Comparison of adverse perinatal outcomes between Asians and Caucasians: a population-based retrospective cohort study in Ontario

Na Zeng, Erica Erwin, Wendy Wen, Daniel J. Corsi, Shi Wu Wen, and Yanfang Guo

Abstract

Background: Racial disparities in adverse perinatal outcomes have been studied in other countries, but little has been done for the Canadian population. In this study, we sought to examine the disparities in adverse perinatal outcomes between Asians and Caucasians in Ontario, Canada.

Methods: We conducted a population-based retrospective cohort study that included all Asian and Caucasian women who attended a prenatal screening and resulted in a singleton birth in an Ontario hospital (April 1st, 2015-March 31st, 2017). Generalized estimating equation models were used to estimate the independent adjusted relative risks and adjusted risk difference of adverse perinatal outcomes for Asians compared with Caucasians.

Results: Among 237,293 eligible women, 31% were Asian and 69% were Caucasian. Asians were at an increased risk of gestational diabetes mellitus, placental previa, early preterm birth (< 32 weeks), preterm birth, emergency cesarean section, 3rd and 4th degree perineal tears, low birth weight (< 2500 g, < 1500 g), small-for-gestational-age (<10th percentile, <3rd percentile), neonatal intensive care unit admission, and hyperbilirubinemia requiring treatment, but had lower risks of preeclampsia, macrosomia (birth weight > 4000 g), large-for-gestational-age neonates, 5-min Apgar score < 7, and arterial cord pH ≤ 7.1, as compared with Caucasians. No difference in risk of elective cesarean section was observed between Asians and Caucasians.

Conclusion: There are significant differences in several adverse perinatal outcomes between Asians and Caucasians. These differences should be taken into consideration for clinical practices due to the large Asian population in Canada.

Background

Racial disparities in health outcomes have been widely recognized [1]. Maternal race provides a significant axis for studies investigating perinatal outcomes, including stillbirth, preterm delivery, gestational diabetes mellitus (GDM), preeclampsia, and low or high birth weight [2, 3].

For example, White women are about one and half times more likely to have preterm birth and almost three times more likely to delivery very preterm birth compared to Black women [4].

Infant mortality rate in Blacks is also doubled as compared to Whites [3]. Racial disparities in perinatal outcomes have been believed due to the complexities of social, genetic and environmental factors [1, 5, 6]. Racial disparities in access to health care and prenatal care as well as insurance coverage are also demonstrated to contribute to differential health outcomes [7–10]. A previous study noted that women belonging to a racial/
ethnic-minority were more likely to be exposed to chronic stressors in their lifetime, enhancing their risk for poor perinatal outcomes [11]. Disparities in perinatal outcomes between Black and Caucasian women have been well documented by a series of studies in the United States (US) [4, 12, 13]. However, health disparities between Asian-Caucasian Americans have been understudied although Asian Americans account for 5.7% of the US population [14], which has promoted more research in the perinatal field to Asian Americans [15]. In Canada, population-based studies examining Asian-Caucasian differences in components of maternal and neonatal outcomes are scarce. Although Canada and the US share some social and economic similarities, results of studies conducted in the US may not be generalizable to the Canadian population due to differing racial composition and population context. 

Asian Canadians comprise the largest and fastest growing minority group in Canada. Ontario, as the most populous province of Canada and with Asian origin accounting for 23% of the total population [16], provides a unique opportunity to investigate variations in adverse perinatal outcomes between Asians and Caucasians. We therefore conducted a retrospective cohort study to examine disparities in adverse perinatal outcomes between Asians and Caucasians in Ontario.

Methods

Study design and data source

The study design is a population-based retrospective cohort study. We used data from Better Outcomes Registry & Network (BORN) Ontario birth registry, which contains comprehensive perinatal information covering virtually all hospital deliveries in Ontario, to conduct this study. Data access to the BORN is managed under the Personal Health Information Protection Act, 2004 (PHIPA) [17]. This study received ethical approval from the Children’s Hospital of Eastern Ontario Research Ethics Board (16/119X) and the Ottawa Health Science Network Research Ethics Board (20160780-01H).

Study population

All Asian and Caucasian women who attended a prenatal screening and resulted in a singleton birth in any Ontario hospital from April 1st, 2015 to March 31st, 2017, were included in this study. If participants had multiple births during the study period, only the first birth was included. We excluded women with missing information on ethnicity or classified as mixed or other racial groups. Women with a history of hypertension were excluded for analysis of gestational hypertension and preeclampsia. Women who were diagnosed with diabetes prior to the index pregnancy were excluded for analysis of GDM.

Outcome measures

Outcome measures considered in this study consist of a range of adverse maternal and neonatal complications. Maternal outcomes included GDM, gestational hypertension, preeclampsia, placental previa, preterm birth (< 37, < 34, < 32 weeks), spontaneous preterm birth, cesarean section (elective, emergency), assisted vaginal delivery, episiotomy, and 3rd and 4th degree perineal tears. Neonatal outcomes included sentinel congenital anomalies, low birth weight (LBW) (< 2500 g, < 1500 g), macrosomia (> 4000 g), small-for-gestational-age (SGA) neonates (defined as < 10th percentile of birth weight for gestational age) [13], SGA neonates (< 3rd percentile), large-for-gestational-age (LGA) neonates (defined as > 90th percentile of birth weight for gestational age), 5-min Apgar score < 7, cord arterial PH ≤ 7.1, hyperbilirubinemia require treatment (limiting to live births), and neonatal intensive care unit (NICU) admission. Values of birth weight outside of the range of 250 g–6000 g and values of arterial cord pH outside of the range of 6.6–7.4 were considered as outliers and were set to missing.

Exposure and covariates

Maternal race (Asian/Caucasian) was the main exposure measure, self-reported and recorded by care providers at the prenatal screening. We considered a series of relevant factors which could be potential confounders for the association between maternal race and perinatal outcomes, including maternal age at delivery(≤18, 19–24, 25–29, 30–34, 35–39, ≥40 years) [1, 2, 18–20], neighbourhood household income (lowest, 2nd, 3th, 4th, highest), parity(0, ≥1) [1, 18, 19, 21], pre-existing physical health problems (hypertension or diabetes or heart disease or pulmonary disease) [1], pre-existing mental health problems (a composite measure of depression and anxiety), previous cesarean section (yes, no) [1], pre-pregnancy body mass index (BMI) (defined as height in kilograms (kg) divided by weight in meters squared(m²) (< 18.5, 18.5–24.9, 25.0–29.9, 30–34.9, 35–39.9, ≥40 kg/m²) [1, 7], assisted reproductive technology (ART) (yes, no) [1], substance use/alcohol exposure/smoking during pregnancy (yes, no) [1, 7, 8, 20], maternal residence area (rural, urban) [2, 18], obstetrician in antenatal care team (yes, no) [2, 7, 18, 19], and hospital level of maternal care at delivery (I, II, III) [22]. We derived neighbourhood household income and maternal residence area data from the 2011 Canadian census using Statistics Canada’s Postal Code Conversion File (PCCF) through the maternal residence postal code because BORN does not collect data on social economic status [23].

Statistical analysis

We first compared baseline characteristics between Asians and Caucasians. Continuously distributed variables were
presented by mean ± standard deviation (SD) and compared by using a t-test. Categorical variables were displayed by counts and percentages and compared by using a chi-square test. We then compared adverse perinatal outcomes between Caucasians and Asians. Generalized estimating equations (GEE) model with a log link function and a Poisson distribution were used to estimate the adjusted relative risks (aRR) and adjusted risk difference (aRD) with their 95% confidence intervals (CI) of perinatal outcomes for Asians, with Caucasians as the reference [24, 25]. Potential confounding variables included in the GEE models were maternal age at delivery, neighborhood household income, pre-existing physical health problems, pre-existing mental health problems, previous caesarean section, pre-pregnancy BMI, parity, ART, substance use/alcohol exposure/smoking during pregnancy. For procedure-related outcomes (assisted vaginal delivery, episiotomy, cesarean section, episiotomy, 3rd and 4th degree vaginal tears, NICU admission) were further adjusted for maternal residence area, obstetrician in antenatal care team, and hospital level of maternal care at delivery, in addition to the aforementioned covariates. Confounders are carefully selected to be adjusted in the multivariable models for each perinatal outcome separately to avoid the occurrence of overadjustment [26, 27]. All confounders in the multivariate regression analysis were selected by ensuring they are independently associated with both race in our source population and perinatal outcomes among Caucasian women (the reference group in this study) only with a cutoff of 0.05 [28]. Multiple imputation method was used to account for missing data in the regression analysis, in which five datasets were imputed by using fully conditional specification (FCS) logistic regression method [29–31], assuming a joint distribution for all variables. Specifically, linear regression model was used for maternal age and pre-pregnancy BMI (kg/m²). Generalized logit model was used for household income quintile, parity, previous caesarean section, assisted reproductive technologies, substance use during pregnancy, mental health, and urban/rural residence. All variables used in multivariable analysis were included in imputation models. Statistical Analysis System (SAS) for windows, version 9.4 (SAS Institute, Cary, NC) was used to perform all of the analysis in this study, the criteria for statistical significance was set at alpha = 0.05.

Results

A total of 237,293 eligible women (30.9% Asians and 69.1% Caucasians) were included in the final analysis (Fig. 1). Compared to Caucasian women, Asian women tended to be older and had a significantly higher rate of being in the lowest income quintile level, living in urban areas, being underweight, having a previous caesarean section, and having an obstetrician on the antenatal care team. On the other hand, Asian women were less likely to be nulliparous, be overweight/obese, partake in alcohol consumption/substance use/smoking during pregnancy, have pre-existing disease, have mental health issues, have a previous cesarean section, have a previous abortion, and have a high BMI.
problems, and also less likely to deliver in alower mater-

Compared with Caucasian women, Asian women had
higher risks of GDM, placental previa, preterm birth (<
37, < 34, < 32 weeks), spontaneous preterm birth, emer-
gency cesarean section, episiotomy and 3rd and 4th de-
gree perineal tears, but lower risks of gestational hyperten-
sion, preeclampsia after adjusting for relevant
confounders (Table 2). No difference was found in risk
of elective cesarean section between these two groups.

Compared with Caucasians, Asians had higher risks of
low birth weight (< 2500 g, < 1500 g), SGA neonates (<
10th percentile, <3rd percentile), NICU admission, and
hyperbilirubinemia requiring treatment, but had lower
risks of sentinel congenital anomalies, macrosomia, LGA
neonates, 5-min Apgar score < 7, and arterial cord pH
≤7.1 after adjusting potential confounders (Table 3).

Discussion
In this population-based study, we have several principal
findings. First, we found that compared with Caucasians,
Asians had elevated risks of GDM, placental previa, pre-
term birth, and emergency cesarean section, whereas
had lower risks of gestational hypertension, preeclamp-
sia. Second, Asians have elevated risk of LBW, SGA,
NICU admission, and hyperbilirubinemia requiring treatment, compared to Caucasians, but are less likely to
have macrosomia, LGA, 5-min Apgar score < 7, sentinel
congenital anomalies, and arterial cord pH ≤7.1. We find
no difference in risk of elective cesarean section was ob-
served between the two groups.

The most substantial difference in adverse maternal
outcomes between Asian and Caucasian women ob-
served in this study was GDM. Asian background has
been associated with markedly increased risk of GDM
[32], and our study finding provided additional evidence
supporting an increased risk of GDM in Asians. A recent
systematic review and meta-analysis showed that the
pooled rate of GDM in Asians was 11.5% (95% CI 10.9–
12.1) [33], which is close to the rate of GDM (13.7%) in
Asians in this study. Another important difference in ad-
verse maternal outcomes observed in this study was that
Asian women had a higher rate of 3rd and 4th degree
perineal tear than Caucasian women, which is consistent
with previous studies [34, 35]. In our study, Asian
women were less likely to have macrosomic babies and
less likely to be nulliparous, which are protective against
perineal tears [36]. This phenomenon is likely associated
with the smaller stature and shorter perineum of Asian
women relative to Caucasian women [37]. Asian women
had higher risk of preterm birth, which is similar to pre-
vious studies [38, 39]. This is more pronounced in the
subgroup of early preterm birth (e.g.,<32 weeks). The
findings of Asians having an elevated risk of placenta
previa is also consistent with our previous studies [40]
which may be explained by cultural influence (such as
stress), nutrition or true genetic differences. Asian
women are observed to have a relatively larger placenta
even though the reasons are still not elucidated [41].

The higher rate of emergency cesarean section among
Asians may be explained by social deprivation or com-
unication difficulties [42]. We speculate that the lower
risk of preeclampsia and gestational hypertension for
Asian women, may in part be explained by their lower
risk of health behaviours such as recreational drugs, al-
cohol, and cigarette smoking during pregnancy that was
observed in this study and many previous studies [43–
45], although it is still unclear.

The most striking difference in neonatal outcomes be-
tween Asians and Caucasians was the size of the newborns, in which Asians had higher risks of low birth weight and SGA but lower risk of macrosomia and LGA than Caucasians. These findings are in general consistent with previous studies [20, 21, 46, 47], although somewhat different from an earlier study by our team compar-
ning birth weight distribution between Caucasian and East Asian (Chinese) [48]. Specifically, we found that while the mean birth weight in Chinese was substantially lower than that of in Caucasians with lower rate of macrosomia, the rate of low birth weight was also lower in Chinese infants [48]. As we have stated earlier, Asians in this study were from different regions in Asia with some distinctive features and lumping them together limited our ability to identify specific differences among them.

The higher rate of NICU admission for neonates deliv-
ered by Asian women might be associated with the in-
creased risk of early preterm birth among Asian women
found in our study. The result of lower rate of 5-min
Apgar score < 7 among Asian women might be expla-
ned by social deprivation or communication difficulties [42]. We speculate that the lower
risk of preeclampsia and gestational hypertension for
Asian women, may in part be explained by their lower
risk of health behaviours such as recreational drugs, al-
cohol, and cigarette smoking during pregnancy that was
observed in this study and many previous studies [43–
45], although it is still unclear.

The finding of higher risk of hyperbilirubinemia re-
quired treatment in Asian infants was consistent with
previou studies [51, 52]. One of the reasons the
phenomenon of increased risk of hyperbilirubinemia re-
quired treatment among Asians may be caused by a
common DNA-sequence variant (Gly71Arg) carried by
Asians, resulting in an amino acid change in the uridine
phosphate glucuronosyl-transferase protein [53]. Asian
women were found to have a slightly lower risk of senti-
nel congenital anomalies, whereas a previous study
found no difference in overall congenital anomalies
Table 1 Comparison of characteristics between Asians and Caucasians, Ontario, Canada, April 1st, 2015-March 31st, 2017 (N = 237,293)

| Characteristics                                           | Asian     | Caucasian | P value |
|-----------------------------------------------------------|-----------|-----------|---------|
|                                                           | n (%)     | n (%)     |         |
| Maternal Age at delivery (years) (Mean ± SD)              | 32.07 ± 4.5 | 31.08 ± 4.98 | <.0001  |
| ≤ 18                                                      | 49 (0.1)  | 1221 (0.7) | <0.001  |
| 19–24                                                     | 3207 (4.4) | 15,229 (9.3) |         |
| 25–29                                                     | 17,792 (24.3) | 41,652 (25.4) |         |
| 30–34                                                     | 30,428 (41.6) | 65,448 (39.9) |         |
| 35–39                                                     | 18,019 (24.7) | 34,207 (20.9) |         |
| ≥ 40                                                      | 3592 (4.9)  | 6116 (3.7)  |         |
| Missing                                                   | 101 (0.1)  | 232 (0.1)  |         |
| Neighbourhood median household income quintiles (link to 2011 Canadian Census data) | <.0001    |           |         |
| Quintile 1 (lowest)                                       | 17,117 (23.6) | 26,877 (16.6) |         |
| Quintile 2                                                 | 16,540 (22.8) | 30,678 (18.9) |         |
| Quintile 3                                                 | 16,544 (22.8) | 33,781 (20.8) |         |
| Quintile 4                                                 | 13,679 (18.9) | 37,563 (23.2) |         |
| Quintile 5 (highest)                                      | 8556 (11.8)  | 33,148 (20.5) |         |
| Missing                                                   | 752 (1.0)   | 2058 (1.3)  |         |
| Maternal pre-existing diseasea                            | <.0001     |           |         |
| No                                                        | 70,579 (96.4) | 151,491 (92.4) |         |
| Yes                                                       | 2609 (3.6)  | 12,544 (7.6) |         |
| Mental health Condition                                   | <.0001     |           |         |
| No                                                        | 66,363 (96.6) | 123,975 (80.8) |         |
| Yes                                                       | 2366 (3.4)  | 29,465 (19.2) |         |
| Missing                                                   | 4459 (6.1)  | 10,665 (6.5) |         |
| Previous cesarean section                                 | <.0001     |           |         |
| Yes                                                       | 60,129 (83.8) | 138,671 (86.5) | <.0001  |
| No                                                        | 11,656 (16.2) | 21,624 (13.5) |         |
| Missing                                                   | 1403 (1.9)  | 3810 (2.3)  |         |
| Pre-pregnancy BMI (kg/m$^2$) (Mean ± SD)                  | 23.4 ± 4.5 | 25.74 ± 6.17 | <.0001  |
| Underweight (< 18.5)                                      | 5958 (9.7)  | 6537 (4.4)  | <.0001  |
| Normal (18.5–24.9)                                        | 36,655 (59.7) | 75,072 (50.8) |         |
| Overweight (25.0–29.9)                                    | 13,409 (21.8) | 36,235 (24.5) |         |
| Obese (30–34.9)                                           | 3982 (6.5)  | 17,044 (11.5) |         |
| Obese (35–39.9)                                           | 1001 (1.6)  | 7982 (5.4)  |         |
| Obese (≥40)                                               | 378 (0.6)   | 4991 (3.4)  |         |
| Missing                                                   | 11,805 (16.1) | 16,244 (9.9)  |         |
| Parity                                                    | <.0001     |           |         |
| 0                                                         | 31,289 (43.1) | 75,996 (46.7) |         |
| ≥ 1                                                       | 41,386 (56.9) | 86,738 (53.3) |         |
| Missing                                                   | 513 (0.7)   | 1371 (0.8)  |         |
| Conception by assisted reproductive technology             | <.0001     |           |         |
| No                                                        | 65,565 (96.2) | 145,616 (95.4) |         |
| Yes                                                       | 2622 (3.8)  | 6978 (4.6)  |         |
There are several strengths of this study. First, this study is based on a large population with comprehensive demographic and health care information, allowing an investigation of a number of adverse perinatal outcomes with appropriate adjustment for potential confounding factors. Second, our study has a large sample size of Asian women, enabling a robust comparison between Caucasians and Asians with greater than at least 90% power to detect the difference for each perinatal outcome with a two-tailed alpha (type 1 error) of 5%, where previous studies had smaller samples of Asians [1, 7, 18, 54, 55]. Third, universal access to quality maternity care helped to isolate maternal factors from health care factors.

Limitations of this study should be acknowledged. First, Asians in this study included women from a variety of regions in Asia. Although these women share some common demographic and cultural background, there are major differences in genetic and environmental factors among them. However, although grouping different Asians together may have limited our ability to reveal some specific differences from Caucasians and to properly interpret specific results, it gives us an overall sense of discrepancies in perinatal outcomes between Asians and Caucasians, which will direct us to focus on some specific outcomes in future work. Second, as race status is considered to be a subjective assessment, which might generate misclassification of race status leading to unavoidable bias. Third, as our study population included women who had undergone prenatal screening.

Table 1  Comparison of characteristics between Asians and Caucasians, Ontario, Canada, April 1st, 2015-March 31st, 2017 (N = 237,293) (Continued)

| Characteristics                                | Asian       | Caucasian   | P value |
|------------------------------------------------|-------------|-------------|---------|
|                                               | n           | %           | n       | %         |               |
| Missing                                       | 5001        | 6.8         | 11,511  | 7.0       | <.0001       |
| Drug use during pregnancy                     |             |             |         |           |               |
| No                                            | 69,375      | 97.9        | 137,147 | 86.7      |               |
| Yes                                           | 1458        | 2.1         | 21,012  | 13.3      |               |
| Missing                                       | 2355        | 3.2         | 5946    | 3.6       |               |
| Alcohol exposure during pregnancy             |             |             |         |           | <.0001       |
| No                                            | 69,833      | 99.1        | 152,805 | 97.2      |               |
| Yes                                           | 612         | 0.9         | 4470    | 2.8       |               |
| Missing                                       | 2743        | 3.7         | 6830    | 4.2       |               |
| Smoking during pregnancy (any time)           |             |             |         |           | <.0001       |
| No                                            | 69,485      | 98.9        | 140,296 | 89.4      |               |
| Yes                                           | 771         | 1.1         | 16,575  | 10.6      |               |
| Missing                                       | 2932        | 4.0         | 7234    | 4.4       |               |
| Maternal residence area                       |             |             |         |           |               |
| Urban                                         | 72,386      | 99.2        | 139,566 | 85.4      |               |
| Rural                                         | 593         | 0.8         | 23,841  | 14.6      |               |
| Missing                                       | 209         | 0.3         | 698     | 0.4       |               |
| Obstetrician in antenatal care team           |             |             |         |           | <.0001       |
| No                                            | 11,171      | 15.3        | 49,579  | 30.2      |               |
| Yes                                           | 62,017      | 84.7        | 114,456 | 69.8      |               |
| Hospital level of maternal care              |             |             |         |           | < 0.001      |
| level I                                       | 1383        | 1.9         | 18,597  | 11.3      |               |
| level II                                      | 60,006      | 82.0        | 101,777 | 62.0      |               |
| level III                                     | 11,799      | 16.1        | 43,661  | 26.6      |               |

*Maternal pre-existing disease includes any of hypertension, diabetes, heart disease, and pulmonary disease
1. Missing data represents missing values for neighborhood household income level and education level, parity, previous caesarean section, drug use, alcohol use, birth weight and antenatal health care provider were excluded from the percentage calculation
2. Bold values mean the risk factor favouring corresponding race group
Table 2 Comparison of risks of adverse maternal outcomes between Asians and Caucasians, Ontario, Canada, April 1st, 2015-March 31st, 2017 (N = 69,734)

| Maternal Outcomes               | Asian               | Caucasian (reference) | Adjusted RR (95% CI) | Adjusted RD (95% CI) |
|---------------------------------|---------------------|-----------------------|----------------------|---------------------|
| Gestational diabetes            | 9793 13.38          | 9077 5.53             | 2.71 (2.68, 2.74)    | 1.00 (0.97, 1.03)   |
| Gestational hypertension        | 2012 2.75           | 6461 3.94             | 0.93 (0.88, 0.98)    | -0.07 (-0.12, -0.02)|
| Preeclampsia                    | 1945 2.66           | 7045 4.29             | 0.84 (0.78, 0.89)    | -0.18 (-0.23, -0.13)|
| Placental previa                | 700 0.96            | 1097 0.67             | 1.30 (1.21, 1.40)    | 0.26 (0.17, 0.36)   |
| Preterm birth (< 37 weeks)      | 5070 6.93           | 10,419 6.35           | 1.23 (1.20, 1.27)    | 0.21 (0.17, 0.24)   |
| Preterm birth (< 34 weeks)      | 1376 1.88           | 2603 1.59             | 1.37 (1.29, 1.44)    | 0.31 (0.24, 0.38)   |
| Preterm birth (< 32 weeks)      | 901 1.23            | 1582 0.96             | 1.49 (1.39, 1.58)    | 0.40 (0.30, 0.49)   |
| Spontaneous preterm birth       | 1994 2.72           | 4103 2.50             | 1.25 (1.20, 1.31)    | 0.23 (0.17, 0.28)   |
| Cesarean section                | 21,694 29.64        | 46,416 28.30          | 1.03 (1.01, 1.05)    | 0.03 (0.01, 0.05)   |
| Elective cesarean section       | 11,542 15.77        | 24,968 15.22          | 0.91 (0.89, 0.94)    | -0.09 (-0.11, -0.07)|
| Emergency cesarean section      | 10,146 13.86        | 21,443 13.07          | 1.22 (1.20, 1.25)    | 0.20 (0.18, 0.22)   |
| Assisted vaginal delivery       | 8521 11.64          | 14,601 8.90           | 1.29 (1.26, 1.31)    | 0.25 (0.23, 0.28)   |
| Episiotomy                      | 10,443 14.27        | 14,552 8.87           | 1.40 (1.38, 1.43)    | 0.34 (0.31, 0.36)   |
| 3rd and 4th degree perineal tears| 2756 4.19           | 3836 2.65             | 1.57 (1.52, 1.62)    | 0.45 (0.40, 0.50)   |

RR: relative risk, CI: confidence interval
1. Generalized estimating equations with a log link function and a poisson distribution were used to estimate the relative risks of the outcomes.
2. Covariates included in the adjusted models for each outcome were selected covariates that showed univariate association of P < 0.05 with both the exposure and the outcome were included in the adjusted model. The covariate for each outcome was fit separately.
3. A fully conditional specification method was used to impute missing values, assuming a joint distribution for all variables. Five imputed datasets were created.

Table 3 Comparison of risks of adverse neonatal outcomes between Asians and Caucasians, Ontario, Canada, April 1st, 2015-March 31st, 2017 (N = 69,734)

| Neonatal outcome                  | Asian             | Caucasian (reference) | Adjusted RR (95% CI) | Adjusted RD (95% CI) |
|-----------------------------------|-------------------|-----------------------|----------------------|---------------------|
| Sentinel Congenital Anomalies     | 1046 1.43         | 2938 1.79             | 0.90 (0.83, 0.98)    | -0.10 (-0.18, -0.03)|
| Low birth weight (< 2500 g)       | 5089 7.00         | 7160 4.40             | 1.81 (1.77, 1.85)    | 0.59 (0.55, 0.63)   |
| Low birth weight (< 1500 g)       | 756 1.40          | 1229 0.76             | 1.59 (1.49, 1.69)    | 0.46 (0.36, 0.56)   |
| Macrosomia (> 4000 g)             | 3459 4.76         | 19,214 11.80          | 0.43 (0.39, 0.46)    | -0.85 (-0.89, -0.82)|
| Small-for-gestational-age neonates (<10th percentile) | 10,396 14.35 | 12,229 7.56 | 1.93 (1.91, 1.96) | 0.66 (0.63, 0.69) |
| Small-for-gestational-age neonates (<3rd percentile) | 2703 3.73 | 2879 1.78 | 2.19 (2.14, 2.25) | 0.78 (0.73, 0.84) |
| Large-for-gestational-age neonates (>90th percentile) | 3610 4.98 | 17,660 10.92 | 0.50 (0.46, 0.53) | -0.70 (-0.73, -0.66)|
| 5- min Apgar score < 7            | 1219 1.69         | 3742 2.32             | 0.89 (0.82, 0.96)    | -0.11 (-0.18, -0.05)|
| Arterial cord pH ≤ 7.1            | 2595 4.04         | 8704 6.11             | 0.71 (0.66, 0.76)    | -0.34 (-0.39, -0.30)|
| NICU admission                    | 8529 11.65        | 18,796 11.46          | 1.18 (1.16, 1.21)    | 0.17 (0.14, 0.19)   |
| Hyperbilirubinemia requiring treatment | 4300 6.95 | 8132 5.52 | 1.41 (1.37, 1.45) | 0.35 (0.31, 0.38) |

RR: relative risk, CI: confidence interval, RD risk difference, NICU neonatal intensive care unit
1. Generalized estimating equations with a log link function and a poisson distribution were used to estimate the relative risks of the outcomes.
2. Covariates included in the adjusted models for each outcome were selected covariates that showed univariate association of P < 0.05 with both the exposure and the outcome were included in the adjusted model. The covariate for each outcome was fit separately.
3. A fully conditional specification method was used to impute missing values, assuming a joint distribution for all variables. Five imputed datasets were created.
so that it only captures approximately 70% of pregnant women in Ontario [56]. Women who attend prenatal screening tend to live in an urban area and high income neighbourhood, to receive prenatal care from an obstetrician, and are more likely be an immigrant or a refugee [57]. Fourth, there were significant differences in baseline characteristics between Asians and Caucasians, which might still have impact on our results due to possible residual confounding. Finally, we did not cover some perinatal outcomes, including placenta accreta, postpartum haemorrhage, neonatal asphyxia and infection in our study due to incomplete information in BORN database, and did not report some underpowered outcomes, such as maternal ICU admission, placental abruption, stillbirth, 5-min Apgar score <4 and neonatal death due to their low incidence rates (less than 1% in Ontario). Despite these limitations, the results of this study are valuable in informing future work on perinatal outcomes in persons from subgroups within the Asian diaspora.

Conclusion
In summary, our population-based study found significant differences in several adverse perinatal outcomes between Asians and Caucasians. Given the heterogeneity in the demographic and social characteristics among different Asian groups, future studies will be valuable to explore these differences among specific Asian groups.

Abbreviations
ART: Assisted Reproductive Technology; BMI: Body Mass Index; BORN: Better Outcomes Registry & Network; CI: Confidence Interval; FCS: Fully Conditional Specification; GDM: Gestational Diabetes Mellitus; GEE: Generalized Estimating Equations; LG A: Large-for-Gestational-Age; NCIU: Neonatal Intensive Care Unit; PCCF: Postal Code Conversion File; PHIPA: Personal Health Information Protection Act; RD: Risk Difference; RR: Relative Risk; SAS: Statistical Analysis System; SD: Standard Deviation; SGA: Small-for-Gestational-Age; US: United States

Acknowledgements
The authors thank Ruth White, Alysha Harvey and Catherine Riddell for managerial oversight and support.

Authors’ contributions
YG and SW contributed to the study concept and design. All of the authors (N2, EE, WW, DC, SW, YG) were involved in the analysis and interpretation of data and the critical revision of the manuscript for important intellectual content. EE conducted the statistical analysis. NZ wrote the first draft. All of the authors approved the final version to be published. YG is the guarantor of the work.

Funding
This study was supported by a Canadian Institutes of Health Research (CIHR) Foundation Grant (FDN 148438). The funding agency was not involved in study design, analysis or interpretation of data, or writing of this manuscript or the decision to submit the article for publication. The data analyzed for this study are held securely at the prescribed registry, BORN Ontario.

Availability of data and materials
The data analyzed during this study are held securely at the prescribed registry BORN Ontario. Data sharing regulations prevent these data from being made available publicly due to the personal health information in the datasets. Enquiries regarding BORN data must be directed to BORN Ontario (Science@BORNOntario.ca).

Ethics approval and consent to participate
This study received ethical approval from the Children’s Hospital of Eastern Ontario Research Ethics Board (16/119X) and the Ottawa Health Science Network Research Ethics Board (20160780-01H). Our research team acquired permissions from BORN local administrator to access the data used in this research.

Consent for publication
Not Applicable.

Competing interests
We have no conflict of interest.

Author details
1School of Epidemiology and Public Health, University of Ottawa, Ottawa, Ontario, Canada. 2OMNI Research Group, Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa, Ontario, Canada. 3Better Outcomes Registry & Network Ontario, Children’s Hospital of Eastern Ontario, Ottawa, Ontario, Canada. 4Ottawa Hospital Research Institute, Ottawa, Ontario, Canada. 5Children’s Hospital of Eastern Ontario Research Institute, Ottawa, Ontario, Canada. 6Department of Obstetrics and Gynecology, University of Ottawa Faculty of Medicine, Ottawa, Ontario, Canada.

Received: 20 September 2020 Accepted: 1 December 2020
Published online: 05 January 2021

References
1. Soffer MD, Naqvi M, Melka S, Gottlieb A, Romero J, Fox NS. The association between maternal race and adverse outcomes in twin pregnancies with similar healthcare access. J Matern Fetal Neonatal Med. 2018;31(18):2424–8.
2. Singh GK, Stella MY. Adverse pregnancy outcomes: differences between US- and foreign-born women in major US racial and ethnic groups. Am J Public Health. 1996;86(6):837–43.
3. Matthews TJ, MacDorman MF. Infant mortality statistics from the 2010 period linked birth/infant death data set. Natl Vital Stat Rep. 2013;62(8):1–26.
4. McKinnon B, Yang S, Kramers MS, Bushnik T, Sheppard AJ, Kaufman JS. Comparison of black-white disparities in preterm birth between Canada and the United States. CMAJ. 2016;188(1):19–26.
5. Hoyert D. Perinatal Mortality in the United States: 1985–91 National Center for Health Statistics. Vital Health Stat. 1995;20(26) Accessed August 16, 2020. https://www.cdc.gov/nchs/data/nvsr/nvsr26/nvsr26_026.pdf.
6. Alhusen JL, Bower KM, Epstein E, Sharps P. Racial discrimination and adverse birth outcomes: an integrative review. J Midwifery Womens Heal. 2016;61(6):707–20.
7. Bryant AS, Worjoloh A, Caughey AB, Washington AE, Bryant A. Racial/ethnic disparities in obstetrical outcomes and care: prevalence and determinants of racial and ethnic disparities in obstetrical outcomes and obstetrical care. Am J Obstet Gynecol. 2010;202(4):335–43.
8. Cullhane JP, Goldenberg RL. Racial disparities in preterm birth: Semin Perinatol. 2011;35(4):234–9.
9. Creanga AA, Bateman BT, Kuldina EV, Callaghan WM. Racial and ethnic disparities in severe maternal morbidity: A multistate analysis, 2008–2010. Am J Obstet Gynecol. 2014;210(5):435.e1–8.
10. Bengiamin MI, Capitman JA, Ruwe MB. Disparities in initiation and adherence to prenatal care: impact of insurance, race/ethnicity and nativity. Matern Child Health J. 2010;14(4):618–24.
11. Latendresse G. The interaction between chronic stress and pregnancy: preterm birth from a biobehavioral perspective. J Midwifery Womens Heal. 2005;50(1):18–17.
12. Keeser AM, Salinas YD, DeWan AT, Havley NL, Donohue PK, Strobino DM. Risks of preterm birth among non-Hispanic black and non-Hispanic white women: effect modification by maternal age. Paediatr Perinat Epidemiol. 2019;33(5):346–56.
13. Kramer MS, Platt RW, Wen SW, Joseph KS, Allen A, Abramowicz M, et al. A new and improved population-based Canadian reference for birth weight for gestational age. Pediatrics. 2001;108(2):E35.
