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 GDM7 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 groups8 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 22.5.6 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.
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. 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.

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. We previously determined prevalent dietary patterns using principal components analysis. Intentional exercise in metabolic equivalent task-minutes per week was assessed with the use of the Typical Week’s Physical Activity Questionnaire.

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. 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]. 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 <0.05 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).

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
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. 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. Furthermore, the overall prevalence of type 2 diabetes is increasing in the United States and is highest in certain racial and ethnic minorities. 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 1 Baseline characteristics of women in Mediators of Atherosclerosis in South Asians Living in America cohort

<table>
<thead>
<tr>
<th></th>
<th>Women with history of GDM (N = 40)</th>
<th>Women without history of GDM (N = 374)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>51.1 (7.0)</td>
<td>54.7 (8.7)</td>
<td>0.01</td>
</tr>
<tr>
<td>Married, %</td>
<td>80.0</td>
<td>85.6</td>
<td>0.35</td>
</tr>
<tr>
<td>Education, %</td>
<td></td>
<td></td>
<td>1.00</td>
</tr>
<tr>
<td>&lt;Bachelor’s degree</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bachelor’s degree</td>
<td>37.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt;Bachelor’s degree</td>
<td>62.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family income, %</td>
<td></td>
<td></td>
<td>0.49</td>
</tr>
<tr>
<td>≤$49 999</td>
<td>23.1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$50-99 999</td>
<td>15.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>$100-199 999</td>
<td>28.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥$200 000</td>
<td>33.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parity</td>
<td>2.2 (0.6)</td>
<td>2.1 (0.8)</td>
<td>0.36</td>
</tr>
<tr>
<td>Total caloric intake, kCal/d</td>
<td>1563 (384)</td>
<td>1573 (443)</td>
<td>0.89</td>
</tr>
<tr>
<td>Years lived in the United States</td>
<td>25.1 (7.7)</td>
<td>26.7 (11.1)</td>
<td>0.22</td>
</tr>
<tr>
<td>Medical insurance, %</td>
<td>92.5</td>
<td></td>
<td>1.00</td>
</tr>
<tr>
<td>Alcohol use, 1 + drinks/wk, %</td>
<td>22.5</td>
<td>18.7</td>
<td>0.53</td>
</tr>
<tr>
<td>Family history diabetes, %</td>
<td>12.2</td>
<td>6.2</td>
<td>0.04</td>
</tr>
<tr>
<td>Weight history, kg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>At age 20 y</td>
<td>51.6 (8.3)</td>
<td>49.1 (7.4)</td>
<td>0.05</td>
</tr>
<tr>
<td>At age 40 y</td>
<td>65.1 (11.1)</td>
<td>61.1 (10.0)</td>
<td>0.02</td>
</tr>
<tr>
<td>Physical activity (MET-min/wk)</td>
<td>1080.8 (849.3)</td>
<td>1296.7 (1392.8)</td>
<td>0.97</td>
</tr>
<tr>
<td>Dietary patterns, % in highest tertile</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Animal protein</td>
<td>26</td>
<td>18</td>
<td>0.40</td>
</tr>
<tr>
<td>High fat dairy, sweets</td>
<td>27</td>
<td>30</td>
<td>0.28</td>
</tr>
<tr>
<td>Fruits, vegetables</td>
<td>33</td>
<td>30</td>
<td>0.27</td>
</tr>
<tr>
<td>Current metabolic health</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glycemic status, %</td>
<td></td>
<td></td>
<td>0.08</td>
</tr>
<tr>
<td>Normal</td>
<td>37.5</td>
<td>49.7</td>
<td></td>
</tr>
<tr>
<td>Prediabetes (IFG)</td>
<td>27.5</td>
<td>30.8</td>
<td>0.68</td>
</tr>
<tr>
<td>Diabetes</td>
<td>35.0</td>
<td>19.5</td>
<td></td>
</tr>
<tr>
<td>HOMA-IR</td>
<td>2.67 (1.40)</td>
<td>3.17 (5.06)</td>
<td>0.57</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>26.7 (3.8)</td>
<td>26.0 (4.3)</td>
<td>0.31</td>
</tr>
<tr>
<td>Waist circumference, cm</td>
<td>231.6 (21.3)</td>
<td>225.5 (25.9)</td>
<td>0.15</td>
</tr>
<tr>
<td>Total cholesterol, mmol/L</td>
<td>5.1 (1.0)</td>
<td>5.0 (0.9)</td>
<td>0.38</td>
</tr>
<tr>
<td>LDL cholesterol, mmol/L</td>
<td>3.0 (0.8)</td>
<td>2.9 (0.8)</td>
<td>0.52</td>
</tr>
<tr>
<td>HDL cholesterol, mmol/L</td>
<td>1.4 (0.4)</td>
<td>1.4 (0.4)</td>
<td>0.71</td>
</tr>
<tr>
<td>Triglycerides, mmol/L</td>
<td>1.4 (0.6)</td>
<td>1.3 (0.6)</td>
<td>0.40</td>
</tr>
<tr>
<td>Blood pressure, mm Hg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diastolic</td>
<td>72.8 (9.0)</td>
<td>69.5 (9.7)</td>
<td>0.04</td>
</tr>
<tr>
<td>Systolic</td>
<td>124.9 (16.5)</td>
<td>122.3 (16.6)</td>
<td>0.35</td>
</tr>
</tbody>
</table>

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.
Abbreviations: CI, confidence interval; HOMA reported GDM in this cross
ings exhibit lower than expected odds of type 2 diabetes after
in comparison to women with normoglycemic pregnancies, our find-
South Asian women living in Canada.9 In this investigation, nearly
progression from GDM to type 2 diabetes in White, Chinese, and
exceedingly high. There are similar findings in a prior study comparing
The prevalence of type 2 diabetes in this population, however, remains
the impact of a positive GDM history was less strong than that
progression to type 2 diabetes after GDM. Despite the high odds,
10 years after an affected pregnancy, with an OR of 9.6 for the
to type 2 diabetes after a history of GDM9 was 13.6. A small UK study
and study
[46x626]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

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

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

aAdjusted for age (y) and weight at age 40 (lbs).

bAdditionally 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 find-
ings 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 GDM10 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 GDM21,22 and type 2 diabetes risk after GDM.23,24
Previously characterized dietary patterns in participants of the
MASALA cohort11 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.5,27,28

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 def-
initions of GDM in countries of origin at the time of diagnosis, under-
diagnosis, 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 pro-
gression from expected. Third, the wording of the question used to
elicit self-report of GDM in the MASALA study: “For Women: Did dia-
betes 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 col-
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 diabe-
tes, 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 cri-
terion 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. 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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