

Contents lists available at [ScienceDirect](https://www.sciencedirect.com)

Canadian Journal of Diabetes

journal homepage:
www.canadianjournalofdiabetes.com


Original Research

Perinatal Outcomes Among Different Asian Groups With Gestational Diabetes Mellitus in Ontario: A Cohort Study



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Key Messages

- Standard birthweight curves underestimate the risk of large-for-gestational-age offspring for Asian women with gestational diabetes mellitus.
- Using ethnicity-specific birthweight curves, large-for-gestational-age offspring risk remains lower only for South Asian women compared with Caucasian women with gestational diabetes mellitus.

ARTICLE INFO

Article history:

Received 22 March 2019

Received in revised form

18 June 2019

Accepted 20 June 2019

Keywords:

Asian ethnicity

birthweight

gestational diabetes

perinatal outcomes

ABSTRACT

Objective: The aim of this study was to determine whether perinatal outcomes differ between Caucasian and Asian subgroups of women with gestational diabetes mellitus (GDM) through use of standard vs ethnicity-specific birthweight curves.

Methods: This retrospective cohort study included 537 women with GDM, within the ethnically diverse province of Ontario, Canada. Study outcomes included large-for-gestational-age (LGA) and small-for-gestational-age (SGA) birthweights in newborns of women from prevalent Asian ethnic groups compared with newborns of Caucasian women. Odds ratios were adjusted for maternal age, parity, prepregnancy body mass index, gestational weight gain and insulin use in pregnancy.

Results: Of the 537 women participating in the study, 228 (35.8%) were Caucasian, 109 (17.1%) South Asian, 141 (22.1%) East Asian and 59 (9.3%) Filipino. Using standard birthweight curves, compared with Caucasian women, the risk of LGA was lower among South Asian (adjusted odds ratio [aOR], 0.065; 95% confidence interval [CI], 0.01 to 0.49) and East Asian (aOR, 0.36; 95% CI, 0.14 to 0.95) women. The aOR for SGA was notably higher among South Asian women (aOR, 2.96; 95% CI, 1.24 to 7.09). Significant effects were not seen among Filipino women. Use of ethnicity-specific birthweight curves largely attenuated these associations, except for LGA in South Asian mothers (aOR, 0.27; 95% CI, 0.09 to 0.81).

Conclusion: South Asian women with GDM are at lower risk of having an LGA newborn, even after accounting for maternal risk factors or the use of an ethnicity-specific birthweight curve.

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<https://doi.org/10.1016/j.jcjd.2019.06.006>

Mots clés:

appartenance à un groupe d'origine ethnique asiatique
poids à la naissance
diabète gestationnel
issues périnatales

R É S U M É

Objectif : Le but de la présente étude était de déterminer si les issues périnatales sont différentes entre les sous-groupes de femmes blanches et de femmes asiatiques ayant un diabète sucré gestationnel (DSG) à l'aide des courbes de poids à la naissance normaux ou spécifiques à l'origine ethnique.

Méthodes : La présente étude de cohorte rétrospective regroupait 537 femmes ayant le DSG, de la province multiethnique de l'Ontario, au Canada. Les résultats de l'étude portaient notamment sur le poids élevé pour l'âge gestationnel (PÉAG) et le faible poids pour l'âge gestationnel (FPAG) à la naissance entre les nouveau-nés des femmes des groupes prévalents d'origine ethnique asiatique et les nouveau-nés des femmes blanches. Les rapports de cotes étaient ajustés à l'âge de la mère, à la parité, à l'indice de masse corporelle avant la grossesse, au gain de poids durant la grossesse et à l'utilisation de l'insuline durant la grossesse.

Résultats : Parmi les 537 femmes qui participaient à l'étude, 228 (35,8 %) étaient des femmes blanches, 109 (17,1 %), des femmes sud-asiatiques, 141 (22,1 %), des femmes est-asiatiques et 59 (9,3 %), des femmes philippines. Selon les courbes de poids normaux à la naissance, le risque de PÉAG était plus faible chez les femmes sud-asiatiques (rapport de cotes ajusté [RCa], 0,065; intervalle de confiance [IC] à 95 %, de 0,01 à 0,49) et les femmes est-asiatiques (RCa, 0,36; IC à 95 %, de 0,14 à 0,95) que chez les femmes blanches. Le RCa des FPAG était notablement plus élevé chez les femmes sud-asiatiques (RCa, 2,96; IC à 95 %, de 1,24 à 7,09). Aucun effet significatif n'a été observé chez les femmes philippines. L'utilisation de courbes de poids à la naissance spécifiques à l'origine ethnique atténuait en grande partie ces associations, excepté le FPAG chez les mères sud-asiatiques (RCa, 0,27; IC à 95 %, de 0,09 à 0,81).

Conclusion : Les femmes sud-asiatiques ayant un DSG sont exposées à un risque plus faible d'avoir des nouveau-nés de FPAG, même si l'on tient compte des facteurs de risque maternels ou de l'utilisation d'une courbe de poids à la naissance spécifique à l'origine ethnique.

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Introduction

Gestational diabetes mellitus (GDM) is a condition of temporary glucose intolerance during pregnancy, and a risk factor for subsequent type 2 diabetes (1,2). GDM is identified and treated in pregnancy to reduce the risk of excess fetal growth (macrosomia or large for gestational age), which serves as a driver for many of the other associated adverse outcomes (3). Fetal overgrowth occurs with increased fetal insulin secretion in the presence of elevated maternal glucose, which can be prevented with tight glycemic control (4).

Although GDM typically only affects around 6% of pregnant women (5), its prevalence is higher in specific non-Caucasian ethnic groups (6–9). In Canada, Asian populations are the most common non-Caucasian ethnic group, and women from Asian countries have much higher rates of GDM compared with the general population (8–11). Data from Ontario indicate that South Asian and Chinese women are at a 7.1% and 6.1% risk of GDM, respectively, compared with 3.3% for the general population (11).

Previous studies have shown that the impact of increased body mass index (BMI) on insulin sensitivity and glycemia is more pronounced in Asian groups (7), which may increase their propensity to develop GDM at a younger age and lower BMI (12,13). Evidence suggests that epigenetic adaptations of fetal pancreatic beta cells in nutrition-poor settings may increase vulnerability to metabolic impairment in adults who are exposed to more nutrient-rich environments (i.e. the “thrifty phenotype” hypothesis) (14). Sociocultural factors may also contribute to these differences. For instance, GDM patients from high-risk ethnic groups underestimated their personal risk of diabetes compared with Caucasian women (15), which may decrease motivation for risk-reducing behaviours. A study of South Asian women with GDM showed that their attitudes toward diabetes and its management were informed by cultural beliefs, which often conflicted with health-care advice (16).

The influence of GDM on outcomes may also differ between Asian and Caucasian women, and across Asian subpopulations. A Canadian study showed that South Asian women with GDM are at higher risk of future type 2 diabetes compared with both Chinese women and the general population (10). In contrast, GDM patients of Chinese and South Asian descent had lower rates of large-for-gestational-age (LGA) offspring (11), and of South Asian women had higher rates of small-for-gestational-age (SGA) offspring, admissions to the neonatal intensive care unit (NICU) and neonatal hypoglycemia. There is also evidence that offspring of Filipino women in general have a higher risk of SGA, prematurity and stillbirth than other East Asian groups (17–20). These findings highlight the importance of studying effects of GDM across specific Asian subpopulations.

Previous studies of birth outcomes in Asian women with GDM used birthweight distribution curves meant for the general Canadian population to estimate LGA and SGA rates, and thus may not be true reflections of LGA and SGA rates for Asian patients. The use of ethnicity-specific birthweight distribution curves has been shown to more accurately estimate LGA and SGA rates for minority populations in Ontario (21–23). Furthermore, it is also known that babies of specific minority ethnicities have lower birthweights compared with the general population (24); thus, standard curves will underestimate LGA rates while overestimating SGA rates. Given that one of the primary goals of treatment in GDM is to prevent macrosomia and LGA, attaining proper data on these outcomes in minority populations with GDM is important to guide more personalized treatment in multiethnic settings.

No study to date has used customized ethnicity-specific birthweight curves to compare the risk of LGA and SGA between offspring of women with GDM from different ethnic backgrounds. The objective of this cohort study was to evaluate differences in birthweight and other perinatal outcomes among different Asian subgroups and Caucasian women with GDM, and to compare risks of LGA and SGA using both standard and customized birthweight distribution curves.

Methods

Study design and data sources

In this retrospective cohort study, we used data from a previously conducted prospective cohort study of 1,347 women with GDM from 2009 to 2013 (25). The original cohort included women diagnosed with GDM after 24 weeks' gestation at 1 of 7 prenatal diabetes clinics across Ontario, Canada. Women were excluded if they did not speak English or had documented prepregnancy diabetes or any major medical or fetal complications that may impact their ability to participate in research. Patients were asked to complete self-administered questionnaires pertaining to their lifestyle and social history during pregnancy and postpartum, and to consent for a medical chart review. The questionnaires were completed either on paper, online or over the telephone. All women attended at least 1 group education class for GDM prior to completing the first survey. The medical chart review collected data from the prenatal diabetes chart and obstetrical delivery records on medical comorbidities, use of medications, parity, gestational weight gain, gestational age at delivery, birthweight, obstetrical and fetal complications and smoking before and during pregnancy. The prenatal questionnaire was completed between 24 and 40 weeks of gestation and included data on age, ethnicity, household income, highest education level and prepregnancy weight and height (25).

Study population

For this study, we included women from the base cohort who completed both the self-administered questionnaire and consented to a medical chart review. As ethnicity and birthweight were both primary variables of interest, patients with these variables missing were excluded. We only included women who reported Caucasian or Asian ethnicity, which was categorized as South Asian (East Indian, Sri Lankan, Bangladeshi, Pakistani), East Asian (Chinese, Korean Japanese, Vietnamese, Thai, Cambodian) or Filipino.

Outcomes

Birthweight data for most subjects were collected directly from delivery records. When birthweight data were not recorded, we used self-reported data from postpartum questionnaires, if available. Our primary outcome was LGA offspring, defined as any birthweight >90th percentile for the corresponding gestational age. To calculate gestational age at delivery, we used the gestational age recorded in the chart at the date of delivery when available, or the gestational age at the date of GDM presentation was added to the time between presentation and delivery.

We also evaluated the odds of SGA birthweight, which was defined as a birthweight <10th percentile for gestational age. For additional comparisons, the 95th and 3rd percentiles were also used to evaluate more severe LGA and SGA, respectively. We estimated rates of LGA and SGA within ethnicity groups, first using the standard World Health Organization Growth Chart for Canada birthweight curves (26), and second using customized ethnicity-based birthweight percentile curves created from Canadian data (27). In a previous study, smoothed birthweight percentile curves were generated for males and females, categorized by maternal world region of birth, from population-based Ontario data of 766,688 singleton live births from 2002 to 2007 (23). We also examined the following secondary perinatal outcomes: preterm birth, unplanned caesarean births, combined neonatal outcome of NICU admissions, hyperbilirubinemia and hypoglycemia.

Statistical analysis

Baseline characteristics were analyzed descriptively using proportions for dichotomous variables and means \pm standard deviations for continuous variables. Linear regression was used to estimate the associations between each Asian ethnicity and fetal birthweight, using Caucasian ethnicity as the referent category. Logistic regression was used to calculate the odds ratios (ORs) and 95% confidence intervals (CIs) for the association between ethnic groups and likelihood of LGA and SGA offspring. Similar analyses

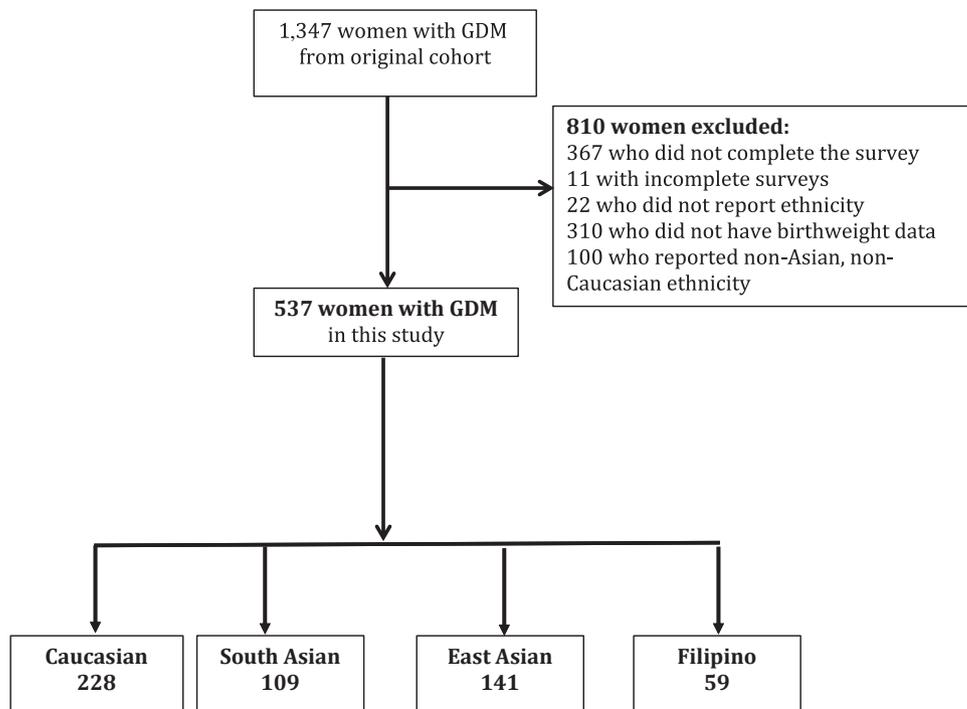


Figure 1. Flowchart of cohort. GDM, gestational diabetes.

were conducted for the secondary outcomes just described. Models were created adjusting for prepregnancy BMI, age, parity, gestational weight gain and insulin use during pregnancy, using Firth's penalized likelihood method to account for small numbers of outcomes. As many women had missing prepregnancy BMI data, we conducted a sensitivity analysis excluding BMI from the models. Analyses were performed using SAS statistical software version 9.4 (SAS Institute, Cary, North Carolina, United States).

Ethics approval

This study received approval from the research ethics board of Women's College Hospital and all participating hospital sites.

Results

Baseline characteristics

After excluding participants with insufficient survey data and those who could not be categorized into the 4 subgroups described earlier, 537 patients (39.9% of base cohort) were included in the study (Figure 1). Baseline clinical and demographics characteristics between the included cohort and the original cohort were similar (data not shown). The majority of the women (96.3%) were diagnosed with GDM based on the 2008 Canadian Diabetes Association guidelines (≥ 2 values exceeding thresholds on 2-h 75-g oral glucose tolerance test; fasting blood glucose, 5.3 mmol/L; 1 h, 10.6 mmol/L; 2 h, 8.9 mmol/L); 30 cohort members were recruited from a centre that used the guidelines of the Society for Obstetricians and Gynaecologists of Canada for GDM diagnosis (≥ 2 values exceeding thresholds on 3-h 100-g oral glucose tolerance test; fasting blood glucose, 5.8 mmol/L; 1 h, 10.6 mmol/L, 2 h, 9.2 mmol/L; 3 h, 8.1 mmol/L). Participants overall had a mean age of 34.1 ± 4.78 years, and over two-thirds were multiparous. Of these women, 228 (42.5%) were Caucasian, 109 (20.3%) South Asian, 141 (26.3%) East Asian and 59 (11.0%) Filipina. Baseline characteristics by ethnicity groups are shown in Table 1. South Asian women were younger and more likely to require insulin during pregnancy when compared with the other groups, and East Asian and Filipina women had lower prepregnancy BMIs than other groups. Other baseline variables were largely similar between ethnic groups.

Outcomes

Birthweight: Birthweight outcomes are presented in Table 2. The majority of birthweight outcomes were recorded from medical chart data (92.2%); the remainder were based on self-report from a postpartum survey. The average birthweight for Caucasian offspring was 3.3 ± 0.6 kg, which was significantly higher than for South Asian offspring (3.1 ± 0.5 kg, $p=0.001$) but did not differ significantly from East Asian (3.2 ± 0.6 kg) or Filipino (3.2 ± 0.7 kg) offspring. Using standard birthweight curves, rates of LGA and SGA offspring were 18.9% and 11.4%, respectively, for Caucasian women. As shown in Table 2, using standard curves, LGA rates were lower and SGA rates were similar or higher in offspring of Asian compared with Caucasian women. However, the rates of LGA increased and SGA rates decreased in Asian groups when customized curves were used. For instance, the rate of LGA rose from 4.6% to 10.1% in offspring of South Asian women, whereas SGA rate decreased from 18.3% to 9.2%. Customized curves showed increased LGA rates for East Asian and Filipina women, with SGA rates decreased in Filipino women (Table 2). Overall trends were similar when the 95th percentile cutoff was used to define LGA and when the 3rd percentile was used to define SGA (data not shown).

On unadjusted analysis, risk of LGA in the Asian subgroups was significantly lower for South Asian and East Asian women

compared with Caucasian women (Table 2). After adjustment for maternal BMI, age, parity, gestational weight gain and insulin use in pregnancy, this difference remained significant only for South Asian women (aOR, 0.065; 95% CI, 0.01 to 0.49). This difference was further attenuated when customized curves were used, but risk of LGA remained significantly lower for South Asian offspring (aOR, 0.27; 95% CI, 0.09 to 0.81). For SGA offspring, the risk was significantly higher for South Asian than for Caucasian women when standard (aOR, 2.96; 95% CI, 1.24 to 7.09; $p=0.015$) but not customized (aOR, 0.93; 95% CI, 0.33 to 2.58) curves were used (Table 2). Findings were similar for all analyses when BMI was removed (data not shown).

Secondary perinatal outcomes: The rate of preterm birth (<37 weeks) was 13.2% for Caucasian women, which was similar in South Asian (13.8%) and Filipina women (13.6%) but lower in East Asian women (8.5%). When we considered the combined perinatal outcome of an NICU admission, hyperbilirubinemia or hypoglycemia, only women of Filipino ethnicity were at a significantly higher risk than Caucasian women (aOR, 2.94; 95% CI, 1.18 to 7.31; $p=0.026$; Table 3).

Discussion

Although excess fetal growth is the main adverse fetal outcome of GDM, this cohort study of GDM patients has demonstrated considerable differences in the risk of LGA and SGA offspring across ethnic groups. We also showed that the use of standard birthweight distribution curves leads to substantial misclassification of LGA and SGA outcomes. With the use of ethnicity-specific birthweight curves and adjustment for other risk factors, risk of LGA remained significantly lower only for South Asian women when compared with Caucasian women. Our findings suggest that the implications of a GDM pregnancy may differ across Asian subgroups, and highlight the importance of using distribution curves customized for ethnicity when evaluating birthweight outcomes.

Previous studies have established a relationship between Asian ethnicity and both incidence (8–11) and fetal outcomes of GDM (11). A population-based Ontario study demonstrated a significantly lower risk of LGA offspring for South Asian and Chinese women with GDM (11). Although that study incorporated a large sample size, birthweight outcomes were based on standard Canadian curves (28), which may have underestimated the risk of LGA in those groups (23). Moreover, they were unable to account for other risk factors, such as maternal BMI and insulin use in pregnancy, which may differ across ethnic groups. Our study also showed significantly lower risks of LGA offspring for both South Asian and East Asian women using standard birthweight curves. However, with the use of customized curves and adjustment for key risk factors, the risk of LGA associated with GDM was comparable between East Asian and Caucasian women but remained significantly reduced only for South Asian women.

The reasons for lower risk of LGA offspring in South Asian women remain unclear. In contrast, GDM has been associated with a higher incidence of maternal type 2 diabetes in South Asian women compared with both the general population and Chinese women (10,29). This may indicate that GDM has a stronger long-term metabolic effect on South Asian women compared with other ethnicities, despite lower rates of offspring LGA. It is also possible that birthweight may not be the best marker of fetal effects of maternal glucose intolerance in South Asian populations, due to differences in fetal adiposity. There is evidence that South Asian neonates have a higher body fat for a given body weight compared with other populations, which has led to the term "thin-fat" babies (30). This differential growth process may be further aggravated by GDM. For instance, Venkataraman et al showed that offspring of

Table 1
Baseline characteristics of the cohort of women with gestational diabetes, by maternal ethnicity

Baseline characteristics	Caucasian (referent), n=228 (35.8%)	South Asian, n=109 (17.1%)	East Asian, n=141 (22.1%)	Filipino, n=59 (9.3%)
Prepregnancy variables				
Age (years), mean ± SD	34.5±4.7	32.7±5.1	34.3±4.5	34.5±4.7
Age >35 years, n (%)	121 (53.1)	40 (36.7)	59 (41.8)	32 (54.2)
Prepregnancy weight (kg), mean ± SD	75.2±22.0	66.5±14.1	60.9±13.1	60.2±13.4
Prepregnancy BMI (kg/m ²), mean ± SD	27.8±7.8	26.6±5.5	23.7±4.6	24.7±5.2
Prepregnancy BMI >25 kg/m ²	105 (56.8)*	37 (46.3)*	31 (27.7)*	15 (35.7)*
Hypertension, n (%)	25 (11.0)	7 (6.4)	6 (4.3)	8 (13.6)
History of prior offspring macrosomia, n (%)	20 (8.8)	4 (3.7)*	10 (7.1)	4 (6.8)
Smoker (prepregnancy), n (%)	31 (15.7)*	6 (7.0)*	6 (5.0)*	6 (12.0)
Born outside of Canada, n (%)	71 (31.3)*	93 (86.9)*	108 (78.3)*	54 (93.1%)*
Postsecondary education, n (%)	208 (91.2)	89 (81.7)	128 (90.8)	56 (94.9)
Income >\$60,000, n (%)	173 (77.2)*	49 (45.4)*	86 (62.8)*	25 (51.0)
Pregnancy variables				
Parity >1, n (%)	151 (67.1)*	65 (60.2)*	94 (66.7)	41 (70.7)*
Gestational weight gain, mean ± SD	12.4±10.9	11.4±9.5	12.5±4.1	10.4±9.6
Insulin use in pregnancy, n (%)	100 (46.5)*	64 (60.4)*	52 (38.8)*	15 (26.8)*

BMI, body mass index; SD, standard deviation.

All data are shown as a number (%) unless otherwise indicated.

* Missing data, overall (Caucasian/South Asian/East Asian/Filipino): prepregnancy BMI, n=118 (43/29/29/17, respectively); history of prior offspring macrosomia, n=1; smoker (prepregnancy), n=85 (31/23/22/9, respectively); born outside of Canada, n=7 (1/2/3/1, respectively); income, n=9 (4/1/4/0, respectively); parity, n=5 (3/1/1, respectively); insulin use in pregnancy, n=26 (13/3/7/3, respectively).

South Asian women with GDM had higher measures of fetal adiposity despite lower lean fetal mass and similar birthweights as women without GDM (31). The metabolic disturbances of GDM may promote epigenetic changes in utero, as described in Hales and Barker's "thrifty phenotype" hypothesis (32). They hypothesized that certain metabolic conditions lead to suboptimal fetal environments, which trigger an adaptive response by the fetus that redirects nutrient delivery primarily toward vital organs. This comes at the expense of other organs (pancreas, kidneys), leading to insulin resistance, and thus predisposing individuals to increased visceral adiposity and the metabolic syndrome (14). Further research is needed to determine the impact of GDM on other fetal outcomes in South Asian women, especially as LGA and macrosomia are the primary adverse outcomes targeted in GDM treatment guidelines (3).

Similar to previous findings (11), we found a higher rate of SGA in offspring of Asian women using standard birthweight curves. These differences were attenuated with customized birthweight curves, which have been favoured as a better way to estimate growth defects for newborns (33). These results are consistent with those of others showing a significant risk of misclassification of LGA and SGA among Asian populations using standard birthweight curves (23,34), underscoring the importance of using ethnicity-specific data to classify birthweight outcomes in non-Caucasian populations.

Interestingly, Filipina women with GDM had an almost 3-fold higher risk of adverse perinatal outcomes, based on the composite of offspring NICU admission, hyperbilirubinemia or hypoglycemia. These findings are consistent with those of others from the United States and Canada, indicating that pregnant women from

Table 2
Logistic regression results for birthweight outcomes of offspring of women with gestational diabetes, by ethnicity (standard and ethnicity-specific birthweight curves)

Birthweight-related outcomes	Caucasian (referent), n=228 (35.8%)	South Asian*, n=109 (17.1%)	East Asian*, n=141 (22.1%)	Filipino*, n=59 (9.3%)
Birthweight (kg), mean ± SD	3.3±0.6	3.1±0.5	3.2±0.6	3.2±0.7
Large for gestational age (90th percentile, standard curve)				
n (%)	43 (18.9)	5 (4.6)	9 (6.4)	6 (10.2)
OR, unadjusted (95% CI)	1.00	0.22 (0.08–0.52) [§]	0.31 (0.14–0.61) [§]	0.52 (0.20–1.17)
OR, fully adjusted [†] (95% CI)	1.00	0.10 (0.01–0.39) [¶]	0.39 (0.14–0.93) [¶]	0.54 (0.14–1.64)
OR, sensitivity analysis [‡] (95% CI)	1.00	0.13 (0.03–0.42) [§]	0.30 (0.11–0.69) [¶]	0.43 (0.11–1.26)
Large for gestational age (90th percentile, ethnicity-specific curve)				
n (%)	43 (18.9)	11 (10.1)	19 (13.5)	8 (13.6)
OR, unadjusted (95% CI)	1.00	0.50 (0.24–0.97) [¶]	0.68 (0.37–1.20)	0.70 (0.30–1.50)
OR, fully adjusted [†] (95% CI)	1.00	0.30 (0.09–0.79) [¶]	1.04 (0.50–2.13)	0.74 (0.22–2.06)
OR, sensitivity analysis [‡] (95% CI)	1.00	0.34 (0.13–0.79) [¶]	0.78 (0.39–1.51)	0.55 (0.17–1.46)
Small for gestational age (10th percentile, standard curve)				
n (%)	26 (11.4)	20 (18.3)	14 (9.9)	8 (13.6)
OR, unadjusted (95% CI)	1.00	1.75 (0.93–3.27)	0.87 (0.43–1.69)	1.26 (0.52–2.80)
OR, fully adjusted [†] (95% CI)	1.00	2.87 (1.22–6.78) [¶]	0.58 (0.20–1.47)	0.97 (0.31–2.70)
OR, sensitivity analysis [‡] (95% CI)	1.00	2.65 (1.19–5.90) [¶]	0.61 (0.22–1.51)	1.25 (0.43–3.24)
Small for gestational age (10th percentile, ethnicity-specific curve)				
n (%)	32 (14.0)	10 (9.2)	14 (9.9)	7 (11.9)
OR, unadjusted (95% CI)	1.00	0.64 (0.29–1.29)	0.69 (0.35–1.31)	0.86 (0.35–1.93)
OR, fully adjusted [†] (95% CI)	1.00	0.96 (0.34–2.50)	0.47 (0.17–1.16)	0.63 (0.18–1.79)
OR, sensitivity analysis [‡] (95% CI)	1.00	0.86 (0.31–2.13)	0.50 (0.18–1.21)	0.82 (0.27–2.18)

BMI, body mass index; OR, odds ratio; SD, standard deviation.

* Compared with offspring of Caucasian women.

[†] Adjusted for prepregnancy BMI, age, parity, gestational weight gain, insulin use in pregnancy.

[‡] Adjusted for age, parity, gestational weight gain, insulin use in pregnancy.

[§] p<0.005 compared with Caucasian group.

[¶] p<0.05 compared with Caucasian group.

Table 3

Other perinatal outcomes of offspring of women with gestational diabetes, by ethnicity

	Caucasian (referent), n=228 (35.8%)	South Asian*, n=109 (17.1%)	East Asian*, n=141 (22.1%)	Filipino*, n=59 (9.3%)
Preterm birth (<37 weeks' gestation)				
n (%)	30 (13.2)	15 (13.8)	12 (8.5)	8 (13.6)
OR, unadjusted (95% CI)	1.0	1.05 (0.54–2.05)	0.61 (0.30–1.24)	1.04 (0.45–2.39)
OR, fully adjusted† (95% CI)	1.0	2.02 (0.83–4.92)	1.70 (0.68–4.23)	1.68 (0.49–5.78)
Caesarean birth				
Any, n (%)	108 (47.4)	49 (45.0)	55 (39.0)	28 (47.5)
Unplanned, n (%)	45 (41.7)	18 (36.7)	21 (38.2)	14 (23.7)
OR, unadjusted (95% CI)	1.0	0.81 (0.41–1.63)	0.87 (0.45–1.68)	1.40 (0.61–3.22)
OR, fully adjusted† (95% CI)	1.0	0.37 (0.13–1.04)	0.72 (0.29–1.77)	1.31 (0.42–4.04)
Other perinatal outcomes				
NICU, hyperbilirubinemia or hypoglycemia, n (%)	43 (18.9)	21 (19.3)	19 (13.5)	11 (18.6)
OR, unadjusted (95% CI)	1.0	1.21 (0.58–1.83)	0.67 (0.37–1.20)	0.99 (0.47–2.06)
OR, fully adjusted† (95% CI)	1.0	0.94 (0.41–2.16)	1.15 (0.53–2.51)	2.94 (1.18–7.31)

BMI, body mass index; CI, confidence interval; NICU, neonatal intensive care unit; OR, odds ratio; SD, standard deviation.

* Compared to offspring of Caucasian women.

† Adjusted for prepregnancy BMI, age, parity, gestational weight gain, insulin use in pregnancy.

the Republic of the Philippines are more vulnerable to adverse perinatal outcomes than other Asian women (17–20). A higher burden of cardiovascular risk factors among Filipina women may partly explain these findings. A Canadian study showed that pregnant Filipina women were more likely to have chronic hypertension and obesity compared with East Asian and Caucasian women (35). Hypertension was also more common among Filipina women with GDM in our study, whereas their prepregnancy BMI based on self-report was substantially lower than other populations. Further research is needed to better understand the unique pregnancy-associated risks and needs for the rapidly growing population of Filipina immigrants.

Strengths of this study include our use of diverse ethnic groups in our assessment of pregnancy-related outcomes as well as the prospective study design. We also grouped patients into ethnic groups based on detailed self-reported categories, and evaluated outcomes across different Asian ethnicities. This is also the first study to utilize ethnicity-specific birthweight distribution curves in women with GDM, providing more robust evidence regarding the impact of GDM on birthweight-related outcomes across Asian subpopulations (21,23). Limitations of this study include exclusion of cohort participants who provided incomplete survey data, which could have introduced a selection bias. We also lacked maternal weight data on a number of participants, a proportion of birthweights were based on self-report, and we did not have measures of glycemic control beyond need for insulin treatment. Power was also limited for less common outcomes and for risk estimates of Filipina women due to the small number of patients within that group. As we did not have data on prenatal glycemic control, we cannot exclude the possibility that our findings were due to differences in treatment and glycemic control between groups. As this was an observational study, we were only able to hypothesize on theoretical causations between ethnicity and birthweight outcomes.

Conclusions

This study has demonstrated that, although birthweight-related outcomes are important in GDM, the impact of GDM on these outcomes may differ for Asian women. As South Asian women with GDM have a lower risk of LGA offspring, birthweight thresholds and treatment targets may need to be modified in South Asian women due to differences in fetal adiposity. For the Filipina population with GDM, other perinatal outcomes may be more important than the traditional measures of fetal overgrowth. Our findings highlight the

need for further research to guide the management of GDM in Asian minority populations.

Acknowledgments

The authors are thankful for the assistance of Sarah McTavish, who oversaw the initial data collection; Tanja Durbic, who coded the data and created the database; Alison Park, who generated the ethnicity-specific birthweight distribution curves; and Christina Yu, who assisted with manuscript preparation. Funding for this study was provided by a research grant from the Lawson Foundation. The funding institution had no role in data collection and analysis or writing of the report. L.L.L. holds a Diabetes Investigator Award from Diabetes Canada.

Author Disclosures

Conflicts of interest: None.

Author Contributions

W.K. contributed to study design, data analysis and interpretation, and coauthored the manuscript; J.R. contributed to patient recruitment, codesigned the study, provided data analysis and interpretation, and edited the manuscript; W.W. conducted data analysis, and edited the manuscript; D.F. contributed to patient recruitment and study design, and edited the manuscript; J.L. contributed to patient recruitment and study design, and edited the manuscript; L.L. provided funding, codesigned the study, coauthored the manuscript, and provided oversight for the cohort study.

References

- Buchanan TA, Xiang A, Kjos AL, Watanabe R. What is gestational diabetes? *Diabetes Care* 2007;30(Suppl):105–11.
- Bellamy L, Casas JP, Hingorani AD, Williams D. Type 2 diabetes mellitus after gestational diabetes: A systematic review and meta-analysis. *Lancet* 2009;373:1773–9.
- Feig DS, Berger H, Donovan L, et al. Diabetes Canada Clinical Practice Guidelines Expert Committee. Diabetes and pregnancy. *Can J Diabetes* 2018;42(Suppl. 1):S255–82.
- Horvath K, Koch K, Jeitler K, et al. Effects of treatment in women with gestational diabetes mellitus: Systematic review and meta-analysis. *BMJ* 2010;340:c1395.
- Feig DS, Hwee J, Shah BR, Booth GL, Bierman AS, Lipscombe LL. Trends in incidence of diabetes in pregnancy and serious perinatal outcomes: A large, population-based study in Ontario, Canada, 1996–2010. *Diabetes Care* 2014;37:1590–6.

6. Mocarski M, Savitz DA. Ethnic differences in the association between gestational diabetes and pregnancy outcome. *Matern Child Health J* 2012;16:364–73.
7. Retnakaran R, Hanley AJ, Connelly PW, Sermer M, Zinman B. Ethnicity modifies the effect of obesity on insulin resistance in pregnancy: a comparison of Asian, South Asian, and Caucasian women. *J Clin Endocrinol Metabol* 2006;91:93–7.
8. Urquia M, Glazier RH, Berger H, Ying I, De Souza L, Ray JG. Gestational diabetes among immigrant women. *Epidemiology* 2011;22:879–80.
9. Hedderson MM, Darbinian JA, Ferrara A. Disparities in the risk of gestational diabetes by race-ethnicity and country of birth. *Paediatr Perinatal Epidemiol* 2010;24:441–8.
10. Mukerji G, Chiu M, Shah BR. Impact of gestational diabetes on the risk of diabetes following pregnancy among Chinese and South Asian women. *Diabetologia* 2012;55:2148–53.
11. Mukerji G, Chiu M, Shah BR. Gestational diabetes mellitus and pregnancy outcomes among Chinese and South Asian women in Canada. *J Matern Fetal Neonatal* 2013;26:279–84.
12. Chiu M, Austin PC, Manuel DG, Shah BR, Tu JV. Deriving ethnic-specific BMI cutoff points for assessing diabetes risk. *Diabetes Care* 2011;34:1741–8.
13. Makgoba M, Savvidou MD, Steer PJ. The effect of maternal characteristics and gestational diabetes on birthweight. *BJOG* 2012;119:1091–7.
14. Fernandez-Twinn DS, Ozanne SE. Mechanisms by which poor early growth programs type-2 diabetes, obesity and the metabolic syndrome. *Physiol Behav* 2006;88:234–43.
15. Mukerji G, Kainth S, Pendrith C, et al. Predictors of low diabetes risk perception in a multi-ethnic cohort of women with gestational diabetes mellitus. *Diabet Med* 2016;33:1437–44.
16. Greenhalgh T, Clinch M, Afsar N, et al. Socio-cultural influences on the behaviour of South Asian women with diabetes in pregnancy: Qualitative study using a multi-level theoretical approach. *BMC Med* 2015;13:120.
17. Fuentes-Afflick E, Hessel NA. Impact of Asian ethnicity and national origin on infant birth weight. *Am J Epidemiol* 1997;145:148–55.
18. Bartsch E, Park AL, Jairam J, Ray JG. Concomitant preterm birth and severe small-for-gestational age birth weight among infants of immigrant mothers in Ontario originating from the Philippines and East Asia: A population-based study. *BMJ Open* 2017;7:e015386.
19. Rao AK, Cheng YW, Caughey AB. Perinatal complications among different Asian-American subgroups. *Am J Obstet Gynecol* 2006;194:e39–41.
20. Wong LF, Caughey AB, Nakagawa S, Kaimal AJ, Tran SH, Cheng YW. Perinatal outcomes among different Asian-American subgroups. *Am J Obstet Gynecol* 2008;199:382.e381–6.
21. Ray JG, Jiang D, Sgro M, Shah R, Singh G, Mamdani MM. Thresholds for small for gestational age among newborns of East Asian and South Asian ancestry. *J Obstet Gynaecol Can* 2009;31:322–30.
22. Urquia ML, Berger H, Ray JG; Canadian Curves Consortium. Risk of adverse outcomes among infants of immigrant women according to birth-weight curves tailored to maternal world region of origin. *CMAJ* 2015;187:E32–40.
23. Ray JG, Sgro M, Mamdani MM, et al. Birth weight curves tailored to maternal world region. *J Obstet Gynaecol Can* 2012;34:159–71.
24. Pasupathy D, McCowan LM, Poston L, et al. Perinatal outcomes in large infants using customised birthweight centiles and conventional measures of high birthweight. *Paediatr Perinatal Epidemiol* 2012;26:543–52.
25. Lipscombe LL, Banerjee AT, McTavish S, et al. Readiness for diabetes prevention and barriers to lifestyle change in women with a history of gestational diabetes mellitus: Rationale and study design. *Diabetes Res Clin Pract* 2014;106:57–66.
26. Dietitians of Canada. WHO Growth Charts. 2017. www.whogrowthcharts.ca. Accessed January 25, 2017.
27. St Michael's Hospital. Birthweight curves for newborns according to maternal ancestry. 2017. www.stmichaelshospital.com/birthweights.php. Accessed January 25, 2017.
28. Kramer MS, Platt RW, Wen SW, et al. A new and improved population-based Canadian reference for birth weight for gestational age. *Pediatrics* 2001;108:E35.
29. Almahmeed B, Shah BR, Mukerji G, Ling V, Booth GL, Feig DS. Effect of multiparity and ethnicity on the risk of development of diabetes: A large population-based cohort study. *Diabet Med* 2017;34:1637–45.
30. Yajnik CS, Fall CH, Coyaji KJ, et al. Neonatal anthropometry: the thin-fat Indian baby. The Pune Maternal Nutrition Study. *Int J Obesity Relat Metab Disord* 2003;27:173–80.
31. Venkataraman H, Ram U, Craik S, Arungunasekaran A, Seshadri S, Saravanan P. Increased fetal adiposity prior to diagnosis of gestational diabetes in South Asians: More evidence for the 'thin-fat' baby. *Diabetologia* 2017;60:399–405.
32. Hales CN, Barker DJ. Type 2 (non-insulin-dependent) diabetes mellitus: The thrifty phenotype hypothesis. *Diabetologia* 1992;35:595–601.
33. McCowan LM, Figueras F, Anderson NH. Evidence-based national guidelines for the management of suspected fetal growth restriction: Comparison, consensus, and controversy. *Am J Obstet Gynecol* 2018;218(Suppl):S855–68.
34. De Souza LR, Urquia ML, Sgro M, Ray JG. One size does not fit all: Differences in newborn weight among mothers of Philippine and other East Asian origin. *J Obstet Gynaecol Can* 2012;34:1026–37.
35. Fuller-Thomson E, Roterhmann M, Ray JG. Elevated risk factors for adverse pregnancy outcomes among Filipina-Canadian women. *J Obstet Gynaecol Can* 2010;32:113–9.