CMAJ OPEN

Research

Causes and consequences of gestational diabetes in South Asians living in Canada: results from a prospective cohort study

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Abstract

Background: The reasons for the increased risk of gestational diabetes among South Asian women are not well understood. We sought to identify the determinants of gestational diabetes and its impact on newborn health in a prospective birth cohort of South Asian women and their babies.

Methods: As part of the South Asian Birth Cohort (START) prospective birth cohort study in Ontario, we recruited 1012 South Asian women with singleton pregnancies in the second trimester of pregnancy between July 11, 2011, and Nov. 10, 2015. We collected health information and physical measurements and administered an oral glucose tolerance test. Birth weight and skinfold thickness measurements were obtained from their newborns, and cord blood glucose and insulin levels were measured.

Results: The incidence of gestational diabetes was 36.3% (95% confidence interval [CI] 33.3%–39.3%); the age-standardized rate was 40.7%. Factors associated with gestational diabetes included maternal age (odds ratio [OR] 1.08 [95% CI 1.04–1.12]), family history of diabetes (OR 1.65 [95% CI 1.26–2.17]), prepregnancy weight (OR 1.025 [95% CI 1.01–1.04]) and low diet quality (OR 1.57 [95% CI 1.16–2.12]). Maternal height was protective against gestational diabetes (OR 0.97 [95% CI 0.95–0.99]). The population attributable risk due to prepregnancy body mass index and low diet quality was 37.3%. Compared to newborns of women without gestational diabetes, those of women with gestational diabetes had a significantly higher birth weight (3267 [standard error (SE) 23] g v. 3181 [SE 17] g, $p = 0.005$), greater skinfold thickness (11.7 [SE 0.1] mm v. 11.2 [SE 0.1] mm, $p = 0.007$) and lower insulin sensitivity (glucose/insulin ratio 0.092 [SE 0.009] mmol/pmol v. 0.129 [SE 0.006] mmol/pmol, $p = 0.001$).

Interpretation: The modifiable risk factors of prepregnancy weight and low diet quality accounted for 37% of the population attributable risk of gestational diabetes in our cohort. Intervention studies to lower prepregnancy weight and to prevent gestational diabetes among South Asian women in high-income countries are needed.

The prevalence of gestational diabetes mellitus is growing worldwide. Gestational diabetes increases the risk of large-for-gestational-age newborns, delivery complications and future type 2 diabetes among both the woman and her baby.[1–4]

South Asian migrants to high-income countries including the United Kingdom, United States and Canada have an excess prevalence of abdominal obesity and type 2 diabetes[5–10] and a twofold increased risk of gestational diabetes compared to white people.[11–14] The reasons for the increased risk of gestational diabetes among South Asians are not well understood. Prior analyses of multiethnic cohorts identified advanced maternal age, family history of diabetes, nonwhite ethnicity, maternal overweight or obesity, and cigarette smoking as common predictors of gestational diabetes.[15–17] Among women living in India, increased age, small stature, urban living, a family history of diabetes, parity of 3 or more children and low vitamin B_{12} levels are associated with the increased prevalence of gestational diabetes.[18–20] Specific prevention strategies for this high-risk ethnic group are lacking.[21–24]

Competing interests: None declared.

This article has been peer reviewed.

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***CMAJ Open* 2017. DOI:10.9778/cmajo.20170027**

In this prospective birth cohort study conducted among South Asian women living in Ontario, we sought to determine 1) the maternal factors associated with gestational diabetes and 2) the impact of gestational diabetes on newborn anthropometric characteristics including birth weight, body fat and insulin sensitivity.

Methods

Design and setting

The South Asian Birth Cohort (START) study is a prospective birth cohort study among South Asian women with singleton pregnancies in Ontario.[25] The goal was to recruit about 1000 participants between July 11, 2011, and Nov. 10, 2015. Participants were recruited during the second trimester of pregnancy from Brampton and Mississauga, Ontario by referral from family practitioners and obstetricians who were familiar with the study.

Maternal measurements

Participants who did not have preexisting diabetes underwent a 75-g oral glucose tolerance test. We classified gestational diabetes using the cut-off values derived from the Born in Bradford cohort of South Asian women: a fasting glucose level of 5.2 mmol/L or higher, or a 2-hour postload level of 7.2 mmol/L or higher.[26] These cut-off values were recently shown to be associated with high infant birth weight (> 90th percentile for gestational age) and adiposity (sum of skinfold measurements > 90th percentile for gestational age) in 5408 babies born to South Asian women in the UK.[26] All participants completed health questionnaires including self-reported personal and family medical history, social and cultural questions, physical activity and sedentary behaviours during work and leisure time,[27] and a previously validated ethnicity-specific food frequency questionnaire.[28] We scored diet quality as follows: 1 point was given for consuming more than the study population median of 1) green vegetables, 2) raw vegetables, 3) cooked vegetables and 4) fruits, or less than the study population median of 5) fried foods and 6) meat (Table 1).[25] The score ranged from 0 to 6; diet quality was classified as low (0 or 1), intermediate (2 or 3) or high (4–6).[29] We determined social disadvantage using a previously validated index that includes employment, marital status and income.[30] We used a standardized protocol to measure resting blood pressure with an oscillometric device (OMRON Healthcare), body weight, height, hip circumference and skinfold thickness. We estimated body fat by summing the skinfold thickness values from triceps and subscapular sites.[31] We calculated weight gain during pregnancy by subtracting the prepregnancy weight (self-reported) from the weight immediately before delivery. Participants were considered to have a family history of diabetes if either their mother or father had a history of type 2 diabetes.

Table 1: Foods in low- versus high-quality diet among South Asians in pregnancy[25]

Foods consumed in greater quantity in low-quality diet	Foods consumed in greater quantity in high-quality diet
Meat, meat dishes, processed meats, organ meats, poultry	Vegetables, raw and cooked
Fish, seafood	Legumes (daals)
Rice	Nuts and seeds
Fried foods	Low-fat dairy products (low-fat and fermented)
Refined grains (breads and cereals)	Whole grains (breads and cereals)
Fast foods	Sweets
Eggs	Fruits

Delivery characteristics and newborn measurements

Type, duration and outcomes of labour as well as birth weight were obtained from hospital charts by trained research assistants. Placental weight was determined by reducing the untrimmed complete placenta weight, as measured at delivery, to a trimmed weight.[32] Infants born at 37 weeks' gestation or later were classified as large for gestational age or small for gestational age by gestational age and sex-specific cut-points of 90th percentile or more, and less than 10th percentile, respectively.[33] Trained research assistants measured the newborns' length using an O'Leary length board, head circumference using a nonstretchable measuring tape, and waist and hip circumference using an Ohaus nonstretchable tape with an attached spring balance. The skinfold thickness of triceps and subscapular sites was measured 3 times and was recorded to the nearest millimetre using Holtain calipers (dial graduation 0.2 mm). The intraclass correlation (reliability) for skinfold measurements was 0.98 for subscapular sites and 0.96 for triceps sites.[34] The ponderal index was calculated as birth weight/length^3.[33] These measures were obtained within 24 hours after delivery in 81.0% of newborns and within 25–96 hours after delivery in 7.6%. If no measurements were obtained within 96 hours, the chart recording of measurement was used, if available.

A cord blood sample was collected from the umbilical vein. Within 2 hours, the sample was centrifuged and sample aliquots were frozen at −70°C and shipped for storage in liquid nitrogen at the Clinical Research Laboratory and Biobank, Hamilton Health Sciences. All suitable samples in which 1 serum aliquot was available were analyzed for glucose and insulin. Glucose level was measured with the UniCel DxC 600 Synchron clinical system (Beckman Coulter) with a timed end-point method. Insulin level was measured with the Elecsys 2010 immunoassay analyzer (Roche Diagnostics) by means of an electrochemiluminescence immunoassay. The coefficients of variation for glucose level and insulin level were 24.4% and 84.6%, respectively.

Statistical analysis

We performed statistical analyses using SAS version 9.4 (SAS Institute). We calculated means (and standard deviations [SDs]) and counts to summarize continuous variables and categorical data, respectively, and means (and standard errors [SEs]) for adjusted continuous results. The incidence of gestational diabetes was directly age-standardized to the general Canadian population with the 2011 census population for women aged 20–44 years as the standard population.[35] We assessed the univariate associations between maternal factors and gestational diabetes using the χ^2 test for categorical variables and the Student t test for continuous variables, as appropriate. Factors with a univariate p value of > 0.10 were then considered for a multivariable logistic regression model; for any set of factors that were highly correlated, only 1 factor was included. We used stepwise selection methods to determine the final model. We assessed the univariate associations between newborn anthropometric characteristics and maternal gestational diabetes using analysis of covariance, adjusting for gestational age, infant's sex and maternal insulin use during pregnancy. We estimated population attributable risk using the Interactive Risk Attributable Program (US National Cancer Institute).[36] Population attributable risk is calculated by considering the frequency of the exposure in the population and the relation of the risk factor to disease. In the current study, population attributable risk quantifies the proportion of cases of gestational diabetes that can be prevented if a specific exposure is eliminated from the study population while other exposures are held constant.

Ethics approval

The study was approved by the Hamilton Integrated Research Ethics Board, William Osler Health System and Trillium Health Partners.

Results

Of the 1012 participants with singleton pregnancies enrolled, 4 with a history of diabetes and 2 who withdrew early were excluded from this analysis. Among the remaining 1006 participants, gestational diabetes status was classified according to the result of the oral glucose tolerance test (performed on average at 26.5 [SD 1.6] weeks' gestation) in 945 and as reported on the birth chart in 61. Of the 1006 women, 365 (36.3% [95% confidence interval (CI) 33.3%–39.3%]) were classified as having gestational diabetes; the age-standardized rate was 40.7%.

Among the 1006 cases, sex, gestational age and birth weight were available for 989 newborns (98.3%).

Characteristics of participants with and without gestational diabetes

Compared to the participants without gestational diabetes, those with gestational diabetes were older (mean age 31.2 [SD 4.0]) yr v. 29.7 [SD 3.8]) yr, $p < 0.001$) and were more likely to have a family history of diabetes (191 [52.5%] v. 228 [35.7%], $p < 0.001$), be multiparous (236 [65.7%] v. 343 [54.8%], $p < 0.001$), have a higher prepregnancy weight (mean 64.9 [SD 12.2] kg v. 61.3 [SD 11.8] kg, $p < 0.001$), be shorter (mean height 161.6 [SD 6.2] cm v. 162.5 [SD 6.3] cm, $p = 0.02$), have a higher prepregnancy body mass index (BMI) (mean 24.9 [SD 4.6] v. 23.2 [SD 4.3], $p < 0.001$), have more body fat (mean sum of skinfold measurements 52.3 [SD 12.3] mm v. 47.9 [SD 12.4] mm, $p < 0.001$) and consume a low-quality diet (121 [33.4%] v. 145 [22.9%], $p < 0.001$) (Table 2). There were no differences between the 2 groups in vegetarianism, physical activity in pregnancy or socioeconomic status.

Women with gestational diabetes were more likely than those without gestational diabetes to have had a cesarean delivery (127 [35.2%] v. 177 [27.9%], $p = 0.02$).

Multivariable predictors of gestational diabetes

Factors independently associated with an increased risk of gestational diabetes included maternal age (per 1-yr increase odds ratio [OR] 1.08 [95% CI 1.04–1.12]), family history of diabetes (OR 1.65 [95% CI 1.26–2.17]), prepregnancy weight (per 1-kg increase OR 1.025 [95% CI 1.01–1.04]) and low diet quality (OR 1.57 [95% CI 1.16–2.12]) (data not shown). The only protective factor was maternal height (per 1-cm increase OR 0.97 [95% CI 0.95–0.99]). Using the prevalence rates and ORs of these independent factors, we estimated that they accounted for 65.3% (95% CI 55.6%–75.1%) of the population attributable risk for gestational diabetes (Figure 1, Table 3). The modifiable risk factors of low diet quality and prepregnancy BMI greater than 23 accounted for 37.3% of the population attributable risk (95% CI 25.9–48.7).

Newborn measurements

Of the 989 infants, 58 (5.9%) were delivered before 37 weeks, and 2 (0.2%) were stillborn. Triceps and subscapular skinfold measurements were available for 937 newborns (94.7%); however, in the current analysis, we included only 839 newborns (84.8%) whose measurements were taken within 4 days of birth.

After adjustment for gestational age, newborn sex and maternal use of insulin during the pregnancy, infants of women with gestational diabetes had a higher birth weight 3267 (SE 23) g v. 3181 (SE 17) g, $p = 0.005$), ponderal index (24.8 [SE 0.2] v. 24.0 [SE 0.1], $p = 0.002$) and skinfold thickness (11.7 [SE 0.1] mm v. 11.2 [SE 0.1] mm, $p = 0.007$) than those of women without gestational diabetes (Table 4). A higher proportion of newborns of women with gestational diabetes than those of women without gestational diabetes were large for gestational age (48 [13.8%] v. 55 [9.0%], $p = 0.02$), and placental weight was higher in the former group (503.2 [SE 8.1] g v. 474.9 [SE 5.8] g, $p = 0.007$).

A cord blood sample was collected in 777 cases (77.2%). Glucose and insulin were analyzed in 638/777 samples (82.1%). No difference in glucose level was observed between the 2 groups. The insulin (log) level was higher in the infants of women with gestational diabetes (76.3 [SE 3.8] pmol/L v. 61.6 [SE 2.8]) pmol/L, $p < 0.002$), and the glucose/insulin ratio was significantly lower (0.092 [SE 0.009] mmol/pmol v. 0.129 [SE 0.006] mmol/pmol, $p = 0.001$), indicating reduced insulin sensitivity (Table 4).

Table 2: Characteristics of participants with and without gestational diabetes mellitus*

Characteristic	Mean ± SD†		
	Gestational diabetes‡ *n* = 365	No gestational diabetes *n* = 641	*p* value
Age, yr	31.2 ± 4.0	29.7 ± 3.8	< 0.001
Length of time in Canada, yr	8.8 ± 7.5	8.2 ± 7.9	0.2
Duration of pregnancy at study enrolment, wk	26.8 ± 2.1	26.6 ± 1.6	0.1
Parity, no. (%)			
Primiparous	123 (33.7)	283 (44.1)	< 0.001
Multiparous	236 (64.6)	343 (53.5)	
Unknown	6 (1.6)	15 (2.3)	
Smoked during pregnancy, no. (%)	0 (0.0)	2 (0.3)	0.5
Vegetarian, no. (%)	125 (34.5)	243 (38.1)	0.2
Diet quality score	2.2 ± 1.4	2.5 ± 1.3	0.002
Low diet quality, no. (%)	121 (33.4)	145 (22.9)	< 0.001
Time spent engaged in active sport per wk, h	1.4 ± 2.2	1.6 ± 2.5	0.4
Physical activity in pregnancy, no. (%)			
Sedentary	97 (26.6)	139 (21.7)	0.2
Mild exercise	202 (55.3)	373 (58.2)	
Moderate exercise	64 (17.5)	128 (20.0)	
Unknown	2 (0.5)	1 (0.2)	
Family history of diabetes, no. (%)	191 (52.5)	228 (35.7)	< 0.001
Social disadvantage index, no. (%)			
High	47 (12.9)	90 (14.0)	0.9
Moderate	118 (32.3)	213 (33.2)	
Low	145 (39.7)	251 39.2)	
Unknown	55 (15.1)	87 (13.6)	
Currently employed, no. (%)	196 (54.0)	349 (54.5)	0.9
Annual household income ≥ $50 000, no. (%)	143 (46.0)	242 (43.6)	0.5
High school education, no. (%)	361 (99.4)	638 (99.5)	0.9
Prepregnancy weight, kg	64.9 ± 12.2	61.3 ± 11.8	< 0.001
Height, cm	161.6 ± 6.2	162.5 ± 6.3	0.02
Prepregnancy body mass index	24.9 ± 4.6	23.2 ± 4.3	< 0.001
Sum of skinfold measurements at enrolment, mm	52.3 ± 12.3	47.9 ± 12.4	< 0.001
Triceps skinfold thickness at enrolment, mm	28.5 ± 6.7	26.5 ± 6.8	< 0.001
Subscapular skinfold thickness at enrolment, mm	24.1 ± 6.6	21.5 ± 6.5	< 0.001
Glucose area under the curve, mmol/min	966.8 ± 164.0	722.4 ± 102.5	< 0.001
Weight gain during pregnancy, kg	13.5 ± 7.5	14.7 ± 7.9	0.02
Weight gain during pregnancy/prepregnancy weight	0.22 ± 0.13	0.25 ± 0.15	< 0.001
Cesarean delivery, no. (%)	127 (35.2)	177 (27.9)	0.02

Note: SD = standard deviation.
*Data missing for some variables.
†Except where noted otherwise.
‡Classified with the cut-off values derived from the Born in Bradford cohort.[26] Participants with a history of diabetes were excluded.

Interpretation

South Asian women living in Ontario had a high burden of gestational diabetes compared to the general population, with the disease affecting upward of one-third of our participants. The major determinants of gestational diabetes accounted for 65.3% of the population attributable risk and included non-modifiable factors (age, family history of type 2 diabetes and height) as well as modifiable factors (prepregnancy weight and low diet quality). Furthermore, newborns of dysglycemic mothers had increased birth weight and body fat, and reduced insulin sensitivity, which may be implicated in their future risk of excess adiposity and type 2 diabetes.

The population attributable risk for gestational diabetes due to modifiable risk factors was 37.3%. This suggests that, if South Asian women could achieve an optimal prepregnancy

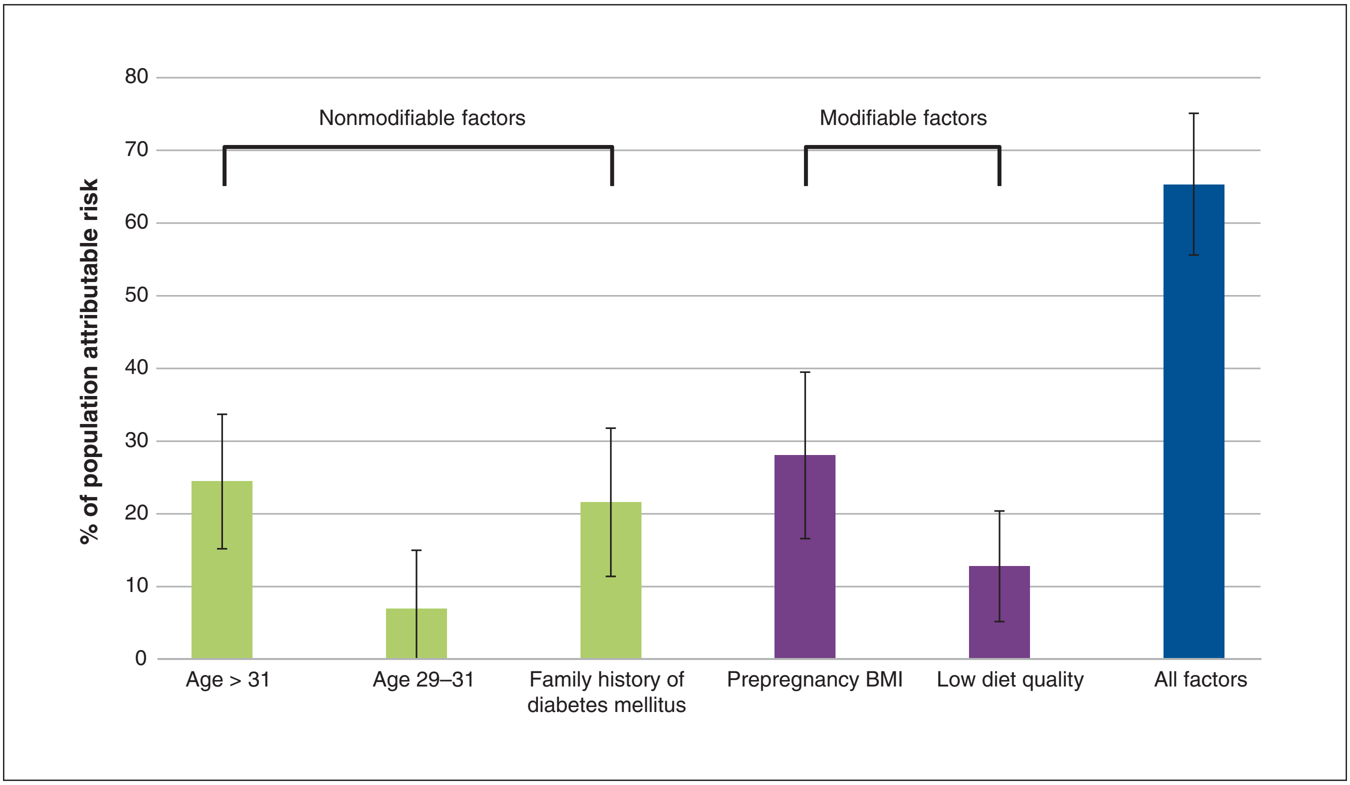

Figure 1: Partial proportional attributable risk for individual risk factors for the development of gestational diabetes mellitus among South Asian women. Error bars represent 95% confidence intervals. Note: BMI = body mass index.

Table 3: Population attributable risk for gestational diabetes

Risk factor	OR (95% CI) from multivariable model	Prevalence, %	Population attributable risk % (95% CI)*
Age 32–43 yr v. < 29 yr	2.10 (1.51 to 2.91)	36.4	24.5 (15.2 to 33.7)
Age 29–31 yr v. < 29 yr	1.34 (0.94 to 1.90)	28.6	7.0 (–1.1 to 15.0)
Family history of diabetes mellitus	1.70 (1.29 to 2.23)	42.1	21.6 (11.4 to 31.8)
Low diet quality	1.62 (1.20 to 2.19)	26.7	12.8 (5.2 to 20.4)
Body mass index > 23 v. ≤ 23	1.80 (1.37 to 2.37)	51.5	28.1 (16.6 to 39.5)
Low diet quality and/or body mass index > 23		63.5	37.3 (25.9 to 48.7)
All factors			65.3 (55.6 to 75.1)

Note: CI = confidence interval, OR = odds ratio.
*Continuous factors needed to be categorized: age was divided into tertiles, and body mass index was split into 3 categories (< 18.5, 18.5–23 and > 23); the highest category was selected as it was significantly different from the lower categories.

Table 4: Newborn characteristics by maternal gestational diabetes status

Characteristic	Mean ± SE*† Gestational diabetes* *n* = 359	Mean ± SE*† No gestational diabetes *n* = 630	*p* value
Male, no. (%)	188 (52.4)	304 (48.2)	
Gestational age, wk	38.8 ± 1.6	39.3 ± 1.4	
Size for gestational age,‡ no. (%)			
Large	48 (13.4)	55 (8.7)	0.02
Average	277 (77.2)	493 (78.2)	
Small	24 (6.7)	64 (10.2)	
Unknown	10 (2.8)	18 (2.8)	
Birth weight, g	3267 ± 23	3181 ± 17	0.005
Length, cm	51.0 ± 0.1	51.1 ± 0.1	0.7
Waist circumference, cm	30.8 ± 0.1	30.3 ± 0.1	0.009
Head circumference, cm	34.1 ± 0.1	34.0 ± 0.1	0.4
Sum of skinfold measurements, mm	11.7 ± 0.1	11.2 ± 0.1	0.007
Triceps skinfold thickness, mm	6.1 ± 0.1	5.9 ± 0.1	0.05
Subscapular skinfold thickness, mm	5.5 ± 0.1	5.2 ± 0.1	0.002
Ponderal index§	24.8 ± 0.2	24.0 ± 0.1	0.002
Placental weight, g	503.2 ± 8.1	474.9 ± 5.8	0.007
Cord blood glucose level, mmol/L	4.1 ± 0.1	4.1 ± 0.0	0.9
Cord blood insulin (log) level, pmol/L	76.3 ± 3.8	61.6 ± 2.8	0.002
Glucose/insulin ratio, mmol/pmol¶	0.092 ± 0.009	0.129 ± 0.006	0.001

Note: SE = standard error.
*Except where noted otherwise.
†Adjusted for gestational age, sex and insulin use by mother during pregnancy.
‡Determined from gestational age and sex-specific percentiles from study data.
§Birth weight (kg)/birth length (m^3).
¶Non log insulin level used.

weight (i.e., BMI < 23) and improve their diet quality, about one-third of cases of gestational diabetes in this population could be prevented. A BMI of 23–25 is often classified as normal prepregnancy weight in white women but likely represents overweight and excess adiposity in South Asian women.[37,38] In our study, women with gestational diabetes had a higher prepregnancy weight (by 3 kg), were shorter (by 1 cm) and had significantly greater body fat than those without gestational diabetes. Prepregnancy BMI was the dominant predictor of gestational diabetes, more so than weight gain during pregnancy, which, as expected, was lower in participants with gestational diabetes than in those without gestational diabetes. This highlights the importance of public health messaging to South Asian women who are contemplating pregnancy to aim for an optimal weight before pregnancy as a prevention strategy against gestational diabetes.[39] To our knowledge, such messaging is not routinely provided by primary care physicians or public health specialists and requires an integrated approach involving primary health care and policy initiatives.[40]

The low-quality diet in the South Asian Birth Cohort (START) study was characterized by higher consumption of meat, rice and fried foods, and was lower in raw or cooked vegetables, whereas a high-quality diet included higher consumption of vegetables, legumes and whole-grain breads.[25] Given that the population attributable risk for gestational diabetes due to low diet quality in our study was 12.8%, a modified diet in which fried foods and meat were replaced with more vegetable protein and raw and cooked vegetables, and refined grains were replaced with whole grains might reduce gestational diabetes in this population by up to 13%. A Cochrane review suggested that dietary interventions are more effective than exercise alone or mixed interventions in preventing gestational diabetes.[41] We identified no randomized trials that aimed to reduce prepregnancy BMI or alter diet quality in pregnancy as a method to prevent gestational diabetes in South Asian women living in high-income countries.

Our observation that a family history of type 2 diabetes is a strong risk factor for gestational diabetes is consistent with prior studies.[15,42–44] Other investigators have hypothesized that women in whom gestational diabetes develops may carry a greater genetic load of variants associated with β-cell dysfunction and insulin resistance, which, in turn, increases their babies' genetic load for these conditions.[45,46] We also observed that maternal hyperglycemia was associated with increased newborn birth weight, more adipose tissue in newborns, a higher proportion of infants who were large for gestational age and a larger placenta. Furthermore, babies of women with gestational diabetes had reduced insulin sensitivity. Chronic exposure of the growing fetus to hyperglycemia may induce changes in the regulation of gene expression, resulting in reduced insulin secretion or action.[47]

Strengths and limitations

Strengths of our study include that it was a large prospective birth cohort study with direct measurement of glycemic status by means of the oral glucose tolerance test. In addition, we directly measured the adiposity of participants and their babies. The study was limited by the fact that our cohort was not a random sample of the population, which may have overestimated the burden of dysglycemia; however, we recruited participants from primary care settings and specialist obstetrical clinics. Furthermore, our dietary questionnaire was self-reported. The lack of random sampling does not affect our association analyses, which remain internally valid, and the food frequency questionnaire is the gold standard of dietary assessment tools.

Conclusion

Gestational diabetes affects up to one-third of South Asian women living in Canada. Modifiable risk factors for this disease include prepregnancy weight and low diet quality. Newborns exposed to the highest maternal glucose levels had increased birth weight, increased body fat and lower insulin sensitivity. Intervention studies to lower prepregnancy weight and to prevent gestational diabetes in this high-risk population are needed.

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Contributors: Sonia Anand conceived the study, and Sonia Anand and Milan Gupta designed the study. Sonia Anand, Milan Gupta, Dipika Desai and Nora Abdalla obtained the data. Karleen Schulze, Mateen Shaikh, Michael Zulyniak and Russell de Souza analyzed the data. Sonia Anand drafted the manuscript. Sonia Anand, Milan Gupta, Koon Teo, Hertzel Gerstein, Karleen Schulze, Dipika Desai, Michael Zulyniak, Russell de Souza, Gita Wahi, Mateen Shaikh, Joseph Beyene, Nora Abdalla and Eileen de Villa contributed to interpreting the data and revising the manuscript critically for important intellectual content. Katherine Morrison contributed to revising the work critically for important intellectual content. Sarah McDonald provided subject matter expertise in gestational diabetes and other obstetrical factors, and contributed to interpreting the data and revising the manuscript critically for important intellectual content. All of the authors approved the final version to be published and agreed to act as guarantors of the work.

Acknowledgements: South Asian Birth Cohort (START) study data were collected as part of a bilateral program funded by the Indian Council of Medical Research/Canadian Institutes of Health Research (grant INC-109205). This study was supported by Heart and Stroke Foundation of Canada grant NA7283. Sonia Anand is supported by a Tier 1 Canada Research Chair in Ethnic Diversity and Cardiovascular Disease, and a Heart and Stroke Foundation/Michael G. DeGroote Chair in Population Health Research at McMaster University. Sarah McDonald is supported by a Tier 2 Canada Research Chair. Hertzel Gerstein is supported by a McMaster–Aventis Population Health Institute Chair in Diabetes Research.

Supplemental information: For reviewer comments and the original submission of this manuscript, please see www.cmajopen.ca/content/5/3/E604/suppl/DC1.