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Association of breastfeeding and gestational diabetes mellitus with the prevalence of prediabetes and the metabolic syndrome in offspring of Hispanic mothers

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Abstract

Background: The effects of breastfeeding (BF) on metabolic syndrome (MetS) and diabetes mellitus in children exposed to gestational diabetes mellitus (GDM) in utero have rarely been evaluated.

Objective: This study assessed BF and GDM in relation to the prevalence of prediabetes and MetS in Hispanic children and adolescents (8–19 y).

Methods: This is a longitudinal study with 229 Hispanic children (8–13 y) with overweight/obesity, family history of diabetes, and an average of four annual visits (AV). Participants were categorized as follows: never (negative for prediabetes/MetS at all AVs), ever (positive for prediabetes/MetS at any visit), intermittent (positive for prediabetes/MetS at 1–2 AVs), and persistent (positive for prediabetes/MetS at greater than or equal to 3 AVs).

Results: Compared with GDM offspring who were not BF (referent), GDM offspring who were BF had lower odds of persistent prediabetes (OR = 0.18; 95% CI, 0.040–82; $P = 0.02$) and MetS (OR = 0.10; 95% CI, 0.02–0.55; $P = 0.008$). Compared with referent group, non-GDM offspring who were BF, and non-GDM offspring not BF had lower odds of persistent prediabetes (OR = 0.10; 95% CI, 0.03–0.39; $P = 0.001$; OR = 0.05; 95% CI, 0.01–0.11; $P < 0.001$) and MetS (OR = 0.14; 95% CI, 0.04–0.59; $P = 0.01$ and OR = 0.04; 95% CI, 0.01–0.11; $P < 0.001$).

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AUTHOR CONTRIBUTIONS

Ms Sarvenaz Vandyousefi and Dr Jaimie N Davis contributed to the acquisition of data, conceptualized the analysis plan, carried out the initial analyses, coordinated the interpretation of results, drafted the initial manuscript, and finalized the manuscript. Dr Michael I Goran conceptualized and designed the study, designed the data collection instruments, collected data, carried out the initial analyses, and critically reviewed and revised the manuscript. Dr Erica P Gunderson coordinated the interpretation of results and critically reviewed the manuscript for important intellectual content. Erfan Khazaee, Matthew J Landry, Reem Ghaddar, and Dr Fiona M Asigbee critically reviewed the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

CONFLICTS OF INTEREST

No conflict of interest was declared.

Conclusions: These results show BF is protective against prediabetes and MetS in offspring regardless of GDM status.

Keywords

breastfeeding; gestational diabetes mellitus; metabolic syndrome; prediabetes

1 | INTRODUCTION

Prediabetes is a condition defined as having higher than normal levels of fasting plasma glucose (FPG), oral glucose tolerance test (OGTT) 2-hour blood glucose, glycated haemoglobin (HbA_{1c}), or a combination of these, but not high enough to be diagnosed as type 2 diabetes.[1] In the United States, the prevalence of prediabetes among adolescent population (12–19 y of age) ranges from 15% to 47%.[2] Early onset of prediabetes during childhood increases risk of type 2 diabetes, the metabolic syndrome (MetS),[3] and cardiovascular disease later in life. According to the SEARCH for Diabetes in Youth study, the prevalence of type 2 diabetes among adolescents younger than 20 years of age, 50% of whom being Hispanics, is estimated to increase fourfold over the next 30 years.[4]

The MetS is a condition described as having at least three of the following cardiometabolic risk factors: abdominal obesity, hypertriglyceridaemia, hyperglycaemia, hypertension, and low highdensity lipoprotein (HDL) cholesterol.[5] Over 30% of US adults had MetS in 2012.[6] Approximately 5% of adolescents and 30% of children who had obesity were diagnosed with MetS in 2010.[7] Hispanics have the highest prevalence of MetS compared with other racial/ethnic groups in the United States.[8] In addition, Hispanic youth have increased risk of obesity-related metabolic diseases, such as type 2 diabetes and cardiovascular disease.[9,10] Goran et al previously showed that over 30% of Hispanic children and adolescents (8–19 y of age) have prediabetes and MetS.[11,12]

Gestational diabetes mellitus (GDM), defined as “any degree of glucose intolerance with onset or first recognition during pregnancy,” is one of the most common metabolic complications of pregnancy worldwide.[13] According to the International Diabetes Federation (IDF), GDM impacted one in seven births in 2017.[14] In the United States, the prevalence of women with GDM was 7.6% between 2007 and 2014.[15] Children born to mothers with GDM are more likely to develop prediabetes, MetS, and increased adiposity later in life.[16,17] A longitudinal cohort of 6- to 11-year-old children showed that GDM offspring who were large for gestational age (LGA) had 3 to 5 times higher prevalence of MetS than non-GDM children born appropriate for gestational age.[18] Another study of 168 Danish offspring born to mothers with GDM found that GDM offspring had a sixfold increased risk of prediabetes (17%) compared with non-GDM offspring (3%).[19] Women of ethnic minority groups in the United States, especially Hispanics, have consistently higher prevalence and risk of GDM, compared with non-Hispanic white (NHW) women.[20–22] Hispanics (9.3%) and Mexican Americans (9.9%) had higher prevalence of GDM compared with NHWs (7.0%) in the United States between 2007 and 2014.[15]

Breast milk has been regarded as the best food for infants to meet their daily nutrients and energy requirements. Breastfeeding (BF) saves the lives of more than 800 000 children

under the age of 5 years annually; however, most infants and children do not receive optimal feeding.[23] The American Academy of Pediatrics and the World Health Organization (WHO) both recommend initiation and continuation of exclusive BF (feeding infants exclusively with breast milk and no other liquids or solids) within 1 hour and 6 months after birth, respectively.[23,24] According to the current Centers for Disease Control and Prevention (CDC) BF Report Card,[25] approximately 52% and 25% of infants in the United States were exclusively breastfed at 3 and 6 months of age in 2014 to 2015, respectively. Data from CDC show that approximately 30% of mothers in southern US states and 19% of mothers in western US states completely stopped BF and/or pumping breast milk in 2014.[26] Compared with NHW mothers, Hispanic and African American mothers have lower rates of exclusive BF.[27]

A few studies have shown that women with GDM throughout pregnancy compared with those without GDM are less likely to exclusively breastfeed in the first hour postpartum, are more likely to formula feed their children, and have delayed onset of lactation mainly due to diabetes, insulin treatment, and obesity.[28,29] Numerous retrospective studies have reported the inverse association between BF history (any duration) and risk factors associated with MetS such as hyperglycaemia, high blood pressure, obesity, cardiovascular disease, type 2 diabetes, and metabolic diseases in both mothers and children later in life.[30] However, research on the association between BF and lower risk of diabetes and MetS is limited in offspring of mothers with GDM.[31] In addition, research suggests that BF may decrease the prevalence of MetS, although not all findings are consistent.[32,33]

To date, no study has examined the association between BF and GDM status on prevalence of MetS and prediabetes in young children, particularly in a high-risk Hispanic population. Therefore, this study aims to assess the effects of BF and GDM on the prevalence of MetS and prediabetes in Hispanic children and adolescents as they age (8–19 y). This study hypothesized that a history of BF for at least 1 month will be associated with decreased MetS and prediabetes risk in older children of mothers reporting previous GDM or no GDM.

2 | METHODS

The design, data collection procedures, and findings of the University of Southern California longitudinal SOLAR (Study of Latino Adolescents at Risk for Diabetes) cohort have been previously described in detail.[34] The present analyses included 229 children (enrolled at ages 8–13 y), with an average of four annual inpatient and outpatient visits (range of 2–7 visits). According to IDF, “MetS should not be diagnosed in children younger than 10 years”[35]; therefore, 198 children (10–19 y of age) who had complete MetS parameters for at least three annual visits were evaluated for persistence of MetS. Data were collected between 2004 and 2013. Participants were recruited from Los Angeles County, California, and met the following inclusion criteria: (a) age 8 to 13 years at baseline, (b) family history of type 2 diabetes in at least one parent, grandparent, or sibling determined by parental self-report, (c) Hispanic origin (all four grandparents of Hispanic origin as determined by parental self-report), and (d) body mass index (BMI) greater than or equal to 85th percentile for age and sex based on CDC growth charts.[36]

Participants taking any medications known to affect fat distribution, body composition, insulin action, or insulin secretion and those diagnosed with diseases that may influence insulin action and secretion such as lipoatrophic diabetes and cystic fibrosis, or body composition and fat distribution such as Cushing and Down syndromes, were excluded from the study. SOLAR was approved by the Institutional Review Board of the University of Southern California. Informed written consent and assent were obtained from both parents and children, respectively, before testing commenced.

2.1 | Anthropometrics and adiposity measures

A licensed paediatric health-care provider performed a detailed physical exam where Tanner staging was determined using established guidelines.[37,38] Height, weight, and waist circumference (at the umbilicus) were measured to the nearest 0.1 cm, 0.1 kg, and 0.1 cm, respectively. Blood pressure was taken in the sitting position, and measures were repeated rapidly in triplicate at each annual visit.[12] BMI and BMI *z* scores were determined by using the EPII 2000 software (version 1.1; CDC, Atlanta, Georgia). Total body fat and soft lean tissue were measured by dual-energy X-ray absorptiometry (DXA) with the use of a Hologic QDR 4500W (Hologic, Bedford, Massachusetts).

2.2 | Oral glucose tolerance test

After an overnight fast, a 2-hour OGTT was administered with a dose of 1.75-g glucose/kg body weight (to a maximum of 75 g). Blood samples were assayed for glucose and insulin after 5 minutes (fasting state) and 2 hours (relative to glucose ingestion).

2.3 | Assays

Glucose from the OGTT was analysed on a Dimension Clinical Chemistry system using an in vitro hexokinase method (Dade Behring, Deerfield, Illinois). Glucose was assayed in duplicate on a Yellow Springs Instrument 2700 Analyzer (Yellow Springs Instrument; Yellow Springs, Ohio) using the glucose oxidase method. Fasting blood samples were also measured for triglycerides, and total and HDL cholesterol using the Vitros chemistry DT slides (Johnson and Johnson Clinical Diagnostics Inc., Rochester, New York).

2.4 | GDM and BF measures

Data on family history of diabetes, maternal GDM status, child's birth weight, and BF initiation and duration were assessed at baseline via parental self-administered questionnaires. In the current study, BF duration was analysed as categorical variables (ie, "No BF Group" who were breastfed 0 or less than 1 month vs "BF Group" who were breastfed greater than or equal to 1 month). Children were divided into four categories based on GDM and BF: (a) mothers without GDM and were breastfed (ie, "non-GDM, BF"), (b) mothers without GDM and were not breastfed (ie, "non-GDM, no-BF"), (c) mothers with GDM and were breastfed (ie, "GDM, BF"), and (d) mothers without GDM and were not breastfed (ie, "GDM, no-BF").

2.5 | Definition of MetS

To date, no standard definition of MetS for children/adolescents has been established.[35] For this analysis, MetS was categorized using a definition proposed by Cruz et al[39] that applies paediatric cut-offs to the Adult Treatment Panel III definition.[40] MetS was defined as having at least three of the following risk factors: abdominal obesity (waist circumference greater than or equal to 90th percentile for age, sex, and Hispanic ethnicity from NHANES III data), elevated blood pressure (systolic or diastolic blood pressure greater than 90th percentile adjusted for height, age, and sex), low HDL cholesterol (HDL cholesterol less than or equal to 10th for age and sex), hypertriglyceridaemia (triglycerides greater than or equal to 90th percentile of age and sex), and impaired glucose tolerance (IGT). Participants with MetS were classified into four groups[12]: "NEVER (negative for MetS at all annual visits); EVER (positive for MetS at any annual visits); INTERMITTENT (positive for MetS at 1 or 2 annual visits); and PERSISTENT (positive for MetS at ≥3 annual visits)."

2.6 | Definition of prediabetes

Prediabetes was defined according to American Diabetes Association (ADA) diagnostic criteria, as FPG levels between 100 and 125 mg/dL (between 5.6 and 6.9 mmol/L) and/or IGT, 2-hour plasma glucose value of at least 140 and less than 200 mg/dL, and/or HbA_{1c} values between 5.7 and 6.4% (39–47 mmol/mol.).[1] Similar to MetS, participants with prediabetes were classified into four groups: "NEVER (negative for prediabetes at all annual visits); EVER (positive for prediabetes at any annual visits); INTERMITTENT (positive for prediabetes at 1 or 2 annual visits); PERSISTENT (positive for prediabetes at ≥3 annual visits)."

2.7 | Statistical analysis

Summary statistics, graphical analyses, and frequency distributions were used to describe the data. Descriptive statistics (ie, mean, standard deviation, range, median and quartiles, histograms, and Q-Q plots) assessed the distribution of the data. First, *t* tests and chi-square analyses were performed to assess differences in baseline and physical characteristics between GDM and non-GDM offspring. Next, multinomial logistic regressions evaluated the effects of BF, GDM, and BF-GDM interaction on the prevalence of MetS and prediabetes over time with sex, Tanner stage, age, total body fat percentage, and birth weight as covariates. All analyses were performed using SAS version 9.4 (SAS, North Carolina). A *P* value of 0.05 was used to denote significance.

3 | RESULTS

Of the 229 children, 26% (n = 60) of children were exposed to GDM in utero, and 57% (n = 130) were breastfed for at least 1 month. Table 1 displays baseline descriptive characteristics of the GDM and non-GDM participants. GDM offspring compared with non-GDM offspring had higher birthweight at baseline. There were no differences in age, sex, Tanner stage, overweight/obesity prevalence, BF status, and MetS prevalence between GDM and non-GDM participants at baseline. Approximately 60% were male with an average age of 11 years at baseline, and 80.1% had obesity. Fifty-seven percent were breastfed for greater than or equal to 1 month, with an average duration of 5.2 ± 7.5 months. Approximately 25% had

MetS at baseline. GDM offspring compared with non-GDM offspring had a higher prevalence of prediabetes at baseline (approximately 58% vs 33%, $P = 0.03$).

Tables 2 and 3 compare baseline physical and metabolic characteristics of the participants with their prediabetes and MetS status (ie, never, ever, intermittent, and persistent), respectively. There were no differences in age, sex, Tanner stage, and birthweight of the participants at baseline and their prediabetes and MetS status at the latest visit. There were significant differences between weight, waiste circumference, total body fat, and overweight/obesity prevalence at baseline and MetS categories (Table 3). However, this result was attenuated for the prediabetes groups (Table 2). There were significant differences between GDM status (ie, being born to GDM vs non-GDM mothers), BF status, BF duration, and fasting blood glucose level at baseline and prediabetes and MetS categories at the latest visit.

Results from the multinomial logistic regression for prevalence of prediabetes are shown in Table 4. Of the 229 children, 27% and 26% had intermittent and persistent prediabetes across time, respectively. Males had three times higher persistent prediabetes than females ($P = 0.04$). Total body percent fat and Tanner stage did not differ across intermittent and persistent prediabetes groups. However, odds of ever prediabetes was four times higher for those in Tanner stage 4 to 5 than those in Tanner stage 1 to 3 ($P < 0.001$). Age of the partcipants with ever prediabetes was significantly higher than those who never had prediabetes. GDM offspring compared with non-GDM offspring had approximately four, two and a half, and six times higher odds of ever, intermittent, and persistent prediabetes, respectively ($P = 0.0002$; $P = 0.03$; $P < 0.001$). Children who were breastfed for at least 1 month had significantly lower odds of ever, intermittent, and persistent ($P = 0.0009$; $P = 0.001$; $P = 0.002$) than those who were never breastfed or breastfed for less than 1 month.

There was an overall significant BF-GDM interaction on the prevalence of prediabetes ($P = 0.04$). “GDM, no-BF” group was entered in the model as the referent group for Bonferroni post hoc comparisons, and all prediabetes groups were compared with the “never prediabetes” group. Compared with the referent group, “non-GDM, BF” group had lower odds of ever prediabetes (OR = 0.07; 95% CI, 0.02–0.24; $P < 0.0001$), intermittent prediabetes (OR = 0.12; 95% CI, 0.03–0.49; $P = 0.003$), and persistent prediabetes (OR = 0.04; 95% CI, 0.010.11; $P < 0.001$). Compared with the referent group, “non-GDM, no BF” group had lower odds of ever and persistent prediabetes (OR = 0.10; 95% CI, 0.03–0.39; $P = 0.001$ and OR = 0.10; 95% CI, 0.03–0.39; $P = 0.001$); however, the prevalence of intermittent prediabetes was not significant for the mentioned group. Among GDM offspring, those who were breastfed compared with those who were not breastfed had lower odds of persistent prediabetes (OR = 0.10; 95% CI, 0.03–0.41; $P = 0.02$); however, this result was attenuated for the prevalence of intermittent prediabetes. Among non-GDM offspring, those who were breastfed compared with those who were not breastfed had lower odds of intermittent prediabetes (OR = 0.23; 95% CI, 0.10–0.54; $P < 0.001$) and persistent prediabetes (OR = 0.29; 95% CI, 0.06–0.28; $P = 0.01$). Figure 1A further displays the results in terms of frequency of prediabetes within all GDM-BF groups.

Results from the multinomial logistic regressions for prevalence of MetS are shown in Table 5. Of the subsample of 198 offspring who were assessed for MetS, 58% never had MetS; 25% and 17% had intermittent and persistent MetS, respectively. Males had about three times higher odds of intermittent and any type of MetS ($P = 0.04$; $P = 0.01$) and five times higher odds of persistent MetS than females ($P = 0.004$). Birthweight, age, and Tanner stage did not differ between MetS groups. Compared with offspring who had never had MetS, those with ever or persistent MetS had higher total body fat percentage ($P = 0.009$; $P = 0.002$). GDM offspring compared with non-GDM offspring had approximately four, three and a half, and six times higher odds of ever, intermittent, and persistent MetS, respectively ($P = 0.002$; $P = 0.01$;$P = 0.001$). Children who were breastfed for at least 1 month had lower odds of ever, intermittent, and persistent MetS ($P < 0.001$) than those who were never breastfed or breastfed for less than 1 month.

There was an overall significant BF-GDM interaction on the prevalence of MetS ($P = 0.03$). Compared with "GDM, no BF" group (referent), "non-GDM, BF" group had significantly lower odds of ever MetS (OR = 0.02; 95% CI, 0.03–0.41; $P < 0.0001$), intermittent MetS (OR = 0.03; 95% CI, 0.01–0.10; $P < 0.001$), and persistent MetS (OR = 0.04; 95% CI, 0.01–0.11; $P < 0.001$). "Non-GDM, no BF" group had lower odds of persistent MetS (OR = 0.14; 95% CI, 0.04–0.59; $P = 0.01$) compared with the "GDM, no BF" group; however, this result was attenuated for the prevalence of intermittent MetS. Among GDM offspring, those who were BF compared with those who were not BF had lower odds of intermittent and persistent MetS (OR = 0.12; 95% CI, 0.02–0.75; $P = 0.02$ and OR = 0.10; 95% CI, 0.02–0.55; $P = 0.008$). Among non-GDM offspring, those BF compared with those not BF had significantly lower odds of ever, intermittent, and persistent MetS, respectively: OR = 0.18 (95% CI, 0.05–0.72) $P = 0.01$; OR = 0.12 (95% CI, 0.02–0.75) $P = 0.02$; OR = 0.10 (95% CI, 0.02–0.55; $P = 0.008$. Figure 1B further displays the frequency of prediabetes within all GDM-BF groups.

4 | DISCUSSION

This study examined the impact of BF and GDM across time on MetS and prediabetes in Hispanic offspring born to mothers with and without GDM. Although research shows that BF has a protective effect on diminishing development of MetS and prediabetes in offspring, there have been conflicting findings, and much less is known about this protective effect of BF on children born to mothers with GDM. Additionally, no previous studies have examined the persistence of MetS and prediabetes in Hispanic offspring exposed to GDM in utero longitudinally. This longitudinal study shows that BF has a protective effect on the prevalence of ever and persistent MetS and prediabetes in both GDM and non-GDM offspring.

It is well established that GDM throughout pregnancy is a contributing factor to prediabetes and type 2 diabetes in women. While many of the mentioned studies controlled for GDM or type of maternal diabetes during pregnancy, few have actually examined the interaction of BF and GDM on glucose/insulin action in children.[41] A prospective cohort of Pima Indians assessed protective effects of BF on type 2 diabetes in GDM offspring and found that offspring of mothers with GDM (n = 21) who were exclusively breastfed had lower

prevalence of type 2 diabetes, compared with those who were not breastfed or were bottle-fed throughout their infancy; however, their results were not statistically significant.[42] The only longitudinal study with quality measurements and quantitative assessment of breastmilk intake was conducted by Gunderson et al and showed that greater BF intensity and duration throughout the first 12 months of life was protective against ponderal growth and weight gain among children of mothers with GDM.[43]

Another study of offspring born to mothers with GDM (n = 29) and type 1 diabetes (n = 83) in Berlin showed that breastfed children of mothers with diabetes had higher risk of developing overweight and IGT at 2 years of age than breastfed offspring of mothers without diabetes.[44] Their conflicting findings may be due to the heterogeneity of maternal type of diabetes and early assessment for prediabetes and overweight in children at or younger than 2 years of age, which is less predictive of overweight and prediabetes status at older ages. Findings of this study show that BF has a protective effect on the prevalence of intermittent prediabetes in non-GDM offspring and persistent prediabetes in GDM offspring across time.

While studies show that BF decreases the risks associated with MetS in children and adolescents, research on the association between BF and MetS is limited and inconclusive.[32] A recent systematic review of studies that examined the relationship between BF and MetS reported that of 11 studies, seven found significant inverse relationships between BF and MetS and four studies found no significant associations. One cross-sectional study with 1770 children and adolescents (7–17 y of age) in China found an inverse association between BF and prevalence of MetS. In contrast, a retrospective study by Yakubov et al with 123 children and adolescents (3–18 y of age) in Israel showed that BF had no protective effect on the prevalence of MetS. However, this study included very young children where MetS might not have yet manifested, which may explain their nonsignificant findings. In addition, the IDF does not suggest MetS diagnosis in children younger than 10 years of age. Of note, all of the above studies were conducted outside the United States, and no study has examined the persistence of MetS in offspring born to mothers with GDM, or in a high-risk Hispanic population. This study found an inverse association between BF and the prevalence of ever, intermittent, and persistent MetS in both GDM and non-GDM Hispanic older children.[32]

The mechanisms by which the risk of MetS and diabetes in offspring increases by intrauterine exposure to diabetes are not fully understood. Exposure to GDM is associated with excess fetal growth and overnutrition in utero, possibly due to hormonal perturbations and alterations in expression of genes that direct the accumulation of body fat or related metabolism in fetus. Research shows that exposure to maternal diabetes in utero results in hyperglycaemia, hyperinsulinaemia, and leptin resistance in offspring.[45] Consequently, exposure to high glucose and insulin concentrations increases levels of fatty acids, glucocorticoids, inflammation, and radicals of oxygen species (ROS) in the maternal-fetal placenta. Increased intrauterine insulin along with generated ROSs can cause altered β-cell differentiation, insulin resistance, and consequently increased risk of prediabetes and type 2 diabetes in offspring later in life. Additionally, increased ROSs in placenta can alter gene expression and metabolic programming of several organs including heart, liver, kidneys, and muscles that can lead to altered insulin signalling pathway, reduced bioavailable nitric oxide,

vascular stiffness, and diastolic dysfunction triggering hypertension and development of MetS in those who were born to mothers with GDM throughout adulthood.[45]

Very little is understood about the composition of breast milk in mothers with GDM, and the precise mechanisms underlying the potential protective effect of BF on diabetes and MetS is still unclear. It is believed that exposure to overnutrition and high glucose levels in breast milk of women with diabetes during pregnancy may increase obesity and metabolic disease risk in offspring later in life. A plausible assumption is that GDM may alter the abundance and composition of free human milk oligosaccharides (HMOs), the highest constituent in breast milk after fat and carbohydrates, and glycosylation of protective proteins in milk.[46,47]

Infants do not have the necessary enzymes for digestion of HMOs; therefore, they remain undigested and will be consumed by specific infant gut microbiota members, which may alter metabolic programming and growth and development of offspring later in life. A few studies have shown that the glycosylation of protective proteins in milk is lower in women with GDM compared with those without GDM. However, no differences were found between the total HMOs and their composition in breast milk of women with and without GDM.[48] Although a few researchers have shown that breast milk from women with glucose intolerance would have adverse effects on health outcomes in children, neither the literature nor these findings support this.[43] In summary, the association between BF and health outcomes in offspring born to GDM mothers remains uncertain, and further research is needed to investigate the effects of these alterations on offspring health outcomes.[48]

There are several limitations of the current study to consider. The study sample included only Hispanic children with overweight or obesity and with a family history of type 2 diabetes; therefore, the results may not be generalizable to Hispanic children of normal weight and other ethnic/racial populations. Replication of this study using nonhomogenous populations is warranted. This study also did not account for GDM mothers receiving treatment, and the severity of the GDM was not known. In addition, GDM status was self-reported and was not confirmed with medical records; however, validity research has shown self-reported GDM status to be accurate with 94% of self-reported GDM cases confirmed by a physician.[49] This study did not assess maternal or paternal BMI, parity, gestational weight gain, or type of delivery mode (ie, C-section vs vaginal birth) for this study, all of which play a role in subsequent obesity and metabolic disease risk in the offspring. Other limitations are that BF was assessed retrospectively and, since little information on BF was collected, exclusive BF could not be assessed. The sample size for GDM offspring is rather small (n = 60) and not enough to examine the various effects of BF duration groups on health outcomes; however, each subject had an average of four annual visits with sophisticated adiposity and metabolic testing, which somewhat offsets this limitation.

In conclusion, childhood prevalence of MetS and prediabetes is rising in the United States, especially among Hispanic children and adolescents. This is the first longitudinal study to examine the association between BF and the prevalence of MetS and prediabetes in Hispanic youth with overweight or obesity across puberty. These findings highlight the need to encourage mothers diagnosed with GDM during pregnancy to breastfeed for at least 1 month. BF is one of the vital modifiable approaches that can have a profound effect on

reducing the persistence of the MetS and prediabetes during adulthood. Continued longitudinal analyses using more precise and valid measures such as exclusivity of BF in relation to MetS and prediabetes are warranted, especially in high-risk populations.

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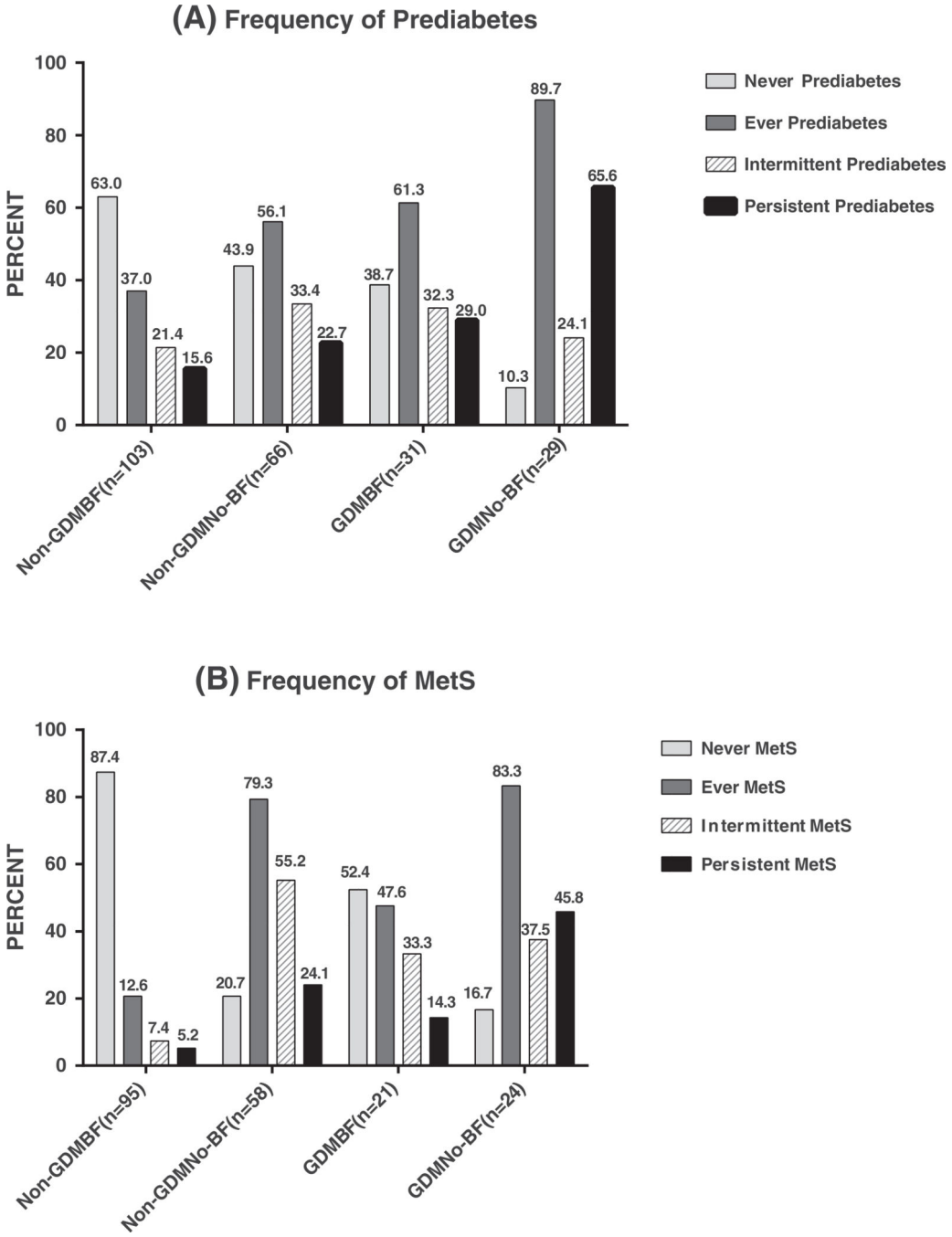

FIGURE 1.

Frequency of each type of prediabetes and metabolic syndrome (MetS) by breastfeeding (BF)-gestational diabetes mellitus (GDM) groups. Never = negative for prediabetes or MetS at all annual visits; ever = positive for prediabetes or MetS at any visit; intermittent = positive for prediabetes or MetS at 1 or 2 visits; persistent = positive for prediabetes or MetS at ≥3 annual visits

TABLE 1

Comparison of baseline physical and metabolic characteristics between GDM and non-GDM offspring[a]

Variable	Total (n = 229)	Non-GDM (n = 169)	GDM (n = 60)	*P* value[b]
Male, n (%)	131.0 (57.2)	106.0 (58.6)	25.0 (52.1)	0.42
Age, y	11.1 ± 1.6	11.0 ± 1.6	11.1 ± 1.6	0.40
Birth weight, kg	3.7 ± 0.9	3.5 ± 0.9	3.9 ± 0.9	**0.03**
Weight, kg	71.7 ± 19.7	69.8 ± 17.9	75.2 ± 23.0	0.06
Waist circumference, cm	92.3 ± 13.5	91.1 ± 13.1	93.4 ± 14.9	0.19
Total body fat, kg	29.1 ± 11.4	26.9 ± 10.1	31.2 ± 12.9	0.48
Tanner stage, n (%)				
1–3	157.0 (68.6)	118.0 (69.9)	39.0 (64.7)	0.87
4–5	72.0 (31.4)	51.0 (30.1)	21.0 (35.3)	
Overweight/obese status, n (%)				
Overweight (>85th to <95th percentile)	44.0 (19.2)	32.0 (18.9)	12.0 (20.6)	0.46
Obese (≥95th percentile)	185.0 (80.1)	137.0 (81.1)	48.0 (79.4)	
BF status, n (%)				
<1 mo	99.0 (43.2)	68.0 (40.2)	31.0 (50.9)	0.08
≥1 mo	130.0 (56.8)	101.0 (59.8)	29.0 (49.1)	
BF duration, mo	5.2 ± 7.5	5.4 ± 7.8	4.6 ± 7.2	0.59
FPG, mg/dL	92.4 ± 6.7	91.7 ± 6.2	93.1 ± 7.9	0.81
Metabolic syndrome, n (%)	57.0 (24.9)	42.0 (25.0)	15.0 (25.5)	0.24
Prediabetes, n (%)	91.0 (39.7)	56.0 (33.3)	35.0 (57.6)	**0.003**

Abbreviations: BF, breastfeeding; FPG, fasting plasma glucose; GDM, gestational diabetes mellitus.

[a]Values are mean ± SD unless otherwise stated.

[b]*t* tests and chi-square tests were run to assess difference in means or % between non-GDM and GDM groups. Significant *P* values (<0.05) are bolded.

TABLE 2

Comparison of baseline physical and metabolic characteristics by prediabetes (PreDM) groups at the latest visit[a]

Variable	Never PreDM (n = 109)	Ever PreDM (n = 120)	Intermittent PreDM (n = 61)	Persistent PreDM (n = 59)	*P* value[b]
Male, n (%)	61.0 (56.0)	70.0 (58.3)	33.0 (54.1)	37.0 (62.7)	0.59
Age, y	11.2 ± 1.7	11.0 ± 1.8	11.0 ± 1.8	11.0 ± 1.7	0.86
Birth weight, kg	3.7 ± 0.9	3.6 ± 0.7	3.6 ± 0.7	3.5 ± 0.8	0.40
Weight, kg	65.9 ± 19.9	64.6 ± 20.0	62.5 ± 16.2	66.7 ± 23.2	0.45
Waist circumference, cm	88.9 ± 14.6	88.6 ± 12.5	87.9 ± 11.0	89.4 ± 13.9	0.82
Total body fat, kg	25.4 ± 10.7	25.3 ± 10.2	24.2 ± 8.3	26.4 ± 11.8	0.52
Tanner stage, n (%)					
1–3	81.0 (74.3)	98.0 (81.7)	52.0 (85.2)	46.0 (78.0)	0.16
4–5	28.0 (25.7)	22.0 (18.3)	9.0 (14.8)	13.0 (22.0)	
Overweight/obese status, n (%)					
Overweight (>85th to <95th percentile)	24.0 (22.0)	16.0 (13.3)	6.0 (9.8)	10.0 (16.9)	0.13
Obese (≥95th percentile)	84.0 (77.1)	104.0 (86.7)	55.0 (90.2)	49.0 (83.1)	
GDM status, n (%)					
Non-GDM	97.0 (89.0)	84.0 (70.0)	48.0 (78.7)	36.0 (61.0)	**0.001**
GDM	12.0 (11.0)	36.0 (30.0)	13.0 (21.3)	23.0 (39.0)	
BF status, n (%)					
<1 mo	32.0 (29.4)	64.0 (53.3)	30.0 (49.2)	34.0 (57.6)	**0.001**
≥1 mo	77.0 (70.6)	56.0 (46.7)	31.0 (50.8)	25.0 (42.4)	
BF duration, mo	6.7 ± 8.6	4.0 ± 6.4	3.4 ± 5.6	4.5 ± 7.1	**0.02**
FPG, mg/dL	92.8 ± 6.1	94.5 ± 7.5	93.2 ± 7.3	95.8 ± 7.5	**0.03**

Abbreviations: BF, breastfeeding; FPG, fasting plasma glucose; GDM, gestational diabetes mellitus.

[a]Values are mean ± SD unless otherwise stated.

[b]Analysis of variance (ANOVA) test was run to assess difference in means or % between metabolic outcomes and baseline variables. Significant *P* values (<0.05) are bolded.

TABLE 3

Comparison of baseline physical and metabolic characteristics by metabolic syndrome (MetS) groups at the latest visit[a]

Variable	Never MetS (n = 117)	Ever MetS (n = 81)	Intermittent MetS (n = 47)	Persistent MetS (n = 34)	*P* value[b]
Male, n (%)	60.0 (51.3)	49.0 (60.0)	29.0 (61.7)	20.0 (58.8)	0.29
Age, y	11.2 ± 1.7	11.0 ± 1.8	11.0 ± 1.8	11.0 ± 1.5	0.45
Birth weight, kg	3.7 ± 0.7	3.5 ± 0.9	3.5 ± 0.7	3.6 ± 1.0	0.71
Weight, kg	63.7 ± 19.9	66.9 ± 19.3	66.9 ± 19.8	64.5 ± 18.8	**0.04**
Waist circumference, cm	87.4 ± 13.5	90.1 ± 13.3	91.1 ± 13.3	89.1 ± 13.3	**0.00**
Total body fat, kg	24.5 ± 10.5	26.1 ± 10.6	26.1 ± 10.5	26.1 ± 10.6	**0.004**
Tanner stage, n (%)					
1–3	88.0 (75.2)	64.0 (79.0)	37.0 (78.7)	27.0 (79.4)	0.53
4–5	29.0 (24.8)	17.0 (20.0)	10.0 (21.3)	7.0 (20.6)	
Overweight/obese status, n (%)					
Overweight (>85th to <95th percentile)	26.0 (22.2)	11.0 (13.6)	4.0 (8.5)	7.0 (20.6)	0.001
Obese (≥95th percentile)	91.0 (77.8)	70.0 (86.4)	43.0 (91.5)	27.0 (79.4)	
GDM status, n (%)					
Non-GDM	95.0 (81.2)	58.0 (71.6)	35.0 (74.5)	23.0 (67.6)	0.001
GDM	22.0 (18.8)	23.0 (28.4)	12.0 (25.5)	11.0 (32.4)	
BF status, n (%)					
<1 mo	29.0 (24.8)	53.0 (65.4)	31.0 (66.0)	22.0 (64.7)	0.001
≥1 mo	88.0 (75.2)	28.0 (34.6)	16.0 (34.0)	12.0 (35.3)	
BF duration, mo	7.1 ± 8.1	3.0 ± 5.9	2.5 ± 5.4	3.5 ± 6.3	0.002
FPG, mg/dL	91.2 ± 4.8	95.6 ± 6.4	95.7 ± 6.2	95.4 ± 6.6	0.048

Abbreviations: BF, breastfeeding; FPG, fasting plasma glucose; GDM, gestational diabetes mellitus.

[a]Values are mean ± SD unless otherwise stated.

[b]Analysis of variance (ANOVA) test was run to assess difference in means or % between metabolic outcomes and baseline variables. Significant *P* values (<0.05) are bolded.

TABLE 4

Logistic multinomial regression of physical and early life predictors on the prevalence of ever, intermittent, and persistent prediabetes

	Ever Prediabetes (n = 120)		Intermittent Prediabetes (n = 61)		Persistent Prediabetes (n = 59)	
Predictors	***P*[a]**	**OR[b] (95% CI)**	***P*[a]**	**OR[b] (95% CI)**	***P*[a]**	**OR[b] (95% CI)**
Covariate adjusted additive model for GDM and BF status separate						
GDM						
No	Referent	1.00	-----	1.00	-----	1.00
Yes	**0.0002**	3.67 (1.87-7.20)	**0.03**	2.40 (1.09–5.29)	**<0.001**	5.60 (2.59–12.06)
BF						
No	Referent	1.00	-----	1.00	-----	1.00
Yes	**0.0009**	0.38 (0.22–0.67)	**0.002**	0.29 (0.13–0.61)	**0.001**	0.26 (0.11–0.58)
Covariate adjusted GDM groups stratified by BF status						
GDM, no BF	Referent	1.00	-----	1.00	-----	1.00
GDM, BF	**0.01**	0.15 (0.03–0.67)	0.59	0.63 (0.11–1.99)	**0.02**	0.18 (0.04–0.82)
Non-GDM, no BF	**0.001**	0.10 (0.03–0.41)	0.35	0.50 (0.12–2.13)	**0.001**	0.10 (0.03–0.39)
Non-GDM, BF	**<0.0001**	0.07 (0.02–0.24)	**0.003**	0.12 (0.03–0.49)	**<0.001**	0.05 (0.01–0.11)
Sex						
Female	Referent	1.00	-----	1.00	-----	1.00
Male	0.05	1.84 (0.99–3.43)	0.45	1.44 (0.56–3.62)	**0.04**	2.98 (1.05–8.45)
Total body % fat	0.23	1.03 (0.98–1.08)	0.28	1.03 (0.98–1.09)	0.36	1.03 (0.97–1.09)
Birthweight	0.06	0.66 (0.43–1.03)	0.43	0.81 (0.48–1.38)	**0.01**	0.47 (0.26–0.85)
Age	**0.01**	1.31 (0.98–1.58)	**0.02**	1.23 (1.02–1.54)	**0.03**	1.27 (0.99–1.62)
Tanner						
1–3	Referent	1.00	-----	1.00	-----	1.00
4–5	**<0.001**	3.91 (1.97–7.79)	0.05	1.71 (0.48–6.06)	0.41	3.18 (0.77–13.21)

Abbreviations: BF, breastfeeding; GDM, gestational diabetes mellitus; OR: odds ratio.

[a]Significant *P* values (<0.05) are bolded.

[b]*P* value for interaction = 0.04.

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TABLE 5

Logistic multinomial regression of physical and early life predictors on the prevalence of ever, intermittent, and persistent MetS[a] rate

	Ever MetS (n = 81)		Intermittent MetS (n = 47)		Persistent MetS (n = 34)	
Predictors	***P*[a]**	**OR[b] (95% CI)**	***P*[a]**	**OR[b] (95% CI)**	***P*[a]**	**OR[b] (95% CI)**
Covariate adjusted additive model for GDM and BF status separate						
GDM						
No	Referent	1.00	-----	1.00	-----	1.00
Yes	**0.002**	4.29 (1.73,10.64)	**0.01**	3.47 (1.29–9.38)	**0.001**	5.72 (2.01–13.29)
BF						
No	Referent	1.00	-----	1.00	-----	1.00
Yes	**<0.001**	0.05 (0.02–0.09)	**<0.001**	0.06 (0.02–0.18)	**<0.001**	0.08 (0.03–0.21)
Covariate adjusted GDM groups stratified by BF status						
GDM, no BF	Referent	1.00	-----	1.00	-----	1.00
GDM, BF	**0.01**	0.18 (0.05–0.72)	**0.02**	0.12 (0.02–0.75)	**0.008**	0.10 (0.02–0.55)
Non-GDM, no BF	0.67	0.76 (0.22–2.67)	0.81	0.88 (0.18–4.13)	**0.01**	0.14 (0.04–0.59)
Non-GDM, BF	**<0.0001**	0.02 (0.03–0.41)	**<0.001**	0.03 (0.01–0.10)	**<0.001**	0.04 (0.01–0.11)
Sex						
Female	Referent	1.00	-----	1.00	-----	1.00
Male	**0.01**	3.02 (1.25–7.27)	**0.04**	2.80 (1.04–5.08)	**0.004**	5.18 (2.67–9.93)
Total body % fat	**0.009**	1.11 (1.03–1.19)	0.12	1.07 (0.98–1.17)	**0.002**	1.17 (1.06–1.29)
Birthweight	0.26	0.72 (0.41–1.26)	0.49	0.81 (0.44–1.49)	0.08	0.55 (0.28–1.08)
Age	0.48	0.91 (0.69–1.19)	0.12	0.79 (0.59–1.05)	0.24	1.22 (0.87–1.70)
Tanner						
1–3	Referent	1.00	-----	1.00	-----	1.00
4–5	0.92	1.05 (0.38–2.84)	0.40	1.79 (0.53–2.58)	0.80	1.18 (0.41–2.73)

Abbreviations: BF, breastfeeding; GDM, gestational diabetes mellitus; MetS, metabolic syndrome; OR: odds ratio.

[a]Significant *P* values (<0.05) are bolded.

[b]*P* value for interaction = 0.03.