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Gestational Diabetes and Cardiovascular Risk Factors and Disease in U.S. Hispanics/Latinas in the Hispanic Community Health Study/Study of Latinos (HCHS/SOL)

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Abstract

Aim—To compare cardiovascular risk and disease prevalence in U.S. Hispanics/Latinas with and without a history of gestational diabetes mellitus (GDM).

Methods—Cross-sectional data from 2008–2011 were analyzed for 8262 (305 with GDM history) parous women, aged 20–73 years, from the Hispanic Community Health Study/Study of Latinos. Women with and without a history of GDM were compared on socio-demographic, cardiovascular risk factor, and disease data from standardized interviews and fasting blood tests, using chi-square tests, t-tests, and logistic regressions to determine odds ratios (OR) and 95% confidence intervals (CI).

Results—Adjusting for covariates, compared to those without a history of GDM, women with a history of GDM: were younger (mean=39.1 [95% CI=37.8, 41.6] vs. 45.5 years [95% CI=44.9, 46.1]) and more likely to have health insurance (68.1% [95% CI=60.3%, 76.0%] vs. 54.9% [95% CI=52.8%, 57.1%]); had greater waist circumference (mean=102.3, [95% CI=100.2, 104.3] vs. 98.1 cm [95% CI=97.4, 98.5]) and higher fasting glucose (116.0 [95% CI=107.8, 124.3] vs. 104.2 mg/dL [95% CI=103.4, 105.1]); and had higher odds of having metabolic syndrome (OR=1.7 [95% CI=1.2–2.6]) or diabetes (OR=3.3 [95% CI=2.2–4.8]). Prevalences of heart and cerebrovascular disease were similar.

Conclusions—GDM history was positively associated with diabetes but not with cardiovascular disease.

Keywords

Gestational diabetes; diabetes; cardiovascular disease; Hispanic/Latina

Introduction

Gestational diabetes mellitus (GDM) is a complication of pregnancy, affecting up to 14% of pregnancies in the United States (DeSisto et al. 2014). During pregnancy, shifts in glucose and insulin resistance occur as a result of the growing needs of the fetus (Coustan 2013). GDM results when a pregnant woman's body is unable to produce sufficient insulin to maintain glucose homeostasis. Consequently, glucose is not absorbed by muscle and adipose tissue and instead builds up in the bloodstream, causing hyperglycemia (Coustan 2013).

Following birth, GDM is associated with increased maternal risk of adverse cardiovascular health outcomes and increased morbidity for the mother (Shah et al. 2008; Sullivan et al. 2012). Compared to women without GDM, women with a history of GDM have increased cardiometabolic risk, including obesity (Buchanan et al. 2012; Lavie et al. 2009), larger waist circumferences, and more likely to have hypertension, dyslipidemia, lower high-density lipoprotein cholesterol (HDL-c), and higher fasting glucose during the decade after the GDM pregnancy (Buchanan et al. 2012). A history of GDM is also a major known risk factor for incidence of type 2 diabetes (T2DM); the incidence of diabetes can be up to 10 times higher in women with a history of GDM compared to those with no history of GDM (Bellamy et al. 2009; Bernstein et al. 2017 & Ferrara et al. 2009; Kim et al. 2002). Given the greater burden of cardiovascular risk factors, women with a history of GDM are at increased risk of incidence of cardiovascular disease (CVD) and events, including myocardial infarction, stroke, coronary angioplasty, coronary artery bypass, and carotid endarterectomy (Shah et al. 2008; Sullivan et al. 2012). Therefore, a diagnosis of GDM is important because it identifies a population of women at increased risk for poorer cardiovascular health outcomes in later life.

Race/ethnicity is a non-modifiable risk factor for GDM, and U.S. Hispanics/Latinas are at two- to fourfold higher risk for GDM compared with non-Latina whites (Ferrara 2007; Fujimoto et al. 2013). From 2000 to 2010 in the U.S., Hispanics/Latinas had the highest increase in GDM incidence (66%), compared with non-Hispanic Whites, Blacks, and Asian/Pacific Islanders (Bardenheier et al. 2015). Compared with other races/ethnicities, U.S. Hispanics/Latinos have also had greater increases in obesity prevalence in the past decade and burden of CVD risk factors, including abdominal obesity, high triglycerides, high blood pressure, and high fasting glucose and low levels of HDL-c (Heiss et al. 2014). Taken together, more obesity and CVD risk factors are related to the development of CVD. Despite presence of these risk factors, the general U.S. Hispanic/Latino population has lower-than-expected rates of CVD and better life expectancy ("Hispanic paradox"; Medina-Inojosa et al. 2014; Shaw et al. 2017). Whether such paradoxical effects of lower-than-expected rates of CVD exist in the subset of Hispanic/Latina women with a history of GDM is unknown.

To address this gap, we compared the prevalence of CVD risk factors and CVD, including coronary heart disease (CHD) with and without angina, and cerebrovascular disease, between U.S. Hispanic/Latina women with and without a prior diagnosis of GDM who participated in the baseline clinic visit of the Hispanic Community Health Study / Study of Latinos (HCHS/SOL). By examining whether evidence existed of paradoxical effects of lower-than-expected rates of CVD within the specific subset of Hispanic/Latina women with

a history of GDM who are expected to have heightened risk of CVD, this paper contributes to the literature on maternal Hispanic/Latina health and the Hispanic paradox.

Material and Methods

Participants

The HCHS/SOL is a prospective cohort study of CVD and risk factors in U.S. Hispanic/Latino populations from randomly selected households recruited March 2008 – June 2011 in Bronx, NY; Chicago, IL; Miami-Dade County, FL; and San Diego, CA. The HCHS/SOL cohort (N=16,415 of which 9,835 are women) was selected through stratified two-stage area household probability sampling in each of the four communities. Briefly, census block groups were randomly sampled with stratification on Hispanic/Latino and socioeconomic status concentration. Using U.S. Postal Service registries, households were randomly selected within strata. To meet the study objective of identifying predictors of disease outcomes, the 45–74 years age group (n=9,714) was oversampled. Screening and recruitment were conducted in-person or by telephone. Of the 39,384 selected, screened, and found eligible, 41.7% enrolled (LaVange et al. 2010). The institutional review boards at each site approved the study protocol, and all participants gave written and signed informed consent. At enrollment, participants were 18–74 years old, self-identified as Hispanic/Latino with representation from persons of Central American, Cuban, Dominican, Mexican, Puerto Rican, and South American ancestry. HCHS/SOL sampling weights are nonresponse adjusted, trimmed, and calibrated weights to the 2010 census target population.

All participants in HCHS/SOL underwent a baseline clinic visit to a HCHS/SOL center and were instructed to fast prior to their appointment. Fasting blood samples and detailed anthropometric measurements were taken. Questionnaires were staff-administered (bilingual staff) and completed in the language preferred by the participants (LaVange et al. 2010).

Analytic Sample

Among the 9835 women in HCHS/SOL aged 18–74 years, 8291 indicated they had previously been pregnant with at least one live birth. Outliers with more than 12 births (N = 29) were excluded. Women reporting a history of GDM had an age range of 20–73 years (Mean=39.1, 95% CI=37.8, 41.6) and the sample of women without a history of GDM was restricted to this age range to equate the age variability between the two groups. Women without a history of GDM outside of the age group 20–73 years were excluded (N=73). The analytic sample comprised 8262 women, 305 with a history of GDM, and 7957 without a history of GDM.

Measurement of GDM and clinical characteristics

Standard questionnaires and interviews were used to collect information on history of GDM. Women were asked, “Have you ever been told by a doctor that you have diabetes?” Women who endorsed the question were then asked, “Was this only when you were pregnant?” Only women who endorsed both questions were classified as having a history of GDM. This classification system originates from the Behavioral Risk Factor Surveillance System (BRFSS) (Nelson et al. 2001), and has been used to classify women with a history of GDM

in at least one other major study (Kieffer et al. 2006). High reliability of the overall BRFSS question about diabetes diagnosis has been reported ($\kappa = 0.60\text{--}0.86$) (Centers for Disease Control 2002). Because we sought to examine prevalence of current diabetes as a cardiovascular risk factor, women with current diabetes were not excluded from the present analyses. Notably, some women with a history of GDM who subsequently developed T2DM may have responded “no” to the classification question “was this (diabetes) only when you were pregnant?”, resulting in misclassification as not having had a history of GDM. Thereby, such misclassification may have biased our results towards the null and underpowered our findings.

Body mass index (BMI) was measured as weight (kg) / [height (cm)/100]². Metabolic syndrome (MetS) components were measured as follows: waist circumference (cm) was measured at the uppermost lateral border of the right ilium to the nearest 0.1 cm using measuring tape. Systolic (SBP) (mmHg) and diastolic blood pressure (DBP) (mmHg) were measured three times in the right arm using an automatic sphygmomanometer after five minutes in the seated position. The average of the three readings was used. Triglycerides (mg/dL), HDL-c (mg/dL) and fasting glucose (mg/dL) were measured from fasting blood samples.

Measurement of metabolic syndrome (MetS) and diabetes

For the subclinical indicator MetS, a dichotomous variable was used based on the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) definition (Grundy 2004). Clinical identification of the MetS was based on meeting any of the three following: waist circumference > 102 cm, triglycerides ≥ 150 mg/dL, HDL-c < 50 mg/dL, systolic/diastolic blood pressure ≥ 130 mmHg/ ≥ 85 mmHg, fasting glucose ≥ 110 mg/dL. Self-reported use of medications (anti-diabetic or hypertensive medications) was used instead of scanned/transcribed medication use.

For diabetes, a dichotomous variable was created based on the American Diabetes Association (ADA) definition in which a diagnosis is made based on meeting any of the following: hemoglobin A1c (HbA1c) is 6.5% or higher, fasting plasma glucose (FPG) is ≥ 126 mg/dL or higher, 2-hour plasma glucose level is ≥ 200 mg/dL or higher during a 75-gram oral glucose tolerance test (OGTT) (ADA 2010).

Measurement of prevalent cardiovascular disease

A digital 12-lead electrocardiogram (ECG) was performed on each participant. Findings were electronically transmitted to a Central ECG Reading Center in Winston-Salem, NC (EPICARE at Wake Forest University School of Medicine). Prior myocardial infarction (MI) was determined based on the Minnesota Code classification system (Prineas et al. 1982). Standard questionnaires and interviews were used to collect self-reported information. Prevalent CHD was a dichotomous variable that combined ECG reports of prior MI and self-reported heart attack and coronary procedures including angioplasty, stent, and bypass surgery to arteries of the heart. Prevalent CHD was also examined as an additional dichotomous variable that also combined ECG reports of prior MI and self-reported heart attack and procedures, and included self-reported angina. Prevalent cerebrovascular disease

was represented as a dichotomous variable that combined information on stroke, transient ischemic attack (TIA), and cerebrovascular procedures including balloon angioplasty or surgery to arteries of the neck.

Measurement of demographic characteristics

Standard questionnaires and interviews were used to collect the following information: age; age at GDM; Hispanic/Latino background group (characterized as Central American, Cuban, Dominican, Mexican, Puerto Rican, South American origin, and other, including more than two background groups); annual household income (measured as > \$30,000 or \$30,000); educational attainment (< high school, high school/GED, high school); birth place (born within the U.S. states or foreign born); Spanish or English preference to complete the standardized interview; and current health insurance status. For foreign-born women, age at immigration and number of years spent residing in the U.S. were collected.

Statistical analyses

To account for HCHS/SOL complex survey design, all analyses were performed using SAS version 9.2 (SAS Institute, Cary, NC) and SAS-callable SUDAAN (version 10.0; Research Triangle Institute, Research Triangle Park, North Carolina) on the overall analytic sample of 8262 women, (305 women with a history of GDM, and the 7957 without indication of a history of GDM). Participants with missing data were excluded from analysis. Of the 8262 participants, the number of missing data ranged from 24–127 (see Table 1 for N's).

Socio-demographic characteristics, cardiovascular risk factors, and cardiovascular disease were compared between the two groups using chi-square or t-tests and estimating 95% confidence intervals (CI). Each CI reported throughout the Results section is a 95% CI. All group comparison estimates except for age, age at immigration, and years in the U.S. were adjusted for age. Logistic regression was used to estimate the odds ratio (OR) for metabolic syndrome, diabetes, prevalent CHD without self-reported angina, prevalent CHD with self-reported angina, and cerebrovascular disease for women with and without a history of GDM. As a measure of model fit, we examined percentage of concordance between observed responses and predicted values (Hosmer & Lemeshow, 2004). Regression analyses were adjusted for age, age at immigration, BMI, health insurance status, annual household income, HCHS/SOL center, and Hispanic/Latino background. Criteria used to identify and include these confounding variables in multivariable models was theoretical and based on consistent, prior findings in the literature of confounding associations between each variable with the outcomes. Interactions were conducted post hoc to examine the effects of 1) multiparity and age on GDM history; 2) obesity and waist girth, and obesity and fasting plasma glucose, on GDM history; and, 3) age and CHD, and age and cerebrovascular disease, on GDM history. These tests were conducted to evaluate the roles of age and obesity in explaining the group differences observed. All continuous variables were centered around their means prior to computing interaction terms.

Results

Socio-demographic characteristics

Annual household income, educational attainment, nativity, and Spanish language interview preference did not differ by history of GDM (Table 1). The majority of both groups had an annual household income below \$30,000. Approximately one third of both groups had an education level below high school, and another third had greater than a high school education. The majority of both groups was foreign-born, with approximately 19 years spent residing in the U.S. Age at immigration among the foreign-born subset was early 20s (mean=23.9 years) for women with a history of GDM compared to late 20s (mean=29.9 years) for women without a history of GDM. Overall, women with a history of GDM reported being diagnosed on average at 30.1 years [95% CI=29.1, 31.1], were younger (39.1 years [95% CI=37.8, 41.6] vs. 45.5 years [95% CI=44.9, 46.1], respectively), and were younger at immigration (for foreign-born women only) than women without a history of GDM. Due to group differences in mean age, all group comparisons were age-adjusted with the exception of age, age at GDM diagnosis, age at immigration, and years spent residing in the U.S. In addition, women with GDM history were more likely to have health insurance (68.1% [95% CI=60.3, 76.0] vs. 54.9% [95% CI=52.8, 57.1], respectively), less likely to have had one birth (7.5% [95% CI=2.3, 12.8] vs. 23.5% [95% CI=22.1, 24.9]), and more likely to have had 3 (32.1% [95% CI=24.3, 39.8] vs. 24.1% [95% CI=22.7, 25.5]) or 4 births (19.2% [95% CI=12.3, 26.3] vs. 11.2% [95% CI=10.1, 12.3]).

Post hoc analysis to examine the role of age in multiparity showed a statistically significant interaction between age and parity in GDM history, $b=-0.00085$, $s.e.=0.00017$, $p<.00001$, suggesting the association between parity and history of GDM differed by age. Prevalence of multiparity was greater among older women (8.9% [95% CI=7.1, 10.2] in the age group 41–50 years; 11.6% [95% CI=9.6, 13.6] in those aged 51–60 years; 21.6% [95% CI=18.2, 25.1] in those aged 61–70 years; 24.8% [95% CI=18.2, 31.3] in those aged 70+ years) than younger women (.8% [95% CI=0, 1.8] aged 20–30 years; 3.9% [95% CI=2.6, 5.1] aged 31–40 years).

The prevalence of GDM was 4.1% [95% CI: 3.5, 4.7] (Table 2). The prevalence of GDM was similar among women of Dominican, Puerto Rican, and Mexican descent: 5.1% [95% CI=2.8, 7.4], 5.0% [95% CI=3.3, 6.7], and 4.8% [95% CI=3.6, 6.0], respectively. When Mexicans were used as the referent group for pairwise comparisons, women of Central American (2.5% [95% CI=1.3, 3.7]), Cuban (1.8%, 95% CI=.4, 3.1), and South American (1.8% [95% CI=.5, 3.1]) descent had significantly lower relative prevalences of GDM. The same pattern of group differences held when Puerto Ricans were used as the referent group.

Cardiovascular risk factors and disease

Women with a history of GDM had significantly greater BMI (Mean=32.1 kg/m² [95% CI=31.1, 32.9] vs. Mean=30.3 kg/m² [95% CI=30.1, 30.5], respectively) and greater overall prevalence of metabolic syndrome than women without a history of GDM (56.9% [95% CI=48.7, 65.2] vs. 41.7% [95% CI=40.1, 43.5], respectively); however, not all metabolic syndrome components were elevated in women with GDM history (Table 3). Waist

circumference (Mean=102.3 cm [95% CI=100.2, 104.3], vs. Mean=98.1 cm [95% CI=97.4, 98.5], respectively) and fasting glucose (Mean=116.0 mg/dL [95% CI=107.8, 124.8] vs. Mean=104.2 mg/dL [95% CI=103.4, 105.6], respectively) were elevated. Post hoc analysis to examine the role of weight in waist circumference and fasting glucose showed a statistically significant interaction only between BMI and waist girth in history of GDM history, $b=-0.000041$, $s.e.=0.000021$ $p=0.05$, suggesting the association between waist girth and history of GDM depended on levels of BMI. After controlling for variance due to age and BMI, group differences in waist circumference were non-significant (Mean=99.4 mg/dL [95% CI=99.2, 99.7] in women without a history of GDM vs. Mean=98.4 mg/dL [95% CI=97.5, 99.2] in women with a history of GDM).

Variables included in the logistic regression models were age, age at immigration, BMI, health insurance status, household income, HCHS/SOL center, Hispanic/Latino background, and history of GDM status. Outcomes were metabolic syndrome, diabetes, coronary heart disease, coronary heart disease including self-reported angina, and cerebrovascular disease. In our logistic regression models, the percentage of concordance ranged from 72.3–76.5%, supporting overall model fit. In multiple logistic regressions (Table 4), women with a history of GDM were more likely to meet the criteria for metabolic syndrome (56.9%) than women without a history of GDM (41.7%), $OR=1.6$ [95% CI=1.1–2.4]. Women with a history of GDM were also more likely to meet criteria for diabetes (35.4%) than women without a history of GDM (20.2%), $OR=3.7$ [95% CI=2.4–5.5]. No difference was observed between women with and without a history of GDM in meeting the criteria for prevalent CHD without self-reported angina ($OR=1.2$ [95% CI=0.5, 2.6]) or prevalent CHD with self-reported angina ($OR=1.6$ [95% CI=0.8, 2.8]). The number of cases of cerebrovascular disease was low in our sample of women with a history of GDM (less than 20 cases). Thus, cerebrovascular disease was not examined as an outcome in logistic regression models due to risk of model overfitting and unreliable estimates given the few cases of cerebrovascular disease relative to a large number of covariates and predictors (Babayak 2004). Post hoc analysis to examine the role of age in CHD and cerebrovascular disease prevalence showed a statistically significant interaction only between age and cerebrovascular disease in history of GDM, $b=0.103$, $s.e.=0.045$, $p=0.021$, suggesting the association between cerebrovascular disease and GDM history may depend on age. Women in older age groups had higher rates of cerebrovascular disease (3.3% [95% CI=2.4, 4.3] in those aged 51–60 years; 7.2% [95% CI=4.6, 9.8] in those aged 61–70 years; 5.0% [95% CI=1.8, 8.2] in those aged 71+ years) than women in younger age groups (0.9% [95% CI=.1, 1.8] in those aged 20–30 years; 0.6% [95% CI=.1, 1.5] in those aged 31–40 years; and 1.9% [95% CI=1.2, 2.6] in those aged 41–50 years).

Discussion

Women with a history of GDM were younger, more likely to have health insurance currently, and had greater average parity (more likely to have 3 and 4 births) compared to women without a history of GDM. Differences were observed in the prevalence of GDM by Hispanic/Latino heritage group. Age-adjusted group differences emerged on some, but not all, cardiovascular risk factors, and prevalences of coronary heart disease and cerebrovascular disease were similar between groups.

Socio-demographic characteristics

Women with a history of GDM were younger than women without a history of GDM, and mean age group differences may be attributed to several factors. First, younger average age in the group with a history of GDM parallels the recent U.S. trend of a greater increase in prevalence of GDM in younger women (<35 years of age), which has been posited to be fueled by the U.S. obesity epidemic (Lawrence et al. 2008). However, we were unable to examine the trend of a greater increase of GDM in younger women over time because the data were cross-sectional. Second, older women with a history of GDM may not have endorsed a history of GDM because they were never screened for GDM or because of variation in screening approaches across U.S. providers and across other countries (1-hour OGTT; 2-hour OGTT; HbA1c level) (Jiwani et al. 2012), which may be relevant for older women who migrated to the U.S. Little published data are available on secular trends in GDM screening in Latin America; however, U.S. secular trends may play a role in that routine screening for GDM was not recommended by the U.S. Preventive Services Task Force until 2014 (for asymptomatic pregnant women after 24 weeks of gestation) (Moyer 2014). Such misclassification would have biased results toward the null, particularly for diagnoses that present at older ages, such as cardiovascular disease. Third, the mean age difference between groups may be related to immigration-related group differences. Foreign-born women constituted the majority of our sample (84%), and women with a history of GDM migrated to the U.S. at a younger average age (early 20s) than women without a history of GDM (late 20s). Greater duration of residence in the U.S. has been related to increased risk of developing type 2 diabetes mellitus for immigrants who migrate to the U.S. at younger than at older ages (Oza-Frank 2011). Whether age at migration has an unfavorable relation to GDM might be considered in future research. It is also possible that recall bias existed such that older women may have been more likely to forget a GDM diagnosis during pregnancy.

Beyond group differences in average age, women with a history of GDM were more likely to have current health care coverage. It may be that having insurance allowed women to be screened and diagnosed with GDM during prenatal care. Alternatively, some women who did not report a history of GDM may have had undiagnosed GDM because they did not have access to health care and were not screened during pregnancy. Younger women may have also been more likely to be diagnosed with GDM because of changes in criteria for GDM. In addition, women with a history of GDM were less likely to have had one birth (primiparous) and more likely to have had 3 or 4 births (multiparous). A greater prevalence of multiparity was observed with increasing age, and group differences in parity may be related to maternal age (Fowler-Brown et al. 2010). Greater parity is also associated with adverse maternal complications and considered a risk factor for type 2 diabetes for women with histories of GDM (Cure et al. 2015; Almahmeed et al., 2017). A separate analysis of HCHS/SOL participants found higher parity (> 5 births) was associated with metabolic dysregulation, specifically low high-density lipoprotein cholesterol and elevated fasting glucose (Vladutiu et al. 2016). Future work may examine relations between multiparity, metabolic dysregulation, and cardiovascular disease in U.S. Hispanic/Latinas.

Lower prevalence of GDM was observed in South Americans, Cubans, and Central Americans, and relatively higher prevalence was observed in Mexicans, Puerto Ricans, and Dominicans. The pattern of differences by Hispanic/Latina background group aligned with prior HCHS/SOL findings that the prevalence of diabetes varied from 10.2% in South Americans (9.8% in women), 13.4% in Cubans (13.5% in women), 17.7% in Central Americans (18.5% in women), 18.1% in Dominicans and Puerto Ricans (18.2% and 19.5% in women, respectively), and 18.3% in Mexicans (17.9% in women) ($p < 0.0001$) (Schneiderman et al. 2014). Given that transcription factor 7-like-2 (TCF7L2) is associated with GDM and is highly prevalent in Mexican-American women (Watanabe et al. 2007), it was not surprising that we observed a high prevalence of history of GDM among the Mexican-American women in our sample. Present and prior HCHS/SOL findings emphasize a need to consider Hispanic/Latina background in the detection and treatment of diabetes, including GDM. Latinas from Mexican, Puerto Rican, and Dominican descent may be particularly important target groups. Several interventions exist to improve the health of Hispanic/Latina women with a history of GDM (Dulce Mothers; PREVENT-DM; STAR MAMA); however, these interventions have primarily recruited samples of majority Mexican descent (Handley et al. 2016; Perez et al. 2015; Philis-Tsimikas et al. 2014). Future interventions may benefit from specifying Hispanic/Latina background, with particular attention to those of Dominican and Puerto Rican backgrounds.

Cardiovascular risk factors and disease

Prior work using samples of women with a history of GDM indicated greater rates of both overall metabolic syndrome and each of its components in women with a history of GDM than in women without a history of GDM (Clausen et al. 2009; Poola-Kella et al. 2017). Yet, most metabolic syndrome components were not elevated among women with a history of GDM in our sample. Rather, only two components were elevated while controlling for age: waist circumference and fasting glucose. Post hoc analyses suggested that the relationship between waist circumference and history of GDM was dependent on obesity. Obesity may moderate the relation between history of GDM and waist circumference. Glycemic control and obesity reduction and prevention are important intervention targets in this population.

Certain cardiometabolic risk factors may be relatively weaker predictors of cardiovascular disease. Prior findings in diabetic samples have shown glycemia to be a weaker predictor of incident cardiovascular disease, relative to dyslipidemia and hypertension (The Emerging Risk Factors Collaboration 2014; Sattar 2013; Sullivan et al. 2012). Present and prior HCHS/SOL findings suggest major cardiometabolic factors are not equally related to metabolic risk. In the present study, women with a history of GDM had elevated fasting glucose, and did not have elevated triglycerides or blood pressure compared with women without GDM history.

Prior HCHS/SOL work found high waist girth to be a more salient contributor to the metabolic syndrome than impaired lipid metabolism or blood pressure, suggesting that more women in the HCHS/SOL met criteria for metabolic syndrome because of high waist circumference than due to abnormal lipid levels or hypertension (Heiss et al. 2014). Another HCHS/SOL analysis of metabolic syndrome components showed HDL cholesterol is poor at

differentiating between Hispanics/Latinos with and without metabolic syndrome, indicating that HDL-c may also not be a salient component of the metabolic syndrome in U.S. Hispanics/Latinos (Arguelles et al. 2015). Similar to triglyceride and hypertension levels, HDL-c did not differ by history of GDM in the present analyses. Taken together, findings from the present study and prior findings with the HCHS/SOL cohort indicate that hyperlipidemia, hypertension, and low HDL cholesterol are not necessarily present among U.S. Hispanics/Latinos at the rate that might be expected given the high rates of metabolic syndrome and diabetes in this population. Future work might seek to understand the extent to which pattern of elevated cardiometabolic risk factors (including hyperglycemia, dyslipidemia, hypertension, waist circumference, HDL-c) is predictive of cardiovascular disease incidence in Hispanics/Latinas with a history of GDM.

Obesity, metabolic syndrome, and diabetes are known risk factors for cardiovascular disease in women with a history of GDM in the decade after GDM-complicating pregnancy (Berggren et al. 2012; Shah et al. 2008; Sullivan et al. 2012). In our study, women with a history of GDM had approximately three-fold greater prevalence of diabetes than women without a history of GDM; yet no difference emerged in prevalences of CHD or cerebrovascular disease. This finding appears to support the Hispanic paradox of lower-than-expected rates of CVD despite increased risk for CVD. Prior HCHS/SOL findings on cardiometabolic health have also found lower than expected rates of cardiovascular disease. In the full group of HCHS/SOL women, only 2.4% were found to have had prevalent CHD (not including angina) and only 1.2% stroke (Daviglius et al. 2014; Gonzalez et al. 2016). The same study showed that CHD and stroke were more prevalent (to 4.5% CHD & 2.0% stroke) as age increased to 45+ years. The present sample of women with a history of GDM had a mean age of 39.1 [95% CI=37.8, 41.6] years and may be characterized as a young sample. Post hoc analyses indicated that women in older age groups had higher rates of cerebrovascular disease than women in younger age groups. It is possible that the observed lack of differences and low overall rates of CVD represent a limited length of follow-up with a relatively young sample, rather than evidence in support of the Hispanic paradox. In addition to annual follow-up with HCHS/SOL participants, the second clinic visit of HCHS/SOL is underway, and the longitudinal analysis may help elucidate the existence of paradoxical effects of CVD in women with a history of GDM over time as more events are likely to occur as the sample of women ages.

Limitations

The present study had several limitations. First, a history of GDM was determined by self-reported prior diagnosis by a clinician during pregnancy. It is possible that a positive diagnosis of GDM was not ascertained by the same GDM screening tool for all women included in our sample. Women with GDM history may have subsequently developed T2DM and responded “no” to the classification question “was this (diabetes) only when you were pregnant?”, resulting in misclassification as not having had a history of GDM, thus biasing our results towards the null. The low prevalence of CVD in the baseline HCHS/SOL cohort is another limitation that may have affected our ability to detect a relation between GDM history and CVD. The present study was not limited to women with singleton births and the rate of GDM recurrence were not included in our data; however, the question was

asked such that the woman provided her age at the time of her first GDM pregnancy regardless of reoccurrence. Also, although GDM happened before our outcomes and was assessed retrospectively, the data were cross-sectional which does not allow for causal inference. We did not have information on pre-pregnancy, pregnancy, or post-pregnancy clinical characteristics (for example, we did not have information on women who also had hypertension during pregnancy). Rather, the data were clinical characteristics at an average of 9 years after diagnosis of GDM. We were unable to examine potential misclassification of GDM diagnosis in older women, and to determine whether pregnancy occurred prior to or after immigration to the U.S. for all foreign-born women. Due to the cross-sectional nature of our data, we were also unable to delineate the temporal relations and thus potentially causal roles of lifestyle variables, including diet and physical activity, to disease. A second in-person examination of the HCHS/SOL cohort is ongoing and will address these limitations and provide additional information for women who have become pregnant since the baseline HCHS/SOL visit.

Conclusions

A history of GDM was associated with metabolic syndrome and diabetes. Women with a history of GDM should be targeted for management of cardiometabolic health and diabetes risk reduction. Despite a history of GDM, the prevalence of cardiovascular disease was low and similar to women without a history of GDM. Findings may be a function of younger average age of women with a history of GDM.

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Table 1.
Socio-demographic characteristics in women with and without a history of gestational diabetes mellitus (GDM)

	No history of GDM (N=7957)		History of GDM (N=305)	
	N	Mean or percentage ^a	Mean or percentage ^a	95% CI
Age ***	8262	45.4	39.1	37.8, 41.6
Age at GDM	305	--	30.1	29.1, 31.1
Annual household income	8262			
> \$30 000	5708	67.7%	73.7%	66.7, 80.8
\$30 000	2030	25.6%	19.6%	13.2, 26.1
missing/NR	524	6.7%	6.6%	3.1, 10.2
Educational attainment	8238			
< High school	3400	36.5%	38.4%	29.8, 46.9
High school/GED	1939	25.8%	24.0%	17.0, 31.0
High school	2899	37.5%	36.9%	29.1, 44.7
Foreign born	8249	84.7%	84.4%	77.7, 91.1
Age at immigration **	7189	29.9	23.9	22.7, 25.2
Years in the US	7189	19.9	19.5	18.3, 20.9
Spanish language	8262	81.1%	79.1%	71.7, 86.4
Healthcare coverage ***	8135	54.9%	68.1%	60.3, 76.0
Parity (no. live births)	8262			
1 ***	1426	23.5%	7.5%	2.3, 12.8
2	2438	31.7%	30.1%	22.5, 38.7
3 **	2237	24.1%	32.1%	24.3, 39.8
4 ***	1107	11.2%	19.2%	12.3, 26.3
5+	1054	9.4%	10.4%	6.9, 13.8

^a All estimates are weighted and age adjusted. Age, age at immigration, and years in the US were not age adjusted.

* p<0.05

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p<0.001 indicates mean or percentage that is significantly different between women with a history of GDM and without a history of GDM.
Note. Row sample sizes may vary because complete case data was used for estimation of means/percentages.

Table 2. Unadjusted prevalence of history of gestational diabetes mellitus by Hispanic/Latina background.

	<i>N</i>	% ^a	95% CI
Overall	305	4.1	3.5, 4.7
Central American ^{**}	25	2.5	1.3, 3.7
Cuban ^{***}	20	1.8	0.4, 3.1
Dominican ^R	36	5.1	2.8, 7.4
Mexican	151	4.8	3.6, 6.0
Puerto Rican	55	5.0	3.3, 6.7
South American ^{**}	10	1.8	0.5, 3.1
More than one heritage/other/missing	8	2.4	0.3, 5.1

^a All estimates are weighted.
*R*_i indicates referent group for pairwise contrasts.
* p<0.05
** p<0.01
*** p<0.001 indicates simple contrast that is significantly different from referent group.

Table 3.
Cardiovascular risk factors and disease in women with and without a history of gestational diabetes (GDM)

	No history of GDM (N=7957)		History of GDM (N=305)	
	Mean or Percentage ^a	95% CI	Mean or Percentage ^a	95% CI
BMI (kg/m ²) ***	30.3	30.1, 30.5	32.1	31.1, 32.9
Metabolic Syndrome components				
Waist circumference (cm) ***	98.1	97.4, 98.5	102.3	100.2, 104.3
Systolic Blood Pressure (mmHg)	121.4	120.8, 121.9	121.3	118.9, 123.5
Diastolic Blood Pressure (mmHg)	72.5	72.1, 72.9	72.5	70.9, 74.0
Triglycerides (mg/dL)	139.1	136.6, 141.6	147.6	130.2, 165.2
High Density Lipoprotein-c (mg/dL)	52.1	51.7, 52.6	50.1	47.6, 52.5
Fasting glucose (mg/dL) ***	104.2	103.4, 105.1	116.0	107.8, 124.3
Metabolic syndrome ***	41.7%	40.1%, 43.5%	56.9%	48.7%, 65.2%
Diabetes ***	20.2%	19.1%, 21.5%	35.4%	29.2%, 41.7%
Coronary Heart Disease	4.5%	3.9%, 5.2%	9.2%	3.8%, 14.6%
Coronary Heart Disease including self-reported angina	6.7%	5.9%, 7.5%	12.9%	7.1%, 18.7%
Cerebrovascular disease	3.1%	2.5%, 3.6%	5.0%	3.7%, 9.6%

^a All estimates are weighted and age adjusted.

* p<0.05

** p<0.01

*** p<0.001 indicates mean or percentage that is significantly different between women with a history of GDM and without a history of GDM.

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Table 4.

Results^a of multiple logistic regression modeling comparing diseases diagnosed in women with and without a history of gestational diabetes mellitus (GDM)

	Odds Ratio ^a	95% CI
Metabolic syndrome *	1.6	1.1, 2.4
Diabetes ***	3.7	2.4, 5.5
Coronary heart disease	1.2	0.5, 2.6
Coronary heart disease including self-reported angina	1.6	0.8, 2.8

^a Variables included in the modeling are: age, age at immigration, body mass index, health insurance status, income, HCHS/SOL center, and Hispanic/Latino background.

* p<0.05.

*** p<0.001.