CANADIAN SURVEILLANCE OF COVID-19 IN PREGNANCY: EPIDEMIOLOGY, MATERNAL AND INFANT OUTCOMES

Report #4: Released June 3rd, 2021

Maternal and Infant Outcomes (March 1, 2020 to March 31, 2021) from Five Canadian Provinces

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(see appendix 1 for list of collaborators)

Funders: Public Health Agency of Canada, the Canadian Institutes for Health Research, the Better Outcomes Registry & Network Ontario and the BC Women's Health Foundation

BACKGROUND

It has been more than a year since the first case of SARS-CoV-2 (COVID-19) infection was documented. Now, with new variants of concern (VOC) and a third wave spreading both nationally and internationally, there is an even greater need for current data to inform clinical guidance and vaccine-related recommendations for priority populations such as pregnant persons. Globally, as of March 31st, 2021 there were more than 120 million cumulative cases of COVID-19 and more than 2.5 million related-deaths.[1] In Canada, since the start of the pandemic, there have been 976,598 cases of COVID-19 and 22,926 deaths.[2]

Three interim reports have been previously released by the Canadian Surveillance of COVID-19 in Pregnancy: Epidemiology, Maternal and Infant Outcomes (CANCOVID-Preg) team. With only a subset of Canadian data, each of the aforementioned reports highlighted increased rates of hospitalization and admission to the intensive care unit (ICU) among pregnant persons diagnosed with COVID-19.[3-5] A growing number of international reports corroborate our Canadian findings.[6-11] For example, a living systematic review found that the odds of admission to an intensive care unit (pooled odds ratio [OR] 2.13, 95% confidence interval [CI]: 1.53 - 2.95; I2=71.2%), invasive ventilation (pooled OR 2.59, 95% CI: 2.28 - 2.94; I2=0%) and need for extracorporeal membrane oxygenation (ECMO) (pooled OR 2.02, 95% CI: 1.22 - 3.34; I2=0%) were higher in pregnant compared to non-pregnant persons.[11]

The last three CANCOVID-Preg reports also described increased frequency of preterm birth and admission to the neonatal intensive care unit (NICU) among pregnant persons with COVID-19 and their infants, compared with usual background rates.[3-5] Consistent with CANCOVID-Preg findings, a prospective, longitudinal, observational study, involving 43 hospitals in 18 countries, found an increased risk of preterm birth (risk ratio [RR] 1.59, 95% CI: 1.30 - 1.94) among pregnant populations diagnosed with COVID-19.[7] The living systematic review, mentioned above, also found that in pregnant persons with COVID-19, the overall rate of preterm birth was 17% (95% CI: 14% - 19%; 70 studies, 9369 pregnant persons) and 33% (95% CI: 24% - 43%; 41 studies, 3323 pregnant persons) of neonates born were admitted to the NICU.[11]

Analogous to the last three CANCOVID-Preg reports, Report #4 continues to add to the growing body of evidence suggesting that pregnant persons and their infants are at increased risk of adverse outcomes related to COVID-19.[6-12] This report highlights preliminary findings from five provinces [British Columbia (BC), Ontario (ON), Manitoba (MB) and Quebec (QC), and Alberta (AB)], participating in CANCOVID-Preg. On behalf of public health officials, with support from the Public Health Agency of Canada, the Canadian Institutes for Health Research, the Better Outcomes Registry & Network (BORN) Ontario, and the BC Women's Health Foundation, this national, prospective, surveillance project was initiated in order to monitor pregnant persons during the pandemic and assess both maternal and infant outcomes related to COVID-19. This national surveillance initiative is supported by central coordination at the University of British Columbia, based at the Women's Health Research Institute in Vancouver, BC.

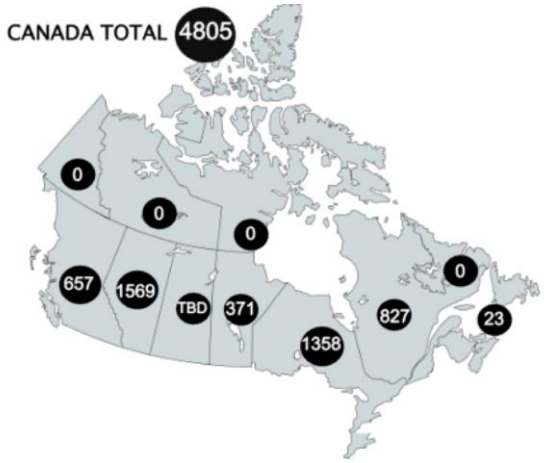
METHODS

Data on laboratory-confirmed (SARS-CoV-2 PCR positive) COVID-19 affected pregnancies were electronically reported to the CANCOVID-Preg team in each province by provincial public health agencies. For BC, MB, QC, and AB, clinical information was abstracted from medical records for affected pregnancies and entered directly into a Research Electronic Data Capture (REDCap) database, which utilizes a robust data confidentiality and security protocol. MB required interprovincial data sharing agreements with each participating hospital/centre in order to enter data into REDCap to be shared with the coordinating centre. Amalgamated data from MB is therefore only provided for data that is governed by a fully executed data sharing agreement. In ON, data were entered at the point of care into a data collection tool and securely transferred to the BORN Information System (where it was linked with the corresponding pregnancy or birth record). Public health laboratory notifications were also submitted to BORN Ontario for linkage to the BORN Information System. Like our previous reports, only high-level summary data were amalgamated (manuscript in preparation). Given the rapidly evolving nature of the pandemic, and the implications that these data have for pregnant populations in Canada, the CANCOVID-Preg Investigative Team resolved to release a series of early interim reports. Of note, the data for this report were censored at March 31st, 2021.

Of the total number of cases known in Canada at the time of this report (4805), available subset data (BC, ON, MB, QC, and AB) for 3678 pregnant positive cases (76.5% of the total number of cases reported to CANCOVID-Preg), from March 1st, 2020 to March 31st, 2021 were amalgamated for this report. We were unable to include the remaining 1127 cases (23.5%) in this report for a few reasons. Firstly, some provinces were unable to enter data into a database without a fully executed data sharing agreement. Also, there is often a time delay between knowledge of a case in pregnancy and entering data for that case. Finally, data on a COVID-19 event may precede data on pregnancy and infant outcomes based on time needing to pass for these events to conclude. Certain data elements were therefore missing or incomplete for some cases leading to varying denominators in the tables below, reflecting those cases for which the information in question was available. After combining provincial data, cells with less than 6 observations were reported as <6, as per privacy requirements.

RESULTS

As of March 31st, 2021, there were 4805 cumulative, pregnant persons with COVID-19 in Canada reported to CANCOVID-Preg (Figure 1).



Last updated
British Columbia: Mar 29, 2021
Alberta: Mar 31, 2021
Saskatchewan: TBD/Nov 11, 2020
Manitoba: Mar 31, 2021
Ontario: Mar 31, 2021
Quebec: Dec 14, 2020
Nova Scotia, New Brunswick and Prince Edward Island: Mar 10, 2021
Newfoundland: Mar 10, 2021
Yukon: Mar 10, 2021
North West Territories: Mar 10, 2021
Nunavut: N/A

FIGURE 1. Number of confirmed pregnant, COVID-19 positive persons in Canada (as of March 31, 2021) reported to CANCOVID-Preg. Saskatchewan has not been included in the total calculation as this site has been unable to provide case numbers to date. NS, NB, and PEI have been combined (n=23) due to small samples sizes and Quebec has not reported since December, 2020.

Table 1 provides crude COVID-19 incidence rates per 1000 pregnancies by province, compared to the general population of all females aged 20-49 (shown visually in Figure 2).[13-18] Although we cannot determine risk of COVID-19 acquisition among pregnant perons from these data, compared to the general population, infection rates appear to be lower among pregnant persons in every province noted below.

TABLE 1. Infection rates in pregnant population and total female population by province (as of March 31st, 2021)

Province	Births in 2019[1]	Corrected births to Mar 31	Pregnant cases[2]	COVID+/1000 pregnant	lower CI	upper CI	Total pop female 20-49[3]	Total cases[4]	COVID+/1000 total	lower CI total	upper CI total
BC	43878	47605	657	13.8	12.8	14.9	1019652	27251	26.7	26.4	27.0
AB	51690	56080	1569	28.0	26.6	29.4	933041	38945	41.7	41.3	42.1
ON	140541	152477	1358	8.9	8.4	9.4	2944223	88059	29.9	29.7	30.1
MB	16500	17901	371	20.7	18.7	22.9	271461	18270	67.3	66.4	68.3

[1] Data Source: Reference 13
[2] Data Source: CANCOVID-Preg (Figure 1 above).
[3] Data Source: Reference 14
[4] Data Source: References 15 through 18
[5] Quebec data not available

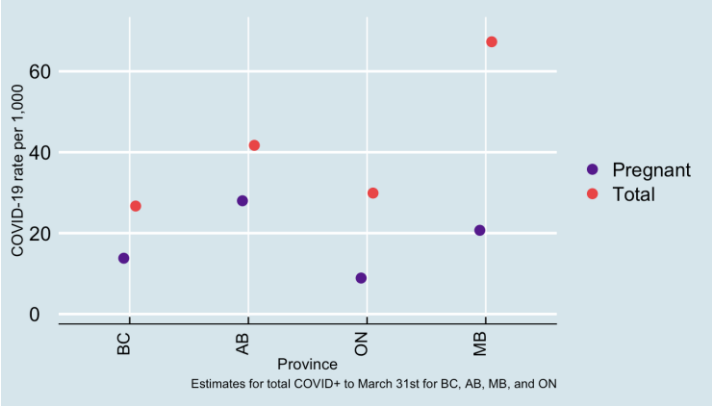


FIGURE 2. Infection rates in pregnant population and total female population by province (as of March 31st, 2021). Confidence intervals seen in Table 1.

Of the 4805 total COVID-19 cases reported, we have at least some outcome data for 3678 cases (76.5%) and these cases are the focus of the remaining tables in this report. Of these, 487 resided in BC, 1358 in ON, 182 in QC, 82 in MB, 1569 in AB. Among pregnant positive persons, 37.5% were between 30 and 34 years of age. Most cases were diagnosed between 14 and 27 weeks' gestation (40.1%), with infection most often acquired via the community-at-large (43.7%). Obesity was the most common underlying condition (12.9%), followed by diabetes (which includes type 1, type 2, and gestational) (11.2%) and cardiovascular disease (which includes hypertension, arrhythmia, and valve conditions) (3.3%) (Table 2).

Table 2. Maternal characteristics from March 1st, 2020 to March 31st, 2021 in BC, ON, QC, MB, and AB

	n	denominator	percent
Gestational age at diagnosis (weeks)			
<14	723	3461	20.9
14-27	1388	3461	40.1
28-38	1092	3461	31.6
>38	258	3461	7.5
Maternal age (years)			
<25	347	3786	9.2
25-30	1119	3786	29.6
30-34	1420	3786	37.5
35-39	728	3786	19.2
>=40	172	3786	4.5
Maternal underlying conditions[1]			
Cardiovascular disease (hypertension, arrhythmia, valve conditions)	72	2172	3.3
Chronic lung disease	<6	2172	N/A
Diabetes mellitus (type 1, type 2, gestational)	244	2172	11.2
Hypertension (chronic and/or gestational)	60	2172	2.8
Immunosuppression	<6	2172	N/A
Obesity (BMI ≥30kg/m2)	281	2172	12.9
Mode of COVID-19 acquisition[1]			
Community	388	888	43.7
Healthcare worker	130	888	14.6
Other	104	888	11.7
Travel	22	888	2.5
Unknown	197	888	22.2

[1] Categories are not mutually exclusive

The most common symptoms associated with a positive COVID-19 diagnosis during pregnancy were cough (38.5%), fever (27.1%), headache (25.6%) and rhinitis (25.5%). Further to this, 8% were asymptomatic (Table 3).

TABLE 3. Maternal COVID-19 symptomatology among n=1791 pregnant positive cases from March 1st, 2020 to March 31st, 2021 in BC, ON, QC, MB, and AB

Symptom[1]	n	Denominator	Percent
Cough	690	1791	38.5
Fever	486	1791	27.1
Headache	458	1791	25.6
Rhinitis	457	1791	25.5
Sore throat	357	1791	19.9
Myalgia	345	1791	19.3
Shortness of breath	278	1791	15.5
Malaise	266	1791	14.9
Anosmia/Ageusia	263	1791	14.7
Nausea/Vomiting	162	1791	9.0
Asymptomatic	143	1791	8.0
Anorexia	123	1791	6.9
Diarrhea	93	1791	5.2
Other	85	1791	4.7
Chest pain	63	1791	3.5

[1] Categories are not mutually exclusive

Among the 1334 persons with complete information about any COVID-19 related hospitalization or ICU admission, 7.1% were hospitalized and 2.8% were admitted to the ICU (Table 4). Non-COVID-19 related hospitalizations have not been included. Notably, compared to their non-pregnant counterparts (females 18-45 years of age who contracted COVID-19), those with COVID-19 during pregnancy were at increased risk of being hospitalized (RR 4.26, 95% CI: 3.45 - 5.10). Of those hospitalized, there was also a higher proportion of infected pregnant individuals admitted to the ICU, relative to infected non-pregnant counterparts (RR 2.68, 95% CI: 2.02 - 3.40) (Table 5).

TABLE 4. Maternal COVID-19 hospitalizations/interventions from March 1st, 2020 to March 31st, 2021 in BC, ON, MB, and QC[1]

Features/Interventions	n	denominator	percent
Hospitalized	95	1334	7.1
Abnormal X-ray or pneumonia	78	1334	5.8
ICU admission	38	1334	2.8
Oxygen	38	1334	2.8
Mechanical ventilation/ECMO	10	1334	0.7
Coagulopathy/sepsis	8	1368	0.6

[1] AB data not included

TABLE 5. COVID-19-related hospitalizations and ICU admissions among pregnant COVID-19 positive persons (18-45 years) in BC, ON, MB, and QC compared to non-pregnant COVID-19 positive females (18-45 years)

	Pregnant positive persons (n=1334) in BC, ON[1], MB, and QC[3]	Non-pregnant positive persons in BC, ON, MB, QC (n=235473)[2]	RR	95% CI
Number and percent hospitalized	95 (7.12%)	3941 (1.53%)	4.26	3.45 to 5.10
Number and percent admitted to ICU	38 (2.50%)	589 (0.25%)	11.39	7.90 to 15.21
Percent admitted to ICU of those hospitalized	40.00%	14.95%	2.68	2.02 to 3.40

[1]Hospital and ICU admission data for ON came from Case Contact Management (CCM) System
[2]Data Sources include: the BC Centre for Disease Control (BC), Case Contact Management (CCM) System (ON), Government of Manitoba (MB), Government of Quebec (QC) [15, 17-19]
[3] AB data not included

Of the reported pregnancy outcomes, 97.4% were live births and 1.0% were stillbirths. Among the 1769 cases with delivery and gestational age data, 87.1% occurred at term and 12.9% at preterm gestation (Table 6). Of 228 preterm births, 34.6% were medically indicated, 39.9% were spontaneous, and 25.4% were missing information on clinical subtype (Table 7).

TABLE 6. Pregnancy outcomes from March 1st, 2020 to March 31st, 2021 in BC, ON, MB, QC, and AB

	n	denominator	percent
Gravidity			
1	455	1568	29.0
≥2	1113	1568	71.0
Multiple pregnancy			
Multiple	30	1661	1.8
Singleton	1631	1661	98.2
Pregnancy outcome (n=all infants)			
Live birth	1774	1821	97.4
SA	28	1821	1.5
Stillbirth (≥20 weeks GA)	19	1821	1.0
Mode of delivery			
Cesearean section	597	1629	36.6
Vaginal	1032	1629	63.4
Labour			
Induced	552	1524	36.2
No labour	272	1524	17.8
Spontaneous	700	1524	45.9
GA at delivery (n=live births + stillbirths)			
Term	1541	1769	87.1
Preterm (<37 weeks)	228	1769	12.9
Late preterm (34-36 weeks)	155	1769	8.8
Moderate preterm (32-33 weeks)	23	1769	1.3
Very preterm (28-31 weeks)	21	1769	1.2
Extremely preterm (<28 weeks)	29	1769	1.6

TABLE 7. Preterm birth subtypes in ON, BC, MB, QC, and AB

	n	denominator	percent
Medically indicated	79	228	34.6
Spontaneous	91	228	39.9
Missing	58	228	25.4

The majority of infants (82.6%) were in the normal range for birth weight (i.e., 2500-4000 grams) and 15.2% were admitted to the NICU (Table 8). To date, 237 infants were tested for SARS-CoV-2 infection, and <6 nasopharyngeal swabs indicated a positive result (Table 9).

TABLE 8. Infant outcomes from March 1, 2020 to March 31, 2021 in BC, ON, MB, QC, and AB

	n	denominator	percent
Apgar (5 minutes)			
<7	35	1133	3.1
≥7	1098	1133	96.9
Birth weight (g)			
Low (<2500 g)	154	1559	9.9
Normal (2500-4000 g)	1287	1559	82.6
High (>4000 g)	118	1559	7.6
NICU admission			
No	1115	1315	84.8
Yes	200	1315	15.2
Small for gestational age (SGA)			

No	1052	1179	89.2
Yes	127	1179	10.8

TABLE 9. Infant SARS-CoV-2 PCR testing March 1, 2020 to March 31, 2021 for BC, ON, MB, QC, and AB

	n[1]	percent
Result pending	6	2.6
Negative	223	95.7
Positive	<6	N/A

[1] The denominator has been removed to prevent the ability to derive the number of positive results, as per our data and privacy obligations.

DISCUSSION

This fourth CANCOVID-Preg report presents ongoing surveillance of the burden of COVID-19 on pregnancy in Canada. These data provide useful information for counseling pregnant persons and their care providers and can be used to inform evidence-based COVID-19 vaccine access decisions.

The findings in this report were consistent with the last three CANCOVID-Preg reports.[3-5] Notably, although the absolute risk is low, compared to their non-pregnant counterparts, persons aged 18-45 who contracted COVID-19 during pregnancy were at increased risk of being hospitalized (RR 4.26, 95% CI: 3.45 - 5.10). Of those hospitalized for COVID-19, there was also a higher a proportion of pregnant individuals admitted to the ICU, relative to non-pregnant counterparts (RR 2.68, 95% CI: 2.02 - 3.40) (Table 5). Increased risk may be related to physiological and immunological changes that occur during pregnancy, resulting in a greater predisposition and susceptibility to more severe consequences of infection.[20] Increased risk of hospitalization may also be related to care provider anxiety and heightened vigilance/caution regarding the clinical care of pregnant perons during a pandemic. However, Table 5 provides an estimate of the number and percent admitted to ICU as well as the proportion of those hospitalized who were admitted to ICU. These findings suggest that that pregnant persons with COVID-19 may require higher levels of care.

Similar to findings reported by the US CDC and a living systematic review of COVID-19 in pregnancy, we found 13.1% of our sample were born preterm.[11,12] The rates of NICU admission in our data were in keeping with rates of prematurity (15.2%). Infant SARS-CoV-2 testing was infrequent in the five Canadian provinces that provided outcome data; however, among infants known to be tested, the majority were negative. This finding supports the growing body of evidence that perinatal infection is uncommon. Importantly, in this sample, stillbirth rates were 10.6 per 1000 (95% CI: 6.6% - 16.8%) compared to 5.44 per 1000 (95% CI: 5.1% - 5.7%) in the general population (derived from CIHI-DAD 2020 data). Although the stillbirth estimate in our COVID-19 positive cases is slightly higher than the general population, the absolute numbers are still quite small.

Limitations

These interim analyses are subject to a number of limitations. First, only five provinces were able to participate in this subset; results are therefore not representative of the entire Canadian context. Subsequent analyses will be conducted using individual-level data and additional provincial/territorial representation for a more comprehensive understanding of the national burden of COVID-19 in pregnancy. In addition, for a number of outcomes, cell sizes were too small to draw meaningful conclusions. Lastly, although the CANCOVID-Preg team recently started capturing data on variants of concern (VOC) and infection following vaccination, these variables were not collected prior to the

March 31st, 2021 cutoff for Report #4. VOC and infection following vaccination will therefore be presented in our next analysis.

Conclusion

Despite limitations, this interim report can be used to inform public policy and continue to inform evidence-based guidelines for clinical care during this rapidly evolving global pandemic. The Canadian maternity care system is a global leader and informs maternity care in many countries internationally. With an assembled pan-Canadian team, we are poised to provide critical Canadian data to guide healthcare for pregnant persons and their infants.

Appendix A: List of Co-investigators/Collaborators/Partners

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Additional Territories – low burden of COVID-19 – will be added should there be a shift in the pandemic

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