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Association of SARS-CoV-2 Infection During Pregnancy With Maternal and Perinatal Outcomes

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IMPORTANCE There are limited high-quality, population-level data about the effect of SARS-CoV-2 infection on pregnancy using contemporaneous comparator cohorts.

OBJECTIVES To describe maternal and perinatal outcomes associated with SARS-CoV-2 infection in pregnancy and to assess variables associated with severe disease in the pregnant population.

DESIGN, SETTING, AND PARTICIPANTS CANCOVID-Preg is an observational surveillance program for SARS-CoV-2–affected pregnancies in Canada. This analysis presents exploratory, population-level data from 6 Canadian provinces for the period of March 1, 2020, to October 31, 2021. A total of 6012 pregnant persons with a positive SARS-CoV-2 polymerase chain reaction test result at any time in pregnancy (primarily due to symptomatic presentation) were included and compared with 2 contemporaneous groups including age-matched female individuals with SARS-CoV-2 and unaffected pregnant persons from the pandemic time period.

EXPOSURE SARS-CoV-2 infection during pregnancy. Incident infections in pregnancy were reported to CANCOVID-Preg by participating provinces/territories.

MAIN OUTCOMES AND MEASURES Maternal and perinatal outcomes associated with SARS-CoV-2 infection as well as risk factors for severe disease (ie, disease requiring hospitalization, admission to an intensive care unit/critical care unit, and/or oxygen therapy).

RESULTS Among 6012 pregnant individuals with SARS-CoV-2 in Canada (median age, 31 [IQR, 28-35] years), the greatest proportion of cases were diagnosed at 28 to 37 weeks' gestation (35.7%). Non-White individuals were disproportionately represented. Being pregnant was associated with a significantly increased risk of SARS-CoV-2–related hospitalization compared with SARS-CoV-2 cases among all women aged 20 to 49 years in the general population of Canada (7.75% vs 2.93%; relative risk, 2.65 [95% CI, 2.41-2.88]) as well as an increased risk of intensive care unit/critical care unit admission (2.01% vs 0.37%; relative risk, 5.46 [95% CI, 4.50-6.53]). Increasing age, preexisting hypertension, and greater gestational age at diagnosis were significantly associated with worse maternal outcomes. The risk of preterm birth was significantly elevated among SARS-CoV-2–affected pregnancies (11.05% vs 6.76%; relative risk, 1.63 [95% CI, 1.52-1.76]), even in cases of milder disease not requiring hospitalization, compared with unaffected pregnancies during the same time period.

CONCLUSIONS AND RELEVANCE In this exploratory surveillance study conducted in Canada from March 2020 to October 2021, SARS-CoV-2 infection during pregnancy was significantly associated with increased risk of adverse maternal outcomes and preterm birth.

Supplemental content

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At the outset of the COVID-19 pandemic, the risk that the novel SARS-CoV-2 pathogen presented to pregnant populations was unclear. Evidence of poor maternal and infant outcomes from past outbreaks of viral respiratory illness, including the coronaviruses SARS[1,2] and Middle East respiratory syndrome (MERS),[3] as well as 2009 influenza A(H1N1),[4,5] suggested that SARS-CoV-2 may also differentially affect pregnant individuals. However, international reports have been varied in the degree of illness severity resulting from SARS-CoV-2 infection[6-15] and the degree and nature of associated adverse pregnancy outcomes, such as preeclampsia, preterm birth, stillbirth, and cesarean delivery.[8-11,14] Since existent studies are highly heterogeneous, with many including only cases of COVID-19 identified at the time of hospital admission for obstetric delivery, they may not adequately represent the full effect of SARS-CoV-2 on pregnant populations, which includes infection acquired throughout pregnancy and a range of disease severity. Furthermore, high-quality, population-level data that use contemporaneous comparator cohorts are limited in the literature to date.

The Canadian Surveillance of COVID-19 in Pregnancy (CANCOVID-Preg) is the only national surveillance program for SARS-CoV-2-affected pregnancies in Canada. The purpose of this program was to contribute to the overarching understanding of SARS-CoV-2 in pregnancy internationally and to generate Canadian-specific data to support national and provincial public health policy. The purpose of this exploratory study was to assess maternal and perinatal outcomes associated with SARS-CoV-2 infection in pregnancy.

Key Points

Question Is SARS-CoV-2 infection during pregnancy associated with increased risk of adverse maternal and perinatal outcomes?

Findings This Canadian surveillance study included 6012 completed pregnancies between March 2020 and October 2021. Among cases of infection during pregnancy compared with cases of infection among the general Canadian population of reproductive-age female individuals, there was a significantly increased risk of SARS-CoV-2–related hospitalization (relative risk, 2.65) and intensive care unit admission (relative risk, 5.46). Among cases of infection during pregnancy compared with pregnant individuals without SARS-CoV-2 infection, there was a significantly increased risk of preterm birth (relative risk, 1.63).

Meaning SARS-CoV-2 infection during pregnancy was significantly associated with increased risk of adverse maternal outcomes and preterm birth.

Methods

Ethical Approval

A waiver of consent was obtained in most provinces and territories for this surveillance work, resulting in data being abstracted from clinical charts and deidentified. Ethical approval was obtained by regional research ethics boards in each province and territory and by the University of British Columbia for the coordinating center and data repository site (H20-01196).

Study Setting and Dates

CANCOVID-Preg was endorsed and funded by the Public Health Agency of Canada as well as the Canadian Institutes for Health Research and received case identification and knowledge translation support from provincial/territorial public health offices. Eight provinces of a total of 13 provinces and territories in Canada had the capacity to collect data during the pandemic. This analysis included data on SARS-CoV-2–affected pregnancies that were completed between March 1, 2020, and October 31, 2021, from 6 Canadian provinces including British Columbia, Alberta, Ontario, Quebec, Manitoba, and Nova Scotia.

Inclusion Criteria

Notifications for incident cases of laboratory-confirmed SARS-CoV-2–affected pregnancy (as identified by a positive SARS-CoV-2 polymerase chain reaction test result at any point in pregnancy) from participating provinces/territories were submitted to the CANCOVID-Preg surveillance team and included in this study. Most cases were identified from testing triggered by symptoms of SARS-CoV-2 or because the individuals were contacts of known SARS-CoV-2–infected persons, not due to routine testing at the time of admission for delivery, thereby largely avoiding pregnancy testing bias. Case identification methodology differed slightly by province/territory, resulting from public health data linkage in some and by a consenting process in others (eTable 1 in Supplement 1).

Data Source

A common standard data set was identified and harmonized with comparable international data collection tools where possible.[13] Sociodemographic and clinical data for each case were abstracted by research staff from relevant clinical charts and hospital records for entry directly into a Research Electronic Data Capture (REDCap) database. The key clinical characteristics and outcomes described in this article are known to have a high degree of completion within clinical charts and accuracy on data abstraction in the Canadian context.[16] Each site conducted checks on accuracy of data abstracted, and data queries were submitted to provincial sites from the coordinating center to address any inconsistent or missing data. To assess potential differences in outcomes by race and ethnicity, these variables were included in this study; data on demographics including race and ethnicity were recorded by clinicians from self-reported patient history and then abstracted to the database. This variable was then given a fixed category reflective of Statistics Canada categories. Clinical data collection included dates of potential SARS-CoV-2 exposure; laboratory reports for maternal and infant SARS-CoV-2 testing; symptomatology, treatment, and outcome of disease to assess severity; COVID-19 vaccination status where available; and pregnancy outcomes including pregnancy complications, mode and timing of delivery, and peripartum complications.

Canadian national population-level outcome data from Statistics Canada of all female, SARS-CoV-2–positive individuals

aged 20 to 49 years were used for comparison with our cohort of pregnant individuals.[17] Summarized national data from the Canadian Institute for Health Information Discharge Abstract Database (CIHI-DAD; data from March-September 2021, excluding data from Quebec) were used to compare the cumulative incidence of adverse perinatal outcomes in SARS-CoV-2–affected pregnancies with unaffected pregnancies during the same time frame. Pregnant persons with a present or past COVID-19 diagnosis on delivery were excluded from the CIHI-DAD data set. Race and ethnicity among pregnant individuals with SARS-CoV-2 infection were compared with 2016 Canadian census proportions of race and ethnicity for female individuals aged 15 to 45 years (eFigure 1 in Supplement 1).[18]

Outcomes

Rates of adverse maternal outcomes were analyzed. Risk factors for severe disease (defined as hospitalization for SARS-CoV-2, intensive care unit [ICU] admission for SARS-CoV-2 including care delivered in equivalent critical care units due to ICU capacity limits, and/or the need for supplemental oxygen therapy) were also analyzed. Hospitalization and admission to an ICU for SARS-CoV-2 were defined as nonobstetrical admissions primarily for symptoms related to SARS-CoV-2. Rates of various perinatal outcomes were also identified, including preterm birth (<37 weeks' gestation), stillbirth (fetal death at ≥20 weeks' gestation), and mode of delivery.

Statistical Analysis

To overcome administrative challenges in sharing data at the time of this analysis, the coordinating center provided directions for Alberta to complete a local analysis with a parallel analysis program (ie, internal to the province); aggregated results were then sent to the coordinating center and combined with data from other provinces/territories for analysis. British Columbia, Alberta, Ontario, and Nova Scotia were able to submit complete provincial data for this analysis, whereas Manitoba and Quebec were able to submit only regional data (ie, from certain hospitals or parts of the province). Nova Scotia was able to provide data only for pregnancies completed up to April 30, 2021. Data sharing agreements between the coordinating center and the provincial centers required that no counts fewer than 6 be reported specifically due to privacy requirements. Due to differences in data entry, and sharing permissions, specific variables were not available for all pregnancies in all provinces, necessitating varying sample sizes among characteristics and outcomes described, as indicated in each table. Missing data were excluded from primary analyses. We conducted a sensitivity analysis using multiple imputation for all provinces except Alberta, where case-level data were unavailable.

All analyses were carried out using R version 4.1.1.[19] Outcomes were compiled monthly, and the proportion of events per month, out of the total number of cases identified in that month, were plotted over the time course of the data collection. The absolute and relative risks of hospitalization, oxygen therapy, and ICU admission were calculated by comorbidities and clinical/demographic factors (ie, body mass index [BMI; calculated as weight in kilograms divided by height in meters squared], preexisting hypertension, preexisting diabetes, asthma, maternal age, gestational age at diagnosis, and race and ethnicity) using mixed-effects log-binomial regression models with province as a random effect. Given the distributed nature of data collection, it was not possible to include covariates in these models. Relative risks compared with non–SARS-CoV-2–affected pregnancies were calculated for preeclampsia, cesarean delivery, preterm birth, and stillbirth using the exact method for confidence intervals. *P* values were calculated using χ^2 tests of 2 proportions. Statistical significance was set at $\alpha = .05$, and all testing was 2-sided. Because of the potential for type I error due to multiple comparisons, findings for these analyses should be interpreted as exploratory.

Results

As of October 31, 2021, there were 8786 cumulative SARS-CoV-2–affected pregnancies reported in Canada (eFigure 2 in Supplement 1). Of the 8786 cases, 6012 were completed pregnancies (loss or delivery) with data abstracted and entered for analysis. Of these, 638 were among individuals residing in British Columbia, 2651 in Alberta, 312 in Manitoba, 529 in Quebec, 1874 in Ontario, and 8 in Nova Scotia.

The mean age of pregnant individuals with SARS-CoV-2 infection was 31 years, with 2381 (39.7%) aged 30 to 35 years (**Table 1**). The most frequently documented race and ethnicity category was White (n = 767 [37.8%]), followed by South Asian (n = 374 [18.4%]), African, Black, or Caribbean (n = 245 [12.1%]), other (including Indigenous) (n = 240 [11.8%]), and East Asian or South East Asian (n = 169 [8.3%]). The race and ethnicity of pregnant SARS-CoV-2–positive individuals was statistically significantly different from the racial and ethnic proportions of the similarly aged Canadian female population as a whole (eTable 2 in Supplement 1). African, Black, or Caribbean; East Asian or South East Asian; South Asian; and other (including Indigenous) races and ethnicities were disproportionately represented among pregnant SARS-CoV-2–positive individuals in Canada. Specifically, there was a much higher proportion of non-White individuals (62%) among SARS-CoV-2–affected pregnancies compared with the general population (20%).[18] The proportion of African, Black, or Caribbean pregnant SARS-CoV-2–positive individuals was 12.1% despite comprising 2.2% of Canadian female individuals aged 15 to 49 years. A similar pattern was observed for East or South East Asian, South Asian, and other pregnant SARS-CoV-2–positive individuals.[18]

The greatest proportion of SARS-CoV-2 infections were diagnosed at 28 to 37 weeks' gestation (n = 2148 [35.7%]). One hundred and forty individuals (3.4%) had preexisting hypertension, 108 (2.6%) had type 1 or 2 diabetes, and 656 (24.3%) had a BMI greater than or equal to 30. During the time period of this analysis, before the Omicron variant, almost all cases of SARS-CoV-2 infection (98.7%) occurred among pregnant persons who had not been previously vaccinated. The characteristics described in Table 1 had less than 1% missing data, with the exception of BMI (data missing for 19.5%) and race and ethnicity (data missing for 39.6%).

Table 1. Demographic and Clinical Summaries for Pregnant Persons Diagnosed as Having SARS-CoV-2 Infection in Canada

Characteristics	Estimate
Age, y	
No. (%)	n = 5993
<30	2419 (40.4)
30-35	2381 (39.7)
≥36	1193 (19.9)
Median (IQR)[a]	31 (28-35) [n = 1418]
Race and ethnicity, No. (%)[b,c]	n = 2031
African, Black, or Caribbean	245 (12.1)
East Asian or Southeast Asian	169 (8.3)
Hispanic or Latinx	91 (4.5)
Middle Eastern	145 (7.1)
Other (including Indigenous)	240 (11.8)
South Asian	374 (18.4)
White	767 (37.8)
Gestational age at diagnosis, No. (%), wk	n = 5967
≤14	1080 (18.1)
15-27	2084 (34.9)
28-37	2148 (35.7)
≥38	666 (11.1)
Days between diagnosis and delivery, median (IQR)[b]	73 (20-140) [n = 3367]
Preexisting hypertension, No. (%)[d]	140 (3.4) [n = 4130]
Type 1 or 2 diabetes, No. (%)[d]	108 (2.6) [n = 4130]
Asthma, No. (%)[d]	147 (3.6) [n = 4130]
Body mass index, No. (%)[b]	n = 2711
<25	1285 (47.5)
25-29	764 (28.3)
≥30	656 (24.3)
Vaccination, No. (%)[b]	n = 3361
0 Doses	3318 (98.7)
1 Dose	28 (0.8)
≥2 Doses	15 (0.5)

[a] Data not available for Alberta and Ontario.

[b] Data not available for Alberta.

[c] Race and ethnicity data were collected by chart review and used specific categories. All possible categories are shown in the table, and "other" was an explicitly chosen category.

[d] Data not available for Ontario.

COVID-19 symptomatology was available for 4972 cases. Among these, only 850 individuals (17.1%) were asymptomatic at the time of testing, reflective of testing criteria within Canada almost exclusively being based on the presence of symptoms. The most common symptoms recorded were cough (n = 2420 [48.6%]) and fever (n = 1229 [24.7%]).

Adverse Maternal Outcomes

Non–SARS-CoV-2–related hospitalizations were excluded from this analysis. Among 6012 pregnancies with complete information about a SARS-CoV-2–related hospitalization or ICU admission, 466 (7.75%) had a hospitalization, 207 (3.4%) required oxygen therapy, and 121 (2.01%) had an ICU admission. When compared with female individuals aged 20 to 49 years in Canada diagnosed with SARS-CoV-2, patients with SARS-CoV-2 during pregnancy were at significantly increased risk of hospitalization (7.75% vs 2.93% [n = 9196]; difference, 4.82% [95% CI, 4.14%-5.50%]; relative risk, 2.65 [95% CI, 2.41-2.88]) and admission to the ICU (2.01% vs 0.37% [n = 1157]; difference, 1.64% [95% CI, 1.29%-2.00%]; relative risk, 5.46 [95% CI, 4.50-6.53]). None of the patients who had received at least 2 doses of a SARS-CoV-2 vaccine experienced any of the adverse maternal outcomes.

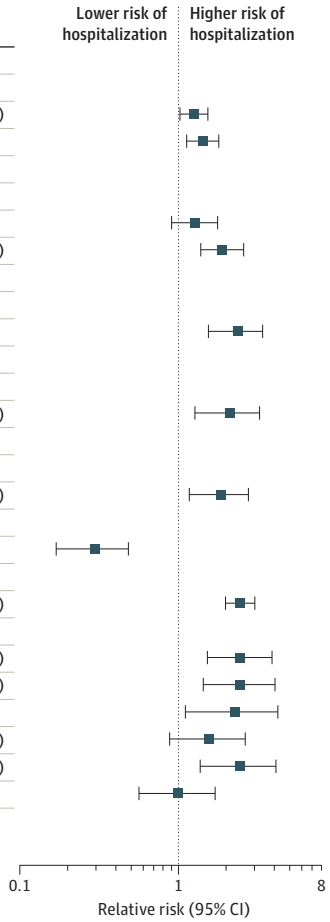
Risk Factors for Adverse Maternal Outcomes

Risk factors for severe maternal disease (hospitalization, ICU admission, and oxygen therapy) were analyzed using bivariable mixed-effects log-binomial regressions (**Figure 1** and **Figure 2**; eFigure 3 in Supplement 1). All models met the assumptions for binary logistic models, including linearity and noncomplete separation. Among pregnant SARS-CoV-2–positive individuals, increasing age was associated with a significantly increased risk of ICU admission (approximately 10% relative increase for each additional year of age). The presence of preexisting hypertension resulted in a significantly increased risk of requiring oxygen therapy (9.40% vs 3.19%; difference, 6.2% [95% CI, 2.4%-10.0%]; relative risk, 3.4 [95% CI, 2.0-5.4]). Greater gestational age at diagnosis was associated with a significantly greater risk of hospitalization and oxygen therapy; among infections diagnosed at 28 weeks' gestation or greater vs infections diagnosed at 15 to 27 weeks' gestation, the relative risk of hospitalization was 2.4 (95% CI, 2.0-3.0) (12.17% vs 4.99%, respectively; difference, 7.2% [95% CI, 5.6%-8.7%]) and the relative risk of oxygen therapy was 3.0 (95% CI, 2.1-4.3) (5.78% vs 1.87%, respectively; difference, 3.9% [95% CI, 2.9%-4.9%]). Body mass index, type 1 or 2 diabetes, asthma, and race and ethnicity were also significantly associated with increased risk of adverse maternal outcomes (Figure 1 and Figure 2; eFigure 3 in Supplement 1). Multiple-imputation analyses resulted in estimates that were very similar to those reported herein for the complete case analyses (eTable 3 in Supplement 1).

Among patients admitted to the hospital for SARS-CoV-2 infection in British Columbia, Manitoba, Ontario, Quebec, and Nova Scotia (n = 278), additional details pertaining to the hospitalization events were available. The median length of hospital stay (including ICU stay if applicable) was 6 days (IQR, 3-11 days; range, 1-180 days). The median length of ICU stay was 4 days (IQR, 2-11 days; range, 1-48 days). The median time between hospital admission and delivery was 34 days (IQR, 3-69 days). Forty-three cases (15.5%) involved overlapping admissions for SARS-CoV-2 infection and delivery. There were fewer than 6 cases with admission for SARS-CoV-2 infection at less than 1 week postpartum but in which the diagnosis had occurred during pregnancy. Among cases involving hospitalization, 18 pregnant individuals (6.5%) received steroid treatment for fetal lung maturation. Eighty-one hospitalized patients (29.1%) received corticosteroids as treatment for SARS-CoV-2 infection. Among patients who received corticosteroids in British Columbia, Manitoba, Quebec, or Nova Scotia (n = 55), 49 (89.1%) received dexamethasone. Other treatments administered included antivirals (<6 cases) and antibi-

Figure 1. Bivariable Log-Binomial Models of Relative Risks for Hospitalization

Variables	No. (%) of patients: Not hospitalized	Hospitalized	Absolute risk difference, % (95% CI)	Relative risk (95% CI)
Age, y				
<30	2262 (93.51)	157 (6.49)	[Reference]	1 [Reference]
30-35	2185 (91.77)	196 (8.23)	1.7 (0.3 to 3.2)	1.25 (1.02-1.53)
≥36	1082 (90.70)	111 (9.30)	2.8 (0.9 to 4.7)	1.42 (1.13-1.8)
Body mass index				
<25	1209 (94.23)	74 (5.77)	[Reference]	1 [Reference]
25-29	708 (92.67)	56 (7.33)	1.6 (-0.7 to 3.8)	1.26 (0.9-1.77)
≥30	585 (89.18)	71 (10.82)	5.1 (2.4 to 7.8)	1.89 (1.38-2.58)
Preexisting hypertension				
No	5343 (92.60)	427 (7.40)	[Reference]	1 [Reference]
Yes	197 (84.19)	37 (15.81)	8.4 (3.7 to 13.1)	2.36 (1.54-3.4)
Type 1 or 2 diabetes				
No	5309 (92.52)	429 (7.48)	[Reference]	1 [Reference]
Yes	231 (86.84)	35 (13.16)	5.7 (1.6 to 9.8)	2.12 (1.27-3.25)
Asthma				
No	3697 (92.82)	286 (7.18)	[Reference]	1 [Reference]
Yes	127 (86.39)	20 (13.61)	6.4 (0.8 to 12)	1.86 (1.17-2.76)
Gestational age at diagnosis, wk				
<14	1064 (98.52)	16 (1.48)	-3.5 (-4.7 to -2.3)	0.3 (0.17-0.48)
14-27	1980 (95.01)	104 (4.99)	[Reference]	1 [Reference]
≥28	2462 (87.83)	341 (12.17)	7.2 (5.6 to 8.7)	2.44 (1.98-3.03)
Race and ethnicity				
African, Black, or Caribbean	216 (88.16)	29 (11.84)	7 (2.7 to 11.3)	2.45 (1.52-3.89)
East Asian or Southeast Asian	149 (88.17)	20 (11.83)	7 (1.9 to 12.1)	2.45 (1.43-4.07)
Hispanic or Latinx	81 (89.01)	10 (10.99)	6.2 (-0.4 to 12.8)	2.28 (1.1-4.24)
Middle Eastern	128 (88.28)	17 (11.72)	6.9 (1.4 to 12.4)	1.55 (0.88-2.64)
Other (including Indigenous)	222 (92.50)	18 (7.50)	2.7 (-1 to 6.3)	2.43 (1.37-4.12)
South Asian	356 (95.19)	18 (4.81)	0 (-2.7 to 2.6)	1 (0.56-1.7)
White	730 (95.18)	37 (4.82)	[Reference]	1 [Reference]



Relative risks and 95% CIs from mixed-effects log-binomial regressions with province as a random effect. Body mass index is calculated as weight in kilograms divided by height in meters squared. See eFigure 3 in Supplement 1 for the model of relative risks for oxygen therapy.

otics (120 cases [43.2%]). Oxygen therapy was administered to 95 hospitalized patients (34.2%), and 52 (54.7%) of these patients were subsequently admitted to the ICU. Twenty-three patients (8.3%) received invasive mechanical ventilation and fewer than 6 received extracorporeal membrane oxygenation. There were a small number of maternal deaths (<6).

The proportion of identified cases that involved adverse maternal outcomes shifted over the course of the pandemic (**Figure 3**). After an initial peak in April 2020, monthly rates of hospitalization, ICU admission, and oxygen therapy remained steady until the second wave in fall 2020, when these rates increased slightly, followed by a rise in spring-summer 2021 during the third wave.

Adverse Perinatal Outcomes

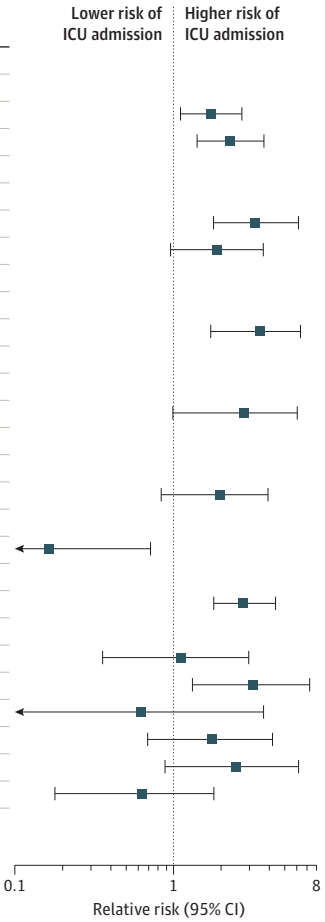
Rates of adverse perinatal outcomes among SARS-CoV-2–affected pregnancies are presented in **Table 2** and compared with Canadian national data on adverse pregnancy outcomes from CIHI-DAD during the pandemic period (March-September 2021), which excluded pregnancies affected by SARS-CoV-2. Rates of preeclampsia, cesarean delivery, and stillbirth did not differ significantly between SARS-CoV-2–affected and unaffected pregnancies in Canada. The rate of overall preterm birth (<37 weeks' gestation) among SARS-CoV-2–affected pregnancies was 11.1%, compared with 6.8% among all unaffected Canadian pregnancies (difference, 4.29% [95% CI, 3.48%-5.10%]; relative risk, 1.6 [95% CI, 1.5-1.8]). Of 175 preterm births with detailed delivery information, 46% were spontaneous and 54% were medically indicated. Preterm birth occurred at an elevated rate, even in cases of mild disease not requiring hospitalization (9.3%).

Discussion

In this Canadian surveillance study, SARS-CoV-2 infection during pregnancy was significantly associated with increased risk of adverse maternal outcomes and preterm birth. Risk of hospitalization and ICU admission was significantly higher among SARS-CoV-2–affected pregnancies compared with reproductive-age nonpregnant female individuals with SARS-CoV-2 infection in this study. The absolute risk increases were gener-

Figure 2. Bivariable Log-Binomial Models of Relative Risks for Intensive Care Unit (ICU) Admission

Variables	No. (%) of patients: Not admitted to ICU	No. (%) of patients: Admitted to ICU	Absolute risk difference, % (95% CI)	Relative risk (95% CI)
Age, y				
<30	2389 (98.76)	30 (1.24)	[Reference]	1 [Reference]
30-35	2327 (97.73)	54 (2.27)	1 (0.3 to 1.8)	1.71 (1.11-2.7)
≥36	1158 (97.07)	35 (2.93)	1.7 (0.6 to 2.7)	2.28 (1.41-3.72)
Body mass index				
<25	1267 (98.75)	16 (1.25)	[Reference]	1 [Reference]
25-29	746 (97.64)	18 (2.36)	1.1 (-0.1 to 2.3)	3.26 (1.79-6.15)
≥30	629 (95.88)	27 (4.12)	2.9 (1.2 to 4.5)	1.87 (0.96-3.69)
Preexisting hypertension				
No	5664 (98.16)	106 (1.84)	[Reference]	1 [Reference]
Yes	220 (94.02)	14 (5.98)	4.1 (1.1 to 7.2)	3.5 (1.72-6.34)
Type 1 or 2 diabetes				
No	5630 (98.12)	108 (1.88)	[Reference]	1 [Reference]
Yes	254 (95.49)	12 (4.51)	2.6 (0.1 to 5.1)	2.78 (0.99-6.05)
Asthma				
No	3908 (98.12)	75 (1.88)	[Reference]	1 [Reference]
Yes	140 (95.24)	7 (4.76)	2.9 (-0.6 to 6.3)	1.98 (0.84-3.95)
Gestational age at diagnosis, wk				
<14	1078 (99.81)	2 (0.19)	-1 (-1.5 to -0.4)	0.16 (0.03-0.55)
14-27	2060 (98.85)	24 (1.15)	[Reference]	1 [Reference]
≥28	2709 (96.65)	94 (3.35)	2.2 (1.4 to 3)	2.76 (1.79-4.41)
Race and ethnicity				
African, Black, or Caribbean	240 (97.96)	5 (2.04)	0.3 (-1.6 to 2.3)	1.12 (0.36-2.99)
East Asian or Southeast Asian	160 (94.67)	9 (5.33)	3.6 (0.1 to 7.1)	3.16 (1.32-7.24)
Hispanic or Latinx	90 (98.90)	1 (1.10)	-0.6 (-2.9 to 1.7)	0.62 (0.03-3.08)
Middle Eastern	139 (95.86)	6 (4.14)	2.4 (-0.9 to 5.8)	1.76 (0.69-4.22)
Other (including Indigenous)	232 (96.67)	8 (3.33)	1.6 (-0.8 to 4.1)	2.48 (0.88-6.16)
South Asian	370 (98.93)	4 (1.07)	-0.6 (-2 to 0.8)	0.63 (0.18-1.8)
White	754 (98.31)	13 (1.69)	[Reference]	1 [Reference]



Relative risks and 95% CIs from mixed-effects log-binomial regressions with province as a random effect. Body mass index is calculated as weight in kilograms divided by height in meters squared. See eFigure 3 in Supplement 1 for the model of relative risks for oxygen therapy.

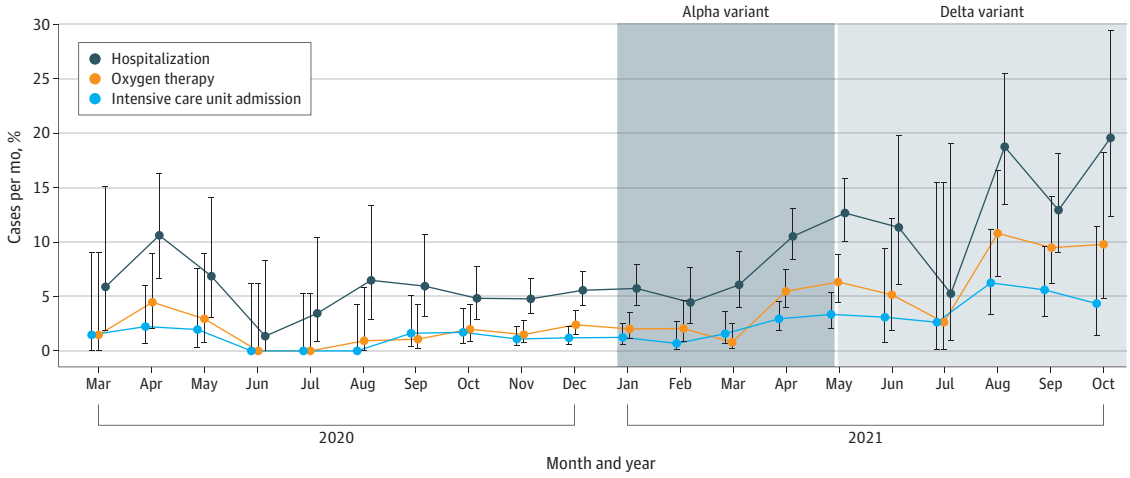
ally not large, but information about relative risks can help inform clinical and public health practice.

This finding is consistent with a Norwegian population-level analysis (hazard ratio for hospitalization, 4.70 [95% CI, 3.51-6.30]),[20] US surveillance reports that have documented a higher risk of admission to the ICU among pregnant individuals with SARS-CoV-2 infection (adjusted relative risk, 3.0 [95% CI, 2.6-3.4]),[6] and an international living systematic review and meta-analysis in which an increased risk of ICU admission was observed (odds ratio, 2.13 [95% CI, 1.53-2.95]).[7] Although some studies have reported that pregnant persons with SARS-CoV-2 infection had higher rates of preeclampsia,[8,9] this was not observed in the Canadian context. Similarly, the literature has been mixed in regard to differential rates of cesarean delivery and stillbirth among SARS-CoV-2–affected pregnancies[9-11,14]; the present study did not find a significantly higher rate of stillbirth. Statistically significant variables associated with severe outcomes related to SARS-CoV-2 infection identified through this study by bivariate analysis included increasing age, non-White race and ethnicity, BMI of 30 or greater, presence of preexisting hypertension, presence of preexisting diabetes, asthma, and greater gestational age at diagnosis.

Compared with the similarly aged Canadian female population, the racial and ethnic distribution of SARS-CoV-2 cases during pregnancy was statistically significantly different. This finding may be the result of a complex interplay of factors affecting ethnic minority Canadian communities that persist despite the presence of a public health care system. The observed differences should be explored further in future analyses.

This surveillance program documented changing proportions of adverse maternal outcomes among identified cases over time. The rise in the proportion of cases of severe disease in the spring and summer of 2021 may reflect the effect of viral variant emergence on pregnant populations. Based on Canadian epidemiology, the first confirmed case of the Alpha variant (B.1.1.7) was identified on December 25, 2020. The first confirmed cases of the Delta variant (B.1.617.2) were identified on April 21, 2021, and shortly thereafter it became the dominant variant until November-December 2021.[21] The increasing rates of adverse maternal outcomes concurrent with the emergence of the Delta vari-

Figure 3. Adverse Maternal Outcomes Associated With SARS-CoV-2 Diagnosis in Pregnancy From March 1, 2020, to October 31, 2021 (N = 6012)



Total No. of SARS-CoV-2 cases by month	68	179	102	74	87	108	185	352	732	916	645	292	379	713	537	97	38	176	232	92

Points are offset a small amount along the x-axis for visualization. Whiskers show 95% CI from binomial tests using a χ^2 approximation. Eight completed pregnancies with missing dates are not included.

Table 2. Adverse Pregnancy Outcomes Among Pregnant Persons Diagnosed as Having SARS-CoV-2 During the Pandemic Compared With Pregnant Persons Not Diagnosed as Having SARS-CoV-2 in Canada

Outcomes	No./total (%)		Absolute risk difference (95% CI)	Relative risk (95% CI)	*P* value
	Persons with SARS-CoV-2 diagnosed during pregnancy[a]	Persons without SARS-CoV-2 diagnosed during pregnancy[b]			
Preeclampsia[c]	91/1260 (7.22)	33201/428 813 (7.74)	−0.52 (−1.95 to 0.91)	0.93 (0.75-1.12)	.53
Cesarean delivery	1965/5696 (34.50)	138 918/428 813 (32.40)	2.10 (0.86 to 3.34)	1.06 (1.03-1.10)	.001
Preterm delivery <37 wk[d]	635/5746 (11.05)	28 394/419 937 (6.76)	4.29 (3.48 to 5.10)	1.63 (1.52-1.76)	<.001
Late preterm (34-36 wk)	480 (8.35)	21 638 (5.15)	3.20 (2.48 to 3.92)	1.62 (1.48-1.76)	<.001
Moderate preterm (32-33 wk)	84 (1.46)	2957 (0.70)	0.86 (0.45 to 1.07)	2.08 (1.64-2.53)	<.001
Very preterm (28-31 wk)	41 (0.71)	2269 (0.54)	0.17 (−0.05 to 0.39)	1.32 (0.93-1.74)	.08
Extremely preterm (20-27 wk)	30 (0.52)	1530 (0.36)	0.16 (−0.03 to 0.34)	1.43 (0.95-1.97)	.60
Stillbirth[e]	35/5743 (0.61)	3695/443 184 (0.83)	−0.22 (−0.43 to −0.02)	0.73 (0.50-0.99)	.07

[a] From the Canadian Surveillance of COVID-19 in Pregnancy (CANCOVID-Preg) program.

[b] From the Canadian Institute for Health Information Discharge Abstract Database.

[c] Data not available from Alberta and Ontario.

[d] Not including stillbirth or intrauterine fetal demise among the total number of fetuses in pregnancies continuing for 20 weeks or longer.

[e] Among the total number of fetuses in pregnancies continuing for 20 weeks or longer or weighing at least 500 g. Includes intrauterine and intrapartum fetal demise. Does not include neonatal mortality.

ant in Canada are consistent with findings internationally.[22] These associations can only be inferred based on the circulating variants in each time period, as individual cases did not have specific variant information available.

Preterm birth was more likely in pregnancies affected by SARS-CoV-2 compared with unaffected pregnancies during the same time frame, even among cases involving milder forms of infection. Although a prior population-based study in 1 Canadian province did not find a difference between preterm birth rates before and during the COVID-19 pandemic,[23] to our knowledge, no study in Canada has looked specifically at pregnancies affected by SARS-CoV-2 and compared the rates of preterm birth in these known cases with SARS-CoV-2–unaffected pregnancies during the pandemic period. Increased risk of preterm birth in the context of SARS-CoV-2 infection has also been documented in other international settings, including the United Kingdom and the Nordic countries.[8,9,14,24]

Strengths of this study include the surveillance approach taken, which approximates population-level data, reducing the potential for selection bias. Unlike other studies that have solely relied on the identification of infection at delivery and miss cases that resolve during pregnancy, this study captured SARS-CoV-2 infections throughout gestation.[25] Additionally, this analysis was able to compare cumulative incidence of pregnancy and birth outcomes from a comprehensive cohort of SARS-CoV-2–affected pregnancies with national-level data on all pregnancies to quan-

tify the differential risks of pregnancy outcomes associated with SARS-CoV-2.

Limitations

This study has several limitations. First, for some of the analyses, there were challenges in obtaining complete national data on SARS-CoV-2–affected pregnancies due to the complexities of data sharing between provinces and territories. Second, most analyses in this study used crude comparisons without adjustment because of a lack of detailed individual-level data. With the inability to perform multivariable analyses, significant associations should not be interpreted as representing independent risk factors. Third, there was substantial missingness for both BMI and race and ethnicity. However, multiple imputation resulted in similar results. Fourth, this data set included pregnancies among SARS-CoV-2–positive individuals only. Fifth, given that the analyses were limited to cases prior to identification of the Omicron variant in Canada, the results cannot be assumed to be generalizable to infections caused by the Omicron variant.

Conclusions

In this exploratory surveillance study conducted in Canada from March 2020 to October 2021, SARS-CoV-2 infection during pregnancy was significantly associated with increased risk of adverse maternal outcomes and preterm birth.

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REFERENCES

1. Wong SF, Chow KM, Leung TN, et al. Pregnancy and perinatal outcomes of women with severe acute respiratory syndrome. *Am J Obstet Gynecol*. 2004;191(1):292-297. doi:10.1016/j.ajog.2003.11.019

2. Shek CC, Ng PC, Fung GPG, et al. Infants born to mothers with severe acute respiratory syndrome. *Pediatrics*. 2003;112(4):e254-e254. doi:10.1542/peds.112.4.e254

3. Rasmussen SA, Smulian JC, Lednicky JA, Wen TS, Jamieson DJ. Coronavirus disease 2019 (COVID-19) and pregnancy: what obstetricians need to know. *Am J Obstet Gynecol*. 2020;222(5):415-426. doi:10.1016/j.ajog.2020.02.017

4. Siston AM, Rasmussen SA, Honein MA, et al; Pandemic H1N1 Influenza in Pregnancy Working Group. Pandemic 2009 influenza A(H1N1) virus illness among pregnant women in the United States. *JAMA*. 2010;303(15):1517-1525. doi:10.1001/jama.2010.479

5. Mosby LG, Rasmussen SA, Jamieson DJ. 2009 pandemic influenza A (H1N1) in pregnancy: a systematic review of the literature. *Am J Obstet Gynecol*. 2011;205(1):10-18. doi:10.1016/j.ajog.2010.12.033

6. Zambrano LD, Ellington S, Strid P, et al; CDC COVID-19 Response Pregnancy and Infant Linked Outcomes Team. Update: characteristics of symptomatic women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status—United States, January 22-October 3, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(44):1641-1647. doi:10.15585/mmwr.mm6944e3

7. Allotey J, Stallings E, Bonet M, et al; PregCOV-19 Living Systematic Review Consortium. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ*. 2020;370:m3320-m3320. doi:10.1136/bmj.m3320

8. Villar J, Ariff S, Gunier RB, et al. Maternal and neonatal morbidity and mortality among pregnant women with and without COVID-19 infection: the INTERCOVID multinational cohort study. *JAMA Pediatr*. 2021;175(8):817-826. doi:10.1001/jamapediatrics.2021.1050

9. Mullins E, Hudak ML, Banerjee J, et al; PAN-COVID Investigators and National Perinatal COVID-19 Registry Study Group. Pregnancy and neonatal outcomes of COVID-19: coreporting of common outcomes from PAN-COVID and AAP-SONPM registries. *Ultrasound Obstet Gynecol*. 2021;57(4):573-581. doi:10.1002/uog.23619

10. Chmielewska B, Barratt I, Townsend R, et al. Effects of the COVID-19 pandemic on maternal and perinatal outcomes: a systematic review and meta-analysis. *Lancet Glob Health*. 2021;9(6):e759-e772. doi:10.1016/S2214-109X(21)00079-6

11. Mark EG, McAleese S, Golden WC, et al. Coronavirus disease 2019 in pregnancy and outcomes among pregnant women and neonates: a literature review. *Pediatr Infect Dis J*. 2021;40(5):473-478. doi:10.1097/INF.0000000000003102

12. Qeadan F, Mensah NA, Tingey B, Stanford JB. The risk of clinical complications and death among pregnant women with COVID-19 in the Cerner COVID-19 cohort: a retrospective analysis. *BMC Pregnancy Childbirth*. 2021;21(1):305-305. doi:10.1186/s12884-021-03772-y

13. Smith ER, He S, Oakley E, Miller L, Tielsch JM. Protocol for a sequential, prospective meta-analysis to describe COVID-19 in pregnancy and newborn periods. *medRxiv*. Preprint posted November 12, 2020. doi:10.1101/2020.11.08.20228056

14. Engjom H, Aabakke AJM, Klungsøyr K, et al. COVID-19 in pregnancy-characteristics and outcomes of pregnant women admitted to hospital because of SARS-CoV-2 infection in the Nordic countries. *Acta Obstet Gynecol Scand*. 2021;100(9):1611-1619. doi:10.1111/aogs.14160

15. Aabakke AJM, Krebs L, Petersen TG, et al. SARS-CoV-2 infection in pregnancy in Denmark-characteristics and outcomes after confirmed infection in pregnancy: a nationwide, prospective, population-based cohort study. *Acta Obstet Gynecol Scand*. 2021;100(11):2097-2110. doi:10.1111/aogs.14252

16. Dunn S, Lanes A, Sprague AE, et al. Data accuracy in the Ontario Birth Registry: a chart re-abstraction study. *BMC Health Serv Res*. 2019;19(1):1001. doi:10.1186/s12913-019-4825-3

17. Statistics Canada. *Preliminary Dataset on Confirmed Cases of COVID-19*. Public Health Agency of Canada; 2021.

18. *2016 Census of Population*. Statistics Canada; 2018.

19. R Core Team. *R: A Language and Environment for Statistical Computing*. R Foundation for Statistical Computing; 2021.

20. Magnus MC, Oakley L, Gjessing HK, et al. Pregnancy and risk of COVID-19: a Norwegian registry-linkage study. *BJOG*. 2022;129(1):101-109. doi:10.1111/1471-0528.16969

21. National Collaborating Centre for Infectious Diseases. Updates on COVID-19 variants of concern. Accessed October 17, 2021. https://nccid.ca/covid-19-variants/

22. Vousden N, Ramakrishnan R, Bunch K, et al. Impact of SARS-CoV-2 variant on the severity of maternal infection and perinatal outcomes: data from the UK Obstetric Surveillance System national cohort. *medRxiv*. Preprint posted July 25, 2021. doi:10.1101/2021.07.22.21261000

23. Shah PS, Ye XY, Yang J, Campitelli MA. Preterm birth and stillbirth rates during the COVID-19 pandemic: a population-based cohort study. *CMAJ*. 2021;193(30):E1164-E1172. doi:10.1503/cmaj.210081

24. Woodworth KR, Olsen EOM, Neelam V, et al; CDC COVID-19 Response Pregnancy and Infant Linked Outcomes Team. Birth and infant outcomes following laboratory-confirmed SARS-CoV-2 infection in pregnancy—SET-NET, 16 jurisdictions, March 29-October 14, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(44):1635-1640. doi:10.15585/mmwr.mm6944e2

25. Palmsten K, Vazquez-Benitez G, Kharbanda EO. Point: uncertainty about estimating the risks of COVID-19 during pregnancy. *Paediatr Perinat Epidemiol*. 2021;00:1-3. doi:10.1111/ppe.12773