors have read and approved the final manuscript and contributed to the overall study design and specific methodologies.

Supporting information

Additional Supporting Information may be found online in the supporting information tab for this article.

Group 2: transition from BF to FF within 3–9 months and Group 3: consistent exclusive/mostly BF. Multivariable mixed linear regression models estimated adjusted mean (95% confidence interval) change in z-scores; weight-for-length (WLZ), weight-for-age and length-for-age.

Results—Compared with intensive BF at 6–9 weeks, FF showed greater increases in WLZ-scores from 6 to 9 weeks to 6 months [+0.38 (0.13 to 0.62) vs. +0.02 (−0.15 to 0.19); $p = 0.02$] and birth to 12 months [+1.11 (0.87 to 1.34) vs. +0.53 (0.37 to 0.69); $p < 0.001$]. For 12-month intensity and duration, Groups 2 and 3 had smaller WLZ-score increases than Group 1 from 6 to 9 weeks to 6 months [−0.05 (−0.27 to 0.18) and +0.07 (−0.19 to 0.23) vs. +0.40 (0.15 to 0.64); $p = 0.01$ and 0.07], and birth to 12 months [+0.60 (0.39 to 0.82) and +0.59 (0.33 to 0.85) vs. +0.97 (0.75 to 1.19); $p < 0.05$].

Conclusions—Among offspring of mothers with GDM, high intensity BF from birth through 1 year is associated with slower infant ponderal growth and lower weight gain.

Keywords

Gestational diabetes mellitus; breastfeeding; growth patterns; prospective cohort; infancy

Introduction

Offspring exposed to maternal diabetes in utero, including mothers with pre-gestational diabetes or gestational diabetes mellitus (GDM), are more likely to become overweight or obese and develop impaired glucose tolerance and type 2 diabetes mellitus during childhood, adolescence and adulthood (1–3). Breastfeeding (BF) provides important health benefits for mothers and children, including protection against becoming overweight or obesity (4–6), upper respiratory infections and diabetes and reduced risk of breast and uterine cancer in women (7). Yet few studies have prospectively evaluated the relationship of infant feeding to attained body size or growth during infancy among offspring exposed to maternal diabetes in utero. Primarily, retrospective studies of toddlers (8,9), and older children (school-age, youth or adolescents) (2,10–12), born to mothers with diabetes consistently have found a lower odds of overweight or type 2 diabetes mellitus associated with BF duration (13,14), although one study showed opposite findings of a twofold higher odds of overweight at age 2 years among infants breastfed for the first 7 days by mothers with diabetes vs. those fed banked breast-milk from mothers without diabetes (15). Overall, these studies are universally limited by lack of perinatal outcomes and GDM phenotype (i.e. severity), as well as unavailable anthropometric measurements during the first year of life for offspring exposed to maternal diabetes in utero.

Only two previous studies have evaluated BF in relation to growth among offspring of mothers with overt diabetes or GDM from birth to 1 year of age. These studies showed mixed findings that do not support the previously reported protective associations between BF duration and subsequent development of overweight or obesity among children exposed to maternal diabetes in utero. A prospective study of 181 GDM infants found that BF 4 months accelerated weight gain from birth to 6 months compared with no BF (16), and a retrospective study of 94 youth exposed to maternal diabetes found a borderline lower body mass index (BMI) gain from birth to 9 months associated with ‘adequate breast-milk

months' (17). However, these studies did not account for reverse causation related to inclusion of early preterm infants (i.e. prematurity leading to slowed growth due to formula supplementation of poor feeders), adverse perinatal health outcomes or unmeasured confounding by severity of GDM that may affect infant growth.

To evaluate the relation of infant feeding methods and infant growth among offspring of mothers with GDM, we conducted the Study of Women, Infant Feeding and Type 2 Diabetes Mellitus after GDM pregnancy and the Growth of their Offspring (The SWIFT Offspring Study) (18). We prospectively quantified BF intensity and duration, and serially measured infant weight and length through 1 year of age. We hypothesized that higher BF intensity and longer duration would lead to slower increases in ponderal growth and weight gain from birth to 12 months after accounting for sociodemographic, gestational metabolic and perinatal risk factors.

Methods

The SWIFT Study enrolled 1,035 women diagnosed with GDM via the Carpenter and Coustan criteria with singleton live births 35 weeks of gestation at Kaiser Permanente Northern California hospitals in 2008–2011 and met other eligibility criteria (19). Briefly, women provided written, informed consent at 6–9 weeks post-delivery (baseline) and attended in-person follow-up visits annually for 2 years, including 2-h 75 gram oral glucose tolerance tests and assessments. Research staff interviewed mothers by telephone during pregnancy to assess BF intention, mailed feeding diaries within 2 weeks of delivery, administered questionnaires at in-person visits and mailed monthly surveys to assess frequency of BF and formula feeding (FF), including water and other feeds since birth. Eligible women were either intensively BF or FF since birth and enrolled at 6–9 weeks (baseline). The BF group also intended to continue the BF 4 months or more.

The SWIFT Offspring Study began in 2009 and enrolled 466 mother-infant dyads from SWIFT Study participants (2009–2011). All infants were healthy, live singleton births 35 weeks of gestation without serious medical conditions (e.g. failure to thrive, physical impairment affecting feeding ability, chronic infectious disease, severe jaundice or metabolic disorders) (18). Mothers provided written consent for three study visits at 6–9 weeks (baseline), 6 months and 12 months to measure their infant's weight, length, three skin-fold thicknesses and head circumference, and completed surveys on infant behaviours and health. After baseline, there were two drop outs, leaving 464 mother-infant pairs. Participant characteristics were similar to the SWIFT Study except for a slightly higher proportion of white, male infants. The Kaiser Permanente Northern California Institutional Review Board approved all study protocols and materials.

Infant feeding measures: breastfeeding intensity and duration

Based on the formula intake since birth and average 24-h formula intake or other feeds in the past 7 days, we categorized infants at baseline as (i) exclusive BF (no formula or other feeds); (ii) mostly BF (< 6 oz of formula); (iii) mixed or inconsistent feeding of breast milk and 7–17 oz of formula, or transition to formula; and (iv) exclusive (no breast milk) or mostly FF since birth or after 3 weeks (>17 oz of formula). These cut-offs are based on

average milk intake of 24 oz among infants aged 6–9 weeks, such that >17 oz of formula represents >65%, and 6 oz of formula is 25% of the daily energy intake (20,21). As previously described (18), we classified exclusive or mostly BF as ‘intensive BF’ and exclusive or mostly FF as ‘intensive FF’ with <10% mixed feeders.

We calculated the BF intensity and duration ratios for each month to construct a summary score for 12 months as described by Piper et al. (22) The score is the number of breast milk feeds (on average in 24 h) divided by the total number of all liquid feeds (on average in 24 h) during the past 7 days to yield a fractional score ranging from 0 to 1.0 that represents BF intensity for each month. A score of ‘zero’ represents exclusive FF, and a score of ‘one’ represents exclusive BF. We summed the 12 months of intensity ratios to obtain a total score from birth to 12 months (range: 0 to 12). A score of 12 represents exclusive BF for 1 year. We categorized these scores as Group 1, consistent exclusive/mostly FF since birth or from 3 months through 12 months (scores: 0 to 3), $n = 163$; Group 2, transition from exclusive/mostly BF to primarily or only FF from 3 to 9 months (scores: >3 to 9), $n = 133$; and Group 3, consistent exclusive/mostly BF from birth through 9 to 12 months (scores: >9 to 12), $n = 168$. The three 12-month intensity/duration categories (Table S1) are shown across the two BF intensity groups at 6–9 weeks. The transition group (Group 2) shows intermediate BF duration relative to Groups 1 and 3 (Fig. S1).

Standardized anthropometric measurements

We obtained mode of delivery, maternal pre-pregnancy and delivery weights, length and gestational age at birth and perinatal health outcomes from electronic health records. At study exams, trained staff measured infant weight, supine length, head circumference, abdominal circumference and three skin-fold thicknesses; subscapular, suprailiac and abdominal circumference using standardized research protocols and quality control measures developed for the World Health Organization Multicenter Growth Reference Study (23). Staff measured weight in the supine position on a digital infant scale (Tanita Corporation of America Inc., Model BD590, Illinois, USA) calibrated to zero and accurate to the nearest 5 g and recumbent infant length from the top of the head to the soles of the feet using an infantometer (Seca North America, Model 417, CA, USA) to the nearest 0.1 cm. For reliability, all measurements were taken in duplicate and averaged. For differences between measurements above 0.1 kg or 1 cm, a third was taken. Skin-fold thicknesses (subscapular, triceps and suprailiac) were measured to the nearest 0.2 mm using a Holtain Tanner/Whitehouse Skinfold Calipers (Seritex Inc.1, NJ, USA) (calibrated at 0 mm at each exam) to assess regional adiposity. If two measurements differed by more than 0.1 mm, a third was taken. Table S2 displays descriptive statistics for the measures and the coefficient of variation and the difference between the two measurements. As recommended by the Centers for Disease Control and Prevention (24), we calculated z-scores for weight-for-length (WLZ), weight-for-age (WAZ) and length-for-age (LAZ) for age and sex for infants <24 months of age based on the World Health Organization Child Growth Standards (25). The WLZ-score evaluates weight relative to length as a ponderal index for body size.

Statistical analysis

All analyses were performed using SAS 9.3, SAS Institute Inc. (Cary, NC, USA); p -values were obtained from two-sided tests (significance <0.05). Descriptive statistics included means $\pm$ SDs for continuous variables and percentages for categorical variables among infant feeding groups evaluated by chi-squared tests and analysis of variance. We evaluated differences in perinatal and newborn health outcomes among infant feeding groups, including GDM severity via 3-h 100 g oral glucose tolerance test z -score sum, GDM treatment type, C-section delivery, size for gestational age at birth, neonatal intensive care unit admissions, newborn Apgar scores and length of hospital stay related to potential reverse causation. We also evaluated cross-sectional differences in anthropometric measures (weight, length), ponderal index (WLZ-score), and markers of growth (WAZ and LAZ-scores) at birth, and ages 6–9 weeks, 6 months and 12 months by BF and FF intensity groups at 6–9 weeks of age.

We used repeated measures linear regression (PROC MIXED) to evaluate associations for intensive BF and FF groups at 6–9 weeks of age, and combined BF intensity and duration groups for mean (95% CI) changes in infant growth z -scores (WLZ, WAZ and LAZ). Models were adjusted for race/ethnicity (White, Black, Hispanic, Asian/other), gestational age at birth, maternal age, parity, education, pre-pregnancy BMI, total gestational weight gain (kg), GDM treatment type, gestational age at diagnosis of GDM and infant age (time). Models also included interaction terms for infant feeding groups and infant age (time) for three intervals and overall change in z -scores from birth to 12 months of age. Repeated measures linear regression models evaluated the associations for 12-month BF intensity and duration categories with changes in z -scores for each time interval accounting for confounders. Inclusion of potential confounders (above) in regression models was based on previously published findings, *a priori* hypotheses, and whether they met the statistical criteria for confounding. Covariates were not included if they were not associated with changes in growth measures independent of other model covariates (significance p -value > 0.05) or did not alter coefficients for BF groups by at least 10% based on addition of covariates. We formally tested effect modification of the infant feeding and associations with WAZ, WLZ and LAZ-scores by infant sex through the introduction of cross-product terms (significant p -value < 0.10).

Results

Of 464 mothers with GDM, 49% were obese, 67% were multiparous, and 68% were of Hispanic, Asian or Black race/ethnicities. Table 1 displays participant characteristics by infant feeding groups from birth to 6–9 weeks of age. Mothers classified as intensively BF ($n = 310$) were slightly older, had higher parity and educational attainment, shorter hospital stay, slightly lower pre-pregnancy BMI, higher BF intention score and more likely to be non-smokers than the intensive FF group ($n = 154$). Infant characteristics were similar by feeding intensity group at 6–9 weeks (baseline) except that the FF infants had slightly longer length at birth, higher mean gestational age, slightly fewer born at 35 to <37 weeks' gestation and earlier complementary feeding than BF infants (all $p < 0.05$). The anthropometric measures

were similar by infant sex, except for slightly lower WLZ-score at birth and smaller sum of skin-folds at 6–9 weeks of age (Table S3).

Unadjusted mean (SD) WLZ-score at birth for the entire sample (Table S2) was below the median (-0.3 ± 1.3), and slightly lower (-0.5 ± 1.3) for baseline FF compared with BF infants (-0.2 ± 1.3) due to longer length at birth among FF infants ($p < 0.05$). Unadjusted mean WAZ and LAZ-scores were significantly higher at ages 6 months ($p < 0.01$) and 12 months for baseline FF compared with BF groups ($p < 0.05$). Unadjusted mean WLZ-scores at age 12 months were higher for FF vs. BF groups ($p < 0.05$).

Fully adjusted repeated measures linear regression models (Fig. 1a–c) showed no differences in infant growth from birth to 6–9 weeks of age (all p -values < 0.05) by intensity of infant feeding groups at 6–9 weeks but showed greater increases in mean (95% CIs) WLZ-scores from ages 6–9 weeks to 6 months [$+0.38$ (-0.15 to 0.19) vs. $+0.02$ (0.13 to 0.62); $p = 0.02$] and overall from birth to 12 months [$+1.11$ (0.87 to 1.34) vs. $+0.53$ (0.37 to 0.69); $p < 0.001$] for FF vs. BF groups (Fig. 1a). Adjusted mean (95% CIs) WAZ-scores also increased more rapidly (Fig. 1b) from ages 6–9 weeks to 6 months [$+0.28$ (0.11 to 0.45) vs. $+0.03$ (-0.08 to 0.15); $p = 0.02$] and from 6 to 12 months [$+0.37$ (0.20 to 0.54) vs. $+0.14$ (0.03 to 0.26); $p = 0.03$] for FF compared with BF groups (Fig. 1b). Mean (95% CIs) change in LAZ-scores for each time interval and overall did not differ by infant feeding groups at 6–9 weeks of age (Fig. 1c). There were no differences in skin-fold thickness measurements by infant feeding intensity groups (Tables S4 and S5).

Increasing 12-month BF intensity/duration scores were inversely associated with unadjusted mean (SD) WLZ, WAZ and LAZ-scores at 12 months of age in a graded manner ($p < 0.001$), but there was no association with unadjusted mean (SD) WLZ-scores at birth, 6–9 weeks, or at age 6 months (Table S3). In multivariable repeated measures regression models, Group 3 (consistent BF) and Group 2 (transition from intensive BF to FF post-baseline) had lower increases in adjusted mean (95% CI) WLZ-scores (Fig. 2a) than Group 1 (consistent FF since birth) from 6 to 9 weeks to 6 months [-0.05 (-0.27 to 0.18) and $+0.07$ (-0.19 to 0.32) vs. $+0.40$ (0.15 to 0.64); $p = 0.01$ and $p = 0.07$, respectively] and birth to 12 months [$+0.60$ (0.38 to 0.82) and $+0.59$ (0.33 to 0.85) vs. $+0.97$ (0.75 to 1.19); all $p < 0.05$]. Groups 1 and 2 showed greater increases in adjusted mean (95% CIs) WLZ-scores than Group 3 from ages 6–12 months, but only differences with Group 2 reached statistical significance ($p = 0.02$).

Compared with Group 1, Groups 2 and 3 had lower increases in adjusted mean (95% CI) WAZ-scores (Fig. 2b) from 6 to 9 weeks to 6 months (all $p < 0.05$), and Group 3 had lower increases in mean (95% CI) WAZ-scores from 6 to 12 months ($p = 0.003$) and birth to 12 months ($p < 0.001$). However, changes in the z -scores did not differ between Groups 1 and 2 during these intervals ($p = 0.37$ and $p = 0.44$). Adjusted mean (95% CI) LAZ-score increases were similar (Fig. 2c), except Group 3 had smaller increases than Groups 1 and 2 from 6 to 12 months ($p = 0.01$) and birth to 12 months ($p = 0.001$).

There were no statistically significant differences in change in WAZ, LAZ or WLZ-scores from birth to 6–9 weeks among infant feeding groups, except for a greater increase in WLZ-

score from birth to 6–9 weeks for Group 3 vs. Group 2 ($p = 0.02$). However, there was no difference in WLZ-score change during this same interval between Groups 1 and 2 ($p = 0.58$). We also found no evidence of effect modification by infant sex for any of the infant feeding group associations with anthropometric z -scores from birth to 1 year of age (all interaction p -values > 0.25).

Discussion

This prospective study of infants of mothers with GDM provides robust evidence that infant feeding method influences ponderal growth during the first year of life. We found that higher BF intensity at 6–9 weeks of age compared with FF was associated with slower increases in ponderal growth and weight gain from 6 to 9 weeks to 6 months and lower attained body size at 12 months of age among infants of mothers with GDM.

We also found that infants who transitioned completely to FF after 3 months but before 9 months had accelerated ponderal growth and weight gain that mirrored the growth of infants primarily fed formula since birth. The mean difference between the groups was 0.36 to 0.45 SD units in WLZ z -score increase, representing a difference in the upward crossing of 14 to 17 growth centiles from age 2 months to 6 months for formula fed compared with breastfed infants. These findings remained after accounting for potential confounding and correlates of reverse causation related to including fetal exposure by maternal GDM phenotype (i.e. severity of dysglycemia), newborn and post-natal health outcomes affecting growth and infant feeding that previous studies of GDM offspring had not considered. The similar growth from birth to 6–9 weeks among infant feeding groups at baseline is consistent with their favourable newborn health outcomes and diminishes the chance of reverse causation. Moreover, infants fed formula since birth or 3 weeks and those breastfed up to a median of 6 months also had similar early growth, consistent with growth not affecting the feeding method.

Accelerated ponderal growth during the first year of life has important implications for future development of overweight and obesity. Previous studies have shown that faster weight gain during the first 6 months of life may elevate future risk of overweight and obesity in children and adults in general (26,27), as well as for offspring of mothers with diabetes (28). Other, mostly retrospective studies of offspring of mothers with diabetes or with GDM, found that longer BF duration was associated with 25–50% lower odds of overweight and 50–76% lower odds of type 2 diabetes in older children at ages 9–14 years (2,10,11), or ages 2–8 years (6,8,12). However, none of these studies evaluated whether ponderal growth or weight gain from birth through the first year of life mediated these associations.

Only one prospective study previously measured growth during the first year of life among infants of GDM mothers. This study of 181 Singaporean infants found that breast milk intake for 4 months was associated with accelerated weight gain from birth to 6 months and higher attained BMI compared to no BF (16). Unmeasured confounding or reverse causation could explain these findings because early preterm births were not excluded, and the analysis did not account for effects of adverse newborn health outcomes or maternal

GDM severity. In a retrospective study of 94 offspring of diabetic mothers, there was no significant difference in BMI gain (weight and length from medical clinic records) from birth to 12 months for 'adequate breast-milk months' (weighted index of mixed feeding via recall at 6–14 years) (17). These findings may arise from low statistical power, heterogeneity in maternal type of diabetes, misclassification of BF intensity or less precision for clinical anthropometric measures.

Findings for infants born to mothers without diabetes have shown that FF may have 'growth-accelerating effects' during infancy (29). Randomized studies showed that the higher protein content of formula causes more rapid growth (30), possibly due to greater stimulation of insulin secretion (31). Observational studies of offspring not exposed to maternal diabetes in utero showed slower ponderal growth during infancy with exclusive BF compared with FF (29,32). Furthermore, the differences in growth emerged from ages 3 to 9 months (33), which also occurred in our study of infants of mothers with GDM.

There currently is no consensus about whether BF slows infant ponderal growth or prevents overweight or obesity later in life (7). Although meta-analyses have shown 22–24% lower risk of overweight independent of lifestyle behaviours across the lifespan (6), experimental designs that randomized clinic sites (cluster-randomized) in eastern Europe to BF support showed no effect on average infant ponderal growth, child BMI or obesity risk (34). However, women were never screened for GDM in the cluster-randomized trial, such that maternal glucose intolerance during pregnancy was unknown in this population (34). The study also lacked a referent group unexposed to BF (i.e. formula only since birth) which may have attenuated differences in average ponderal index or BMI by infant feeding method (i.e. bias towards the null).

Specific properties and constituents of breast milk are hypothesized to affect growth and future obesity, including higher adiponectin and insulin (35,36). Human milk oligosaccharides may promote slower ponderal growth and lower body fat during infancy by influencing the gut microbiome (37). Moreover, exclusive BF also fosters an anti-inflammatory cytokine milieu that may decrease future risk of obesity (38). By contrast, accelerated growth with FF may have implications for metabolic imprinting of insulin secretion that promotes greater adipose tissue storage during the first year of life (39).

Our study strengths include the prospective design and much larger ($n = 464$) and more diverse (28% White, 36% Hispanic, 26% Asian, 8% Black, 2% other) sample of GDM offspring than the only previous prospective study of infants of mothers with GDM. We also employed quantitative methodologies to assess BF intensity and duration prospectively and standardized serial anthropometric growth measurements (weight and length) from birth during the first year of life. The SWIFT Study accounted for early life health outcomes that may influence the feeding method, such as newborn health status (i.e. size for gestational age at birth, neonatal intensive care unit admissions, Apgar scores or length of hospital stay) as well as potential confounders (i.e. gestational age at GDM diagnosis, GDM severity and treatment) of infant feeding and growth that previous studies of infants exposed to maternal diabetes have not considered. Our findings are generalizable to the diverse GDM population with singleton gestations of 35 weeks or longer.

Limitations include the loss-to-follow up, although 84% were measured at 1 year of age. Our study was not a randomized trial; therefore, residual or unmeasured confounding may influence the findings, and reverse causation cannot be completely ruled out in this study. Finally, our study was unable to directly evaluate the metabolic constituents of breast milk.

Our findings show that high intensity BF and longer duration throughout the first year of life among GDM offspring may slow ponderal growth and weight gain compared with FF. This evidence is consistent with previous findings that BF protects against obesity or diabetes among older children exposed to maternal diabetes in utero based on retrospective studies with less robust measures of BF via recall a decade or more later. Our findings support the hypothesis that early infant feeding may counteract the adverse metabolic programming occurring from exposure to maternal dysregulation of metabolic fuels during fetal life. Further investigations are needed to evaluate the direct effects of BF on early post-natal metabolism, breast-milk constituents and possible epigenetic effects that may set the stage for mitigating the trans-generational transmission of obesity, metabolic dysfunction and diabetes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

BF

breastfeeding

BMI

body mass index

C-Section

Cesarean section delivery

CI (statistics)

confidence interval

FF

formula feeding

GDM

gestational diabetes mellitus

LAZ

length for age z-score

SWIFT

Study of Women, Infant Feeding, and Type 2 Diabetes After GDM Pregnancy

SWIFT Offspring Study

Study of Women, Infant Feeding and Type 2 Diabetes After GDM Pregnancy and Infant Growth in their Offspring

WAZ

weight-for-age z-score

WLZ

weight-for-length z-score

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a

Overall adjusted mean WLZ-score change from birth to 12 months			
	Mean	95%CI	p-value
Intensive FF	1.11	0.87 to 1.35	<.0001
Intensive BF	0.53	0.37 to 0.69

b

Overall adjusted mean WAZ-score change from birth to 12 months			
	Mean	95%CI	p-value
Intensive FF	0.21	0.05 to 0.36	<.0001
Intensive BF	-0.22	-0.34 to -0.10

C

Overall adjusted mean LAZ-score change from birth to 12 months			
	Mean	95%CI	p-value
Intensive FF	-0.73	-0.93 to -0.53	0.08
Intensive BF	-0.94	-1.08 to -0.80

Figure 1.

(a–c) Infant growth measures [WLZ, WAZ, and LAZ-scores, mean, 95% confidence intervals (CI)] for each age and differences in the mean change in z-scores (slopes) for three time intervals (birth to 6–9 weeks, 6–9 weeks to 6 months, and 6 months to 12 months) and overall from birth to 12 months. Comparisons between infant feeding intensity groups at 6–9 weeks of age: intensive BF vs. intensive FF groups; *p*-values test the differences in mean change in z-scores; **p* < 0.05, †*p* = 0.01, ‡*p* < 0.001. (a) Adjusted change in WLZ-score. (b) Adjusted c in WAZ-score. (c) Adjusted changes in LAZ-score. (a–c) Repeated measures linear regression models for infant feeding groups and infant age including an interaction by infant age (time) adjusted for race/ethnicity (White, Black, Hispanic, Asian/ other), gestational age at birth (weeks), maternal age, parity, education (years), pre-pregnancy BMI (kg/m²), total gestational weight gain (kg), GDM treatment type and gestational age at diagnosis of GDM (weeks); *p*-values for group differences in change in z-score measures of infant growth within each time interval (three time intervals), and overall time interval from birth to 12 months in the tables beside the graph. **p* < 0.05, †*p* = 0.01, ‡*p* < 0.001. WLZ, weight-for-length; WAZ, weight-for-age; LAZ, length-for-age; BF, breastfeeding; FF, formula feeding.

a

Overall adjusted mean WLZ-score change from birth to 12 months			p-value comparison to Group 1
	Mean	95%CI	
Group 1 Consistent mostly or exclusive FF from birth or >3 months	0.97	0.75 to 1.19	referent
Group 2 Transition from BF to FF from 3 to 9 months	0.59	0.33 to 0.85	0.03
Group 3 Consistent mostly or exclusive BF from birth to >9 months	0.60	0.38 to 0.82	0.02

b

Overall adjusted mean WAZ-score change from birth to 12 months			p-value comparison to Group 1
	Mean	95%CI	
Group 1 Consistent mostly or exclusive FF from birth or >3 months	0.15	-0.01 to 0.31	referent
Group 2 Transition from BF to FF from 3 to 9 months	0.05	-0.13 to 0.23	0.44
Group 3 Consistent mostly or exclusive BF from birth to >9 months	-0.35	-0.49 to -0.21	<.0001

C

Overall adjusted mean LAZ-score change from birth to 12 months	Mean		p-value comparison to Group 1
	Mean	95%CI	
Group 1 Consistent mostly or exclusive FF from birth or >3 months	-0.75	-0.93 to -0.57	referent
Group 2 Transition from BF to FF from 3 to 9 months	-0.56	-0.78 to -0.34	0.18
Group 3 Consistent mostly or exclusive BF from birth to > 9 months	-1.18	-1.36 to -1.00	0.001

Figure 2.

(a–c) Infant growth shown as mean z-scores (95% confidence intervals) at each age and the differences in mean change in z-scores for three time intervals (birth to 6–9 weeks, 6–9 weeks to 6 months, and 6 months to 12 months) and overall from birth to 12 months. Comparisons of growth among combined intensity and duration scores (range 0 to 12) and the referent is Group 1; *p*-values test the change in z-scores (slope) differences for each interval and overall from birth to 12 months. **p* < 0.05, †*p* = 0.01, ‡*p* < 0.001. (a) Comparison of adjusted changes in WLZ-scores (Groups 1, 2 and 3). (b) Comparison of adjusted changes in WAZ-scores (Groups 1, 2 and 3). (c) Comparison of adjusted changes in LAZ-scores (Groups 1, 2 and 3). (a–c) Repeated measures linear regression estimates of infant growth measures for three groups for combined intensity and duration infant feeding scores: Group 1 is Intensive FF since birth or from 3 months of age through 1 year (Referent), Group 2 is Transition from BF to FF mid-year, and Group 3 is Intensive BF through one year. All models are adjusted for infant age and an interaction by infant age (time), race/ethnicity (White, Black, Hispanic, Asian/other), gestational age at birth (weeks), maternal age, parity, education (years), pre-pregnancy BMI (kg/m²), total gestational weight gain (kg), GDM treatment type, and gestational age at diagnosis of GDM (weeks). **p* < 0.05, †*p* = 0.01, ‡*p* < 0.001 for pairwise comparisons. WLZ, weight-for-length; WAZ, weight-for-age; LAZ, length-for-age; BF, breastfeeding; FF, formula feeding.

Table 1

Characteristics of women with GDM and their infants; entire cohort ($n = 464$) and by infant feeding intensity groups at 6–9 weeks of age

Maternal and Infant characteristics	Entire cohort $n = 464$	Intensive BF at 6–9 weeks $n = 310$	Intensive FF at 6–9 weeks $n = 154$
Sociodemographic			
Age (years)	33.2 $\pm$ 4.7	33.5 $\pm$ 4.5	32.5 $\pm$ 5.0 *
Education (years of formal schooling)	14.5 $\pm$ 3.0	14.8 $\pm$ 3.0	13.8 $\pm$ 3.0 ‡
Race/ethnicity, n (%)			
Non-Hispanic White	130 (28)	89 (28.7)	41 (26.6)
Non-Hispanic Black	38 (8)	21 (6.8)	17 (11.0)
Hispanic	165 (36)	106 (34.2)	59 (38.3)
Asian	120 (26)	89 (28.7)	31 (20.1)
Other	11 (2)	5 (1.6)	6 (3.9)
WIC recipient, n (%)	130 (28)	83 (26.8)	47 (30.5)
Smoking, n (%)			
Current (Prenatal and/or post-natal)	19 (4.1)	7 (2.3)	12 (7.8) *
Past (pre-conception)	86 (18.5)	57 (18.4)	29 (18.8)
Never	359 (77.4)	246 (79.4)	113 (73.4)
Prenatal			
Pre-pregnancy BMI (kg/m ²)	30.4 $\pm$ 7.4	29.8 $\pm$ 6.9	31.6 $\pm$ 8.1 *
Pre-pregnancy weight status n (%)			
BMI <25 kg/m ²	122 (26)	89 (28.7)	33 (21.4)
25 kg/m ² BMI < 30 kg/m ²	136 (29)	92 (29.7)	44 (28.6)
BMI $\geq$ 30 kg/m ²	206 (45)	129 (41.6)	77 (50.0)
Prenatal 3-h OGTT z -score	0.1 $\pm$ 2.8	0.0 $\pm$ 2.9	0.3 $\pm$ 2.6
Treatment of GDM, n (%)			
Diet modification only	306 (66)	207 (66.8)	99 (64.3)
Oral hypoglycemic agents	136 (29)	86 (27.7)	50 (32.5)
Insulin	22 (5)	17 (5.5)	5 (3.2)
Gestational age at GDM Diagnosis (weeks)	25.1 $\pm$ 7.7	25.5 $\pm$ 7.4	24.5 $\pm$ 8.2
Gestational weight gain (kg)	10.1 $\pm$ 7.0	10.1 $\pm$ 7.3	10.2 $\pm$ 6.3
Gestational weight gain above IOM, n (%)	158 (34.0)	99 (31.9)	59 (38.3)
Infant feeding intentions score	7.3 $\pm$ 1.1	7.5 $\pm$ 1.1	7.1 $\pm$ 1.1 ‡
Parity n (%)			
Primiparous	154 (33)	91 (29.4)	63 (40.9) ‡
Multiparous	310 (67)	219 (70.6)	91 (59.1)
Labor and delivery			
Caesarean section, n (%)	135 (29)	84 (27.1)	51 (33.1)
Length of hospital stay (days)	2.5 $\pm$ 1.1	2.4 $\pm$ 1.0	2.7 $\pm$ 1.4 *

	Entire cohort <i>n</i> = 464	Intensive BF at 6–9 weeks <i>n</i> = 310	Intensive FF at 6–9 weeks <i>n</i> = 154
Maternal and Infant characteristics			
Infant Characteristics			
Sex, <i>n</i> (%)			
Male	254 (55)	149 (48)	61 (40)
Female	210 (45)	161 (52)	93 (60)
Newborn, Mean SD			
Birth weight (g)	3435.9 ± 501.5	3426 ± 504.3	3455 ± 497.0
Length (cm)	50.7 ± 2.3	50.5 ± 2.3	51.0 ± 2.3 *
Gestational age (weeks)	39.0 ± 1.1	38.9 ± 1.2	39.2 ± 1.0 *
Length hospital of stay (days)	2.2 ± 1.4	2.2 ± 1.5	2.2 ± 1.2
Type of nursery, <i>n</i> (%)			
Regular	418 (90)	282 (91)	136 (88)
Intermediate	23 (5)	12 (4)	11 (7)
Intensive care unit (NICU)	23 (5)	16 (5)	7 (5)
Gestational age, <i>n</i> (%)			
35–36 weeks	28 (6)	24 (8)	4 (3) *
37–39 weeks	338 (73)	228 (73)	110 (71)
40 weeks or more	98 (21)	58 (19)	40 (26)
Birth weight, <i>n</i> (%)			
1,500–2,499 g	11 (2)	8 (3)	3 (2)
2,500–2,999 g	76 (16)	53 (17)	23 (15)
3,000–3,999 g	317 (68)	210 (68)	107 (69)
4,000–4,499 g	47 (10)	30 (10)	17 (11)
4,500 g or more	13 (3)	9 (3)	4 (3)
Size for Gestational Age, <i>n</i> (%)			
Large (LGA)	123 (27)	79 (26)	44 (29)
Appropriate (AGA)	331 (71)	224 (72)	107 (69)
Small (SGA)	9 (2)	6 (2)	3 (2)
Apgar score at 5 min, <i>n</i> (%)			
6 or lower	4 (1)	2 (1)	2 (1)
7 or higher	456 (98)	305 (98)	151 (98)
Missing	4 (1)	3 (1)	1 (1)
Breastfeeding duration (months), Mean (SD)	9.1 ± 7.0	11.9 ± 6.3	3.5 ± 4.5 †
Breastfeeding Intensity and duration 12-month score (range 0 to 12)	6.3 ± 4.6	8.5 ± 3.6	1.8 ± 2.6 †
Sleep at 6–9 weeks of age (hours)	15.0 ± 3.2	15.1 ± 3.1	14.8 ± 3.4
Initiation of complementary feeding, <i>n</i> (%)			
Early (<4 months)	84 (19)	46 (16)	38 (26) *
Later (≥ 4 months)	358 (81)	249 (84)	109 (74)

Data are mean ± SD or *n* (%) unless otherwise specified. Chi-squared or Fisher's exact test was used for categorical variables; *t*-test was used for continuous variables. Missing values: *n* = 3 length at birth, *n* = 22 complementary feeding. Approximately 5% of intensive FF group were mixed BF and FF.

*
 $p < 0.05$.

†
 $p < 0.01$.

‡
 $p < 0.001$.

AGA, size appropriate for gestational age; BF, breastfeeding; BMI, body mass index; FF, formula feeding; GDM, gestational diabetes mellitus; IOM, Institute of Medicine; LGA, size large for gestational age; NICU, neonatal intensive care unit; OGTT, oral glucose tolerance test; SGA, size small for gestational age; WIC, Special Supplemental Nutrition Program for Women, Infants and Children.