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RESEARCH ARTICLE

Type 2 diabetes after gestational diabetes mellitus in South Asian women in the United States

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Abstract

Aims: Gestational diabetes mellitus (GDM) is a major risk factor for type 2 diabetes. The incidence of both GDM and type 2 diabetes is exceedingly high in South Asian populations. However, the risk of type 2 diabetes after GDM in South Asian women in the United States is unknown.

Methods: South Asians aged 40 to 84 years without known cardiovascular disease were enrolled in a community-based cohort called Mediators of Atherosclerosis in South Asians Living in America study. A history of GDM was elicited through self-report, and type 2 diabetes was ascertained by an oral glucose tolerance test. We performed a multivariable logistic regression analysis to examine the odds of type 2 diabetes after GDM history in this cross-sectional analysis.

Results: About 9.7% of women in the Mediators of Atherosclerosis in South Asians Living in America study self-reported a history of GDM, and were significantly younger, with higher mean diastolic blood pressure and self-reported weight at age 20 and 40 years than women without a history of GDM. In a model adjusted for age, weight at age 40, family history of diabetes, education, income, physical activity, caloric intake, alcohol use, and cigarette smoking, women with a history of GDM had increased odds of having type 2 diabetes compared with women without GDM (OR 3.2; 95% CI 1.3, 7.5).

Conclusions: A history of GDM further increases the risk of type 2 diabetes in US South Asian women. Our findings underscore the importance of early postpartum screening in a population at high risk for type 2 diabetes.

KEYWORDS

Asian diabetes, GDM, prevention, type 2 diabetes

1 | INTRODUCTION

Gestational diabetes mellitus (GDM) affects approximately 8% of pregnancies in the United States, and its incidence is increasing.[1] The prevalence of GDM has been observed to be much higher in certain racial and ethnic minority populations,[1,2] where it can reach up to 14%. As the population of the United States continues to become more racially and ethnically diverse, awareness of this increased risk is highly relevant.[3] South Asians are at particularly high risk for this complication of pregnancy, despite relatively low body mass index (BMI) and independent of other important risk factors such as maternal age.[4,5]

The GDM is a well-established and major risk factor for the subsequent development of type 2 diabetes. Women with a pregnancy complicated by GDM have a 7-fold increased risk of developing type 2 diabetes.[6] This risk is affected by underlying and persistent insulin resistance after GDM[7] and by factors such as obesity, a sedentary lifestyle, and poor nutrition. South Asians in the United States are at higher risk for type 2 diabetes than many other racial or ethnic groups[8] and have unique risks for type 2 diabetes that are both intrinsic and environmental. In the Mediators of Atherosclerosis in South Asians Living in America (MASALA) study, the adjusted diabetes prevalence in South Asian women in the United States was 22%.[8] The elevated risk of GDM among South Asian women compounds their preexisting increased risk for type 2 diabetes; however, the extent of this excess risk in the United States is unknown.[9]

In this investigation, we aimed to be the first to characterize the prevalence of type 2 diabetes in women with a previous pregnancy complicated by GDM in MASALA, a cohort of South Asians in the United States.

2 | METHODS

We conducted a cross-sectional investigation of 906 South Asians who participated in the MASALA community-based cohort study. The detailed methods have been described elsewhere.[8] Briefly, MASALA is a prospective cohort study in which we enrolled community-dwelling individuals living in the San Francisco Bay and the greater Chicago areas from 2010 to 2013. Participants, self-identified as having South Asian ancestry, were aged 40 to 84 years and had no known CVD. Those on nitroglycerin, with active cancer, impaired cognitive ability, a life expectancy less than 5 years, who lived in a nursing home, or had plans to relocate were excluded. The University of California, San Francisco and Northwestern University institutional review boards approved the study protocol, and all study participants provided written informed consent. Over 30 months of recruitment, 906 participants were enrolled in the MASALA study.[8]

Each participant underwent in-person interviews to determine age, sex, smoking status, and medical history, including a self-reported history of GDM determined by the following questions: "Has a doctor ever told you that you have any of the following: diabetes (sugar in blood)?" and "For Women Only: did diabetes occur ONLY during pregnancy?" All visits were conducted by trained bilingual study staff, and all consent forms were translated into Hindi and Urdu. We gathered information on participant demographic data, tobacco use, alcohol consumption, and medication use. We also asked about the estimated weight of each participant at age 20 and 40 years. Food group intake was collected with the Study of Health Assessment and Risk in Ethnic groups South Asian FFQ, which was developed and validated in South Asians in Canada.[10] We previously determined prevalent dietary patterns using principal components analysis.[11] Intentional exercise in metabolic equivalent task-minutes per week was assessed with the use of the Typical Week's Physical Activity Questionnaire.[12]

Participant weight was determined with the use of a digital scale, height with a stadiometer, and waist circumference with the use of a measuring tape halfway between the lower ribs and the anterior superior iliac spine, at the site of greatest circumference. Seated resting blood pressure was measured 3 times with the use of an automated blood pressure monitor (V100 Vital Signs Monitor, GE Healthcare) taking the mean of the last 2 readings for analysis. Hypertension was defined as self-reported treatment for hypertension or a systolic blood pressure >140 mm Hg or diastolic blood pressure >90 mm Hg. Blood samples were obtained after a requested 12-hour fast. Fasting plasma glucose was measured with the use of a glucose oxidase method (Ortho Clinical Diagnostics, Johnson & Johnson), and fasting serum insulin was measured by the sandwich immunoassay method (Roche Elecsys 2010, Roche Diagnostics). Diabetes was classified if a participant was using a glucose-lowering medication or had a fasting plasma glucose of at least 126 mg/dL.

Plasma concentrations of total cholesterol, high-density lipoprotein cholesterol, and triglycerides were measured with the use of enzymatic methods (Quest), and low-density lipoprotein cholesterol was calculated with the use of the Friedewald formula.[13] An oral glucose tolerance test was performed in which participants consumed a 75-g oral glucose solution, and blood samples for plasma glucose and insulin were taken after 120 minutes. An assessment of insulin resistance, homeostatic model assessment-insulin resistance, was calculated as [Glucose (mmol/L) 3 Insulin (uIU/mL)/22.5].[14] Values are presented in the text and tables as means and odds ratios (ORs) (95% CIs).

2.1 | Statistical analyses

Basic demographic and metabolic characteristics at baseline were compared between women with a self-reported history of GDM and those without a history of GDM. We used independent *t* tests, Wilcoxon Rank Sum, Fisher exact tests, and chi-square measures to compare baseline characteristics of women with a reported history of GDM and those without. Separate multivariate logistic regression models were used to assess the association between prevalent type 2 diabetes (outcome) and a self-reported history of GDM (exposure). Variables that were found to be significant at a probability value of ≤.05 in either the bivariate or multivariate analyses were included in the final multivariate models, in addition to known risk factors for diabetes (family history of diabetes, income, education, exercise, and caloric intake). Data analyses were completed with SAS (version 9.3; SAS Institute, Research Triangle Park, North Carolina) and STATA software (version 11, College Station, Texas).

3 | RESULTS

A total of 414 women in the MASALA cohort had available data on GDM history. Among the women analyzed, 9.7% self-reported a history of GDM. Although women with a history of GDM were significantly younger than women without GDM, women with a history of GDM had a higher prevalence of type 2 diabetes, mean diastolic blood pressure, and self-reported weight at age 20 and 40 years. Women with a history of GDM were also indistinguishable from their non-GDM counterparts in BMI, waist circumference, cholesterol levels, physical activity, dietary patterns, family income, and education levels (Table 1).

In unadjusted models, women with GDM had increased odds of having type 2 diabetes compared with women without GDM (OR 2.4; 95% CI 1.1, 5.2). With adjustment for age and weight at age 40 years, women with a history of GDM had over 3 times the odds of having diabetes (OR 3.3; 95% CI 1.4, 7.8) (Table 2) as women without a history of GDM. This association held after additional adjustment for known risk factors for diabetes: family history of diabetes, caloric intake, exercise, alcohol use, tobacco use, income, and education (OR 3.2; 95% CI 1.3, 7.5). Fasting glucose was significantly higher amongst women with a history of GDM in all models ($P < .01$). We found no association between a history of GDM and subsequent prediabetes or homeostatic model assessment-insulin resistance (Table 2). As a sensitivity analysis, we restricted the cohort to women who had ever had a pregnancy (excluding n = 25 women), and the results were not significantly different.

4 | DISCUSSION

In the MASALA cohort, South Asian women in the United States with a self-reported history of past GDM had higher diastolic blood pressure

TABLE 1 Baseline characteristics of women in Mediators of Atherosclerosis in South Asians Living in America cohort

	Women with history of GDM (N = 40)	Women without history of GDM (N = 374)	*P* value
Age, y	51.1 (7.0)	54.7 (8.7)	0.01
Married, %	80.0	85.6	0.35
Education, %			1.00
<Bachelor's degree	0	2.1	
Bachelor's degree	37.5	38.1	
>Bachelor's degree	62.5	59.8	
Family income, %			0.49
≤$49 999	23.1	14.7	
$50-99 999	15.4	20.3	
$100-199 999	28.2	34.5	
≥$200 000	33.3	30.5	
Parity	2.2 (0.6)	2.1 (0.8)	0.36
Total caloric intake, kCal/d	1563 (384)	1573 (443)	0.89
Years lived in the United States	25.1 (7.7)	26.7 (11.1)	0.22
Medical insurance, %	92.5	90.9	1.00
Alcohol use, 1 + drinks/wk, %	22.5	18.7	0.53
Family history diabetes, %	12.2	6.2	0.04
Weight history, kg			
At age 20 y	51.6 (8.3)	49.1 (7.4)	0.05
At age 40 y	65.1 (11.1)	61.1 (10.0)	0.02
Physical activity (MET-min/wk)	1080.8 (849.3)	1296.7 (1392.8)	0.97
Dietary patterns, % in highest tertile			
Animal protein	26	18	0.40
High fat dairy, sweets	27	30	0.28
Fruits, vegetables	33	30	0.27
Current metabolic health	**Women with history of GDM (N = 40)**	**Women without history of GDM (N = 374)**	***P* value**
Glycemic status, %			0.08
Normal	37.5	49.7	
Prediabetes (IFG)	27.5	30.8	0.68
Diabetes	35.0	19.5	
HOMA-IR	2.67 (1.40)	3.17 (5.06)	0.57
BMI, kg/m^2	26.7 (3.8)	26.0 (4.3)	0.31
Waist circumference, cm	231.6 (21.3)	225.5 (25.9)	0.15
Total cholesterol, mmol/L	5.1 (1.0)	5.0 (0.9)	0.38
LDL cholesterol, mmol/L	3.0 (0.8)	2.9 (0.8)	0.52
HDL cholesterol, mmol/L	1.4 (0.4)	1.4 (0.4)	0.71
Triglycerides, mmol/L	1.4 (0.6)	1.3 (0.6)	0.40
Blood pressure, mm Hg			
Diastolic	72.8 (9.0)	69.5 (9.7)	0.04
Systolic	124.9 (16.5)	122.3 (16.6)	0.35

Abbreviations: BMI, body mass index; GDM, gestational diabetes mellitus; HDL, high-density lipoprotein; HOMA-IR, homeostatic model assessment–insulin resistance; IFG, impaired fasting glucose; LDL, low-density lipoprotein; MET, metabolic equivalent of task.

and self-reported weight at age 20 and 40 years. Women with a history of GDM were found to have a 3-fold increased risk of prevalent type 2 diabetes. This association persisted after adjustment for known diabetes risk factors, as well as age and weight at age 40 years, which were found to be significant confounders.

Gestational diabetes mellitus is a major risk factor for the subsequent development of type 2 diabetes; up to 60% of women with a history of GDM go on to develop type 2 diabetes.[1,6,15] South Asians are at especially high risk for this pregnancy complication. Population-based studies from Canada, New York City, and Australia have all shown a higher relative risk of GDM in minorities, especially South Asians, compared with White women.[16,17] Furthermore, the overall prevalence of type 2 diabetes is increasing in the United States and is highest in certain racial and ethnic minorities.[8,18] The Multi-Ethnic Study of Atherosclerosis and MASALA studies have shown that type 2 diabetes affects 23% of South Asians, significantly more than White,

TABLE 2 Type 2 diabetes in women with vs. without a history of GDM in Mediators of Atherosclerosis in South Asians Living in America cohort

Odds (OR [95% CI])	Unadjusted	Model 1[a]	Model 2[b]
Type 2 diabetes	2.39 [1.10-5.19]	3.30 [1.39-7.84]	3.16 [1.33, 7.46]
Prediabetes	1.18 [0.53, 2.67]	1.31 [0.57, 3.02]	0.81 [0.37, 1.78]
Glycemia (β, *P* value)			
Fasting glucose (mmol/L)	0.50 (0.010)	0.60 (0.00)	0.60 (0.00)
HOMA-IR	−0.50 (0.57)	−0.50 (0.57)	−1.08 (0.20)

Abbreviations: CI, confidence interval; HOMA-IR, homeostatic model assessment–insulin resistance; OR, odds ratio.

[a]Adjusted for age (y) and weight at age 40 (lbs).

[b]Additionally adjusted for exercise (metabolic equivalent task-min/wk), family history of diabetes, smoking history, alcohol use (1 + drinks/wk), caloric intake (kCal/24 hr), income, education.

Chinese-American, Latino, and African-American populations.[8] Additional risk factors for type 2 diabetes include elevated BMI, sedentary lifestyle, poor diet, and endothelial dysfunction. An accumulation of these risk factors, in conjunction with a history of GDM, heightens and accelerates the risk of subsequent type 2 diabetes.

In a systematic review of 20 cohort studies investigating type 2 diabetes after a pregnancy complicated by GDM, Bellamy et al found over a 7-fold increased risk of type 2 diabetes in women with a history of GDM compared with women with a prior normoglycemic pregnancy.[6] While we found that the risk of type 2 diabetes in this South Asian cohort is 3-fold higher in women with a history of GDM in comparison to women with normoglycemic pregnancies, our findings exhibit lower than expected odds of type 2 diabetes after reported GDM in this cross-sectional study in a high-risk population. The prevalence of type 2 diabetes in this population, however, remains exceedingly high. There are similar findings in a prior study comparing progression from GDM to type 2 diabetes in White, Chinese, and South Asian women living in Canada.[9] In this investigation, nearly one-third of South Asian women developed type 2 diabetes in the 10 years after an affected pregnancy, with an OR of 9.6 for the progression to type 2 diabetes after GDM. Despite the high odds, the impact of a positive GDM history was less strong than that observed for non-Hispanic White women, whose odds of progression to type 2 diabetes after a history of GDM[9] was 13.6. A small UK study showed similar trends in progression among South Asians.[19]

Modifiable factors contribute significantly to risk for both GDM and type 2 diabetes and may play a key role in their prevention. The Indian Diabetes Prevention Program showed that either intensive diet and lifestyle intervention or metformin reduces the incidence of type 2 diabetes in individuals at high risk.[20] Dietary patterns have strong associations with GDM[21,22] and type 2 diabetes risk after GDM.[23,24] Previously characterized dietary patterns in participants of the MASALA cohort[11] were not significantly different between those with and without a history of GDM, and adjustment for caloric intake only strengthened the odds of progression to type 2 diabetes after GDM. Maternal pre-pregnancy BMI and abdominal adiposity have been shown to contribute to risk for GDM.[25,26] Similarly, BMI and weight change after a pregnancy complicated by GDM are strongly tied to subsequent type 2 diabetes risk.[6,27,28]

In our analysis, the relationship between history of GDM and development of type 2 diabetes may be affected by several patient and study-level factors and limitations. In this cohort, history of GDM was elicited through self-report and was not able to be validated given elapsed time since the event. Women in this cohort experienced pregnancies both in the United States and in their country of origin, and there may be inaccurate reporting due to recall bias, differing definitions of GDM in countries of origin at the time of diagnosis, underdiagnosis, or misdiagnosis of GDM. Second, a high background rate of type 2 diabetes in South Asians may also contribute to a lower than expected rate of progression from reported GDM to type 2 diabetes in this population. A recent report from Norway shows that South Asian women are more likely to be insulin resistant in early pregnancy (prior to 20 weeks) than White women, and a compensatory increase in beta cell function was significantly lower.[29] In our population, type 2 diabetes may have been diagnosed in early pregnancy, precluding diagnosis of GDM. If made in early pregnancy, the diagnosis may also have been unclear, contributing to an apparent decrease in rate of progression from expected. Third, the wording of the question used to elicit self-report of GDM in the MASALA study: "For Women: Did diabetes occur ONLY during pregnancy?" modeled after the Behavioral Risk Factor Surveillance System, may have precluded some women who had a known history of both GDM and type 2 diabetes from answering yes, thus decreasing the proportion of GDM cases captured. The authors acknowledge that this is a limitation in baseline data collection that may have lead to under-ascertainment of GDM prevalence in our study population. On review of our data, however, there were 11 women who reported both a history of GDM and of type 2 diabetes, suggesting that the wording of the question was not a universal barrier to gathering accurate data on GDM history. Moreover, the prevalence of GDM in our cohort was very similar to the prevalence of GDM in Asian Indians in the United States estimated using other data sources,[4] potentially indicating less under-ascertainment of GDM prevalence in the MASALA study. Lastly, the MASALA cohort enrollment criteria excluded participants with diagnosed CVD. As a prior history of GDM is a risk factor for subsequent CVD,[30,31] this criterion may have preferentially excluded more women with prior GDM from the entire cohort.

This remains the first characterization of type 2 diabetes incidence after a reported history of GDM in a large cohort of South Asian women residing in the United States. Among women with an elevated BMI and fasting glucose in the Diabetes Prevention Program, type 2 diabetes developed at a 48% higher frequency in women with a history of GDM than in women without a history of GDM. In the same study, both intensive lifestyle intervention and metformin drastically reduced

the incidence of type 2 diabetes over 10 years after an affected pregnancy.[32] This highlights the modifiability of type 2 diabetes risk even after a diagnosis of GDM and the prominent role of early postpartum screening and lifestyle alterations to reduce or delay its incidence in South Asian women.

In conclusion, the incidence of type 2 diabetes after GDM in South Asian women living in the United States is significantly higher than for those women without a history of GDM. Attention to this important risk factor in the growing population of South Asians in the United States is critical to aid in efforts at prevention of type 2 diabetes.

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CONFLICT OF INTEREST

All authors have declared that no competing interests exist.

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AUTHOR CONTRIBUTIONS

The roles for each author are as follows. MDG and ROF conceived of the analytic design and performed the analysis; AMK and NRK contributed to the interpretation of the results and reviewed and edited the manuscript; MDG wrote the manuscript; and AMK conceived of the project idea. MDG had primary responsibility for final content. All authors have read and approved the final manuscript.

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