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Obstetrical and Newborn Outcomes among Patients with SARS-CoV-2 during Pregnancy

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Running head: Pregnancy Outcomes among Patients with SARS-CoV-2

ABSTRACT

We report on the perinatal outcomes of pregnant patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from 2 hospitals in Montréal, Québec. Outcomes of 45 patients with SARS-CoV-2 during pregnancy were compared with those of 225 patients without infection. Sixteen percent of patients with SARS-CoV-2 delivered preterm, compared with 9% of patients without ($P = 0.28$). Median gestational age at delivery (39.3 (interquartile range [IQR] 37.7–40.4) wk vs. 39.1 [IQR 38.3-40.1] wk) and median birthweight (3250 [IQR 2780-3530] g vs. 3340 [IQR 3025-3665] g) were similar between groups. The rate of cesarean delivery was 29% for patients with SARS-CoV-2. Therefore, we did not find important differences in outcomes associated with SARS-CoV-2. Our findings may be limited to women with mild COVID-19 diagnosed in the third trimester.

RÉSUMÉ

Nous faisons état des issues périnatales de patientes enceintes atteintes du coronavirus 2 du syndrome respiratoire aigu sévère (SARS-CoV-2) vues dans deux hôpitaux de Montréal, au Québec. Les issues périnatales de 45 patientes ayant contracté le SARS-CoV-2 pendant la grossesse ont été comparées à celles de 225 patientes non infectées. Au total, 16 % des patientes atteintes du SARS-CoV-2 ont accouché avant terme comparativement à 9 % chez les

patientes non infectées (p = 0,28). L'âge gestationnel médian à l'accouchement (39,3 SA [intervalle interquartile [EIQ] : 37,7-40,4] vs 39,1 SA [EIQ : 38,3-40,1]) et le poids médian à la naissance (3 250 g [EIQ : 2 780-3 530] vs 3 340 g [EIQ : 3 025-3 665]) étaient comparables entre les groupes. Le taux de césariennes était de 29 % chez les patientes atteintes du SARS-CoV-2. Par conséquent, nous n'avons pas trouvé de différence importante dans les issues périnatales associées au SARS-CoV-2. Nos résultats pourraient se limiter aux femmes ayant reçu un diagnostic de COVID-19 légère au cours du troisième trimestre.

Key Words: COVID-19, coronavirus, pregnancy, outcomes, preterm delivery, cesarean delivery

Introduction

Despite mounting evidence demonstrating increased susceptibility of pregnant women to severe manifestations of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the effects of the virus on perinatal outcomes remain incompletely understood.[1] Among pregnant patients with Coronavirus Disease (COVID-19), high rates of preterm delivery (up to 39%) and cesarean delivery (CD) (33-96%) have been reported.[2-5] Concerns regarding maternal status and potential fetal compromise may influence obstetrical management, including timing and mode of delivery. Thus, more information regarding obstetrical and newborn outcomes associated with COVID-19 is urgently needed to guide clinical decision-making. We conducted a multicentre retrospective matched cohort study aiming to 1) report on obstetrical and newborn outcomes among patients with SARS-CoV-2 during pregnancy, and 2) evaluate whether positive testing for SARS-CoV-2 is associated with any major adverse pregnancy outcomes, which could be identified in a limited sized cohort.

Methods

All pregnant women who delivered between March 22 and July 31, 2020 at the two study sites were eligible for inclusion. Pregnant patients with SARS-CoV-2 were identified according to a prospective log of admitted obstetric patients who tested positive. At both centres, testing was initially restricted to at-risk patients, identified through a screening questionnaire. Starting May 2020, universal testing was implemented for all pregnant patients admitted to both hospitals. In all cases, SARS-CoV-2 testing was performed with polymerase-chain-reaction (PCR) on nasopharyngeal swabs. Women who tested positive for SARS-CoV-2

were matched to patients who did not test positive for SARS-CoV-2 during pregnancy and delivered within one day and at the same centre, at a ratio of 1:5.

Data were extracted from electronic medical records using a standardized data collection form. Data on maternal baseline characteristics collected included age, ethnicity, parity, current pregnancy plurality, and presence of underlying medical and pregnancy-associated conditions. Ethnicity was recorded from the electronic medical record demographics when available, or from the antenatal record. Underlying medical conditions of interest included asthma and other respiratory conditions, diabetes mellitus (pre-gestational), cardiac conditions, chronic hypertension, and obesity (defined as pre-pregnancy or first obstetrical visit body mass index (BMI) ≥30 kg/m^2). Pregnancy-associated conditions of interest included gestational diabetes, hypertensive disorders (gestational hypertension and pre-eclampsia), and intra-uterine growth restriction (IUGR). Adverse maternal and newborn outcomes evaluated included preterm delivery, preterm premature rupture of membranes (PPROM), intrapartum complications, CD, low birthweight (<2500 grams), very low birthweight (<1500 grams) and neonatal intensive care (NICU) admission. Preterm delivery was considered 'medically-indicated' or 'iatrogenic' if it occurred due to obstetrical intervention, as opposed to preterm labour or PPROM.[6] Intrapartum complications included major intrapartum fetal heart rate tracing (FHRT) abnormalities and emergency CD. Major intrapartum FHRT were defined as either requiring to stop oxytocin, or to perform an instrumental vaginal or CD. Indications for emergency CD included failure to progress, failed trial of labour after cesarean (TOLAC), fetal distress, or worsening maternal clinical status.

Maternal demographic characteristics were described using means, medians, standard deviations, and interquartile ranges [IQR], as appropriate. Obstetrical and newborn outcomes

between exposed (with SARS-CoV-2) and unexposed (without SARS-CoV2) groups were compared for continuous variables using a Mann-Whitney test and for categorical variables using the Chi-square or Fisher test. P-values were considered statistically significant if ≤0.05. As sample size was limited by the number of available cases, an a priori power calculation was not performed. Instead, post-hoc power calculations were assessed for two of the outcomes reported: preterm delivery and median gestational age (GA). Obstetrical and newborn outcomes among patients with severe COVID-19 were also reported. All statistical analyses were performed using The Statistical Package for Social Sciences (SPSS, Version 27, 2020, IBM, NY).

This study was conducted in accordance with the TCPS 2, Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (2018). Research Ethics Board (REB) approval was obtained (CIUSSS West-Central Montreal REB, Project #2021-2346).

Results

Of 2253 patients who delivered during the study period at both centres, we identified 45 patients with SARS-CoV-2 during pregnancy. These patients were matched to 225 patients who did not test positive for SARS-CoV-2. Maternal demographic and baseline characteristics are summarized in Table 1 and are similar between groups. Nearly all patients with SARS-CoV-2 (44/45; 98%) were diagnosed in the third trimester. The majority of patients with SARS-CoV-2 reported experiencing symptoms (32/44; 72%), with 13% (6/45) requiring antepartum hospital admission for COVID-19. Four (4/45; 9%) patients met World Health

Organization (WHO) criteria for severe COVID-19,[7] and one (1/45; 2%) patient required mechanical ventilation. There were no maternal deaths.

Obstetrical and newborn outcomes are summarized in Table 2. Among patients with SARS-CoV-2, 16% (7/45) delivered preterm, compared to 9% (21/225) of unexposed patients (p=0.28). Median GA at delivery was 39.3 weeks (interquartile range [IQR] 37.7-40.4) among exposed patients, compared to 39.1 weeks (IQR 38.3-40.1) among unexposed patients. Among patients with SARS-CoV-2, three preterm deliveries were medically-indicated (worsening maternal clinical status [n=2], preeclampsia with adverse conditions [n=1]), two were spontaneous preterm deliveries, and two deliveries occurred following PPROM.

Overall rates of CD and emergency CD were respectively 29% (13/45) and 20% (8/40) among patients with SARS-CoV-2, compared to 34% (76/225) and 22% (43/192) among patients without SARS-CoV-2 (p=0.45 and p=0.74). Among patients with SARS-CoV-2 who underwent an emergency CD, indications for CD included worsening maternal clinical status (n=2), fetal distress (n=2), failure to progress (n=3), and failed TOLAC (n=1).

In total, 13% (6/47) of infants born to women with SARS-CoV-2 had a NICU admission, compared to 10% (22/227) of infants born to women without SARS-CoV-2 (p=0.60). Infants born to women with SARS-CoV-2 had a median birthweight of 3250 grams (IQR 2780-3530), compared to 3340 grams (IQR 3025-3665) for infants born to women without SARS-CoV-2 (p=0.08).

Pregnancy outcomes among patients with severe COVID-19 are presented in the Appendix. The small number of patients with severe COVID-19 in this cohort precluded a comparative sub-analysis among these patients.

Discussion

Summary of Findings

Patients who tested positive for SARS-CoV-2 in pregnancy from our cohort had a 16% rate of preterm delivery. Median GA at delivery was similar between exposed and unexposed patients. We did not find an increased risk of CD among patients with SARS-CoV-2. Median birthweight was similar for infants born to exposed vs. unexposed mothers. As such, in our patient population, we did not find significant differences in pregnancy and newborn outcomes among women with and without SARS-CoV-2.

Interpretation

Previous studies have reported rates of preterm delivery among patients with COVID-19 up to 39%.[2-5] The Centers for Disease Control and Prevention (CDC) reported a 12.6% rate of preterm delivery among pregnant patients with SARS-CoV-2 in the United States.[8] Preterm delivery was three times more common among symptomatic patients than among asymptomatic patients (23% vs. 8%, $p<0.05$).[8] In our study, 16% of patients with SARS-CoV-2 delivered preterm, most of whom were symptomatic at time of delivery. Moreover, median GA was similar between groups, and post hoc analysis revealed that we were sufficiently powered to detect a three-week difference in GA at delivery had there been one. In our cohort, two patients were delivered preterm for worsening maternal status (2/7; 30%); therefore, these deliveries can be considered iatrogenic preterm deliveries for reasons related to COVID-19. The absence

of a difference in median GA at delivery between groups may reflect a non-interventionalist approach to avoid iatrogenic preterm delivery among patients with COVID-19 at our institutions. Indeed, we previously described that most (6/8; 75%) patients with severe COVID-19 treated at our institutions were discharged from hospital undelivered, including two patients who had required mechanical ventilation.[10]

Although COVID-19 is not an indication for CD, high rates of CD among SARS-CoV-2-positive patients are reported.[2-5] In a systematic review of 33 studies from ten different countries, which included 252 patients with SARS-CoV-2, 69% delivered by cesarean.[4] In our study, we found that the overall rate of CD among patients with SARS-CoV-2 during pregnancy was similar to our institutional rates (30%). In addition, the rate of emergency CD among patients with SARS-CoV-2 was comparable to that of controls, with two emergency CDs performed for reasons related to COVID-19 among patients with SARS-CoV-2.

Due to the association between low birthweight and other respiratory viruses, such as prior coronaviruses and influenza, there is concern that SARS-CoV-2 infection during pregnancy may affect fetal growth.[9] In our study, median birthweight among infants born to mothers with SARS-CoV-2 was similar to that of infants born to unexposed mothers, with the difference of 90 grams between groups unlikely to be of clinical significance.

Strengths and Limitations

As designated COVID-19 hospitalization centres in Canada's epicenter for COVID-19 during the first wave of infection, this study provides valuable data on the initial Canadian experience treating pregnancies complicated by SARS-CoV-2. Importantly, we were able to

discern whether COVID-19 influenced obstetrical management, including timing and mode of delivery.

Due to our small sample size, our study was underpowered to demonstrate statistically significant differences for some of our findings. Nevertheless, no major signal suggesting a link between SARS-CoV-2 and the adverse perinatal outcomes observed was detected. However, most patients in this cohort had mild disease diagnosed in the third trimester. Therefore, results may not be generalizable to patients with severe disease or diagnosed earlier in pregnancy.

Conclusion

We did not find a major difference in the frequency of adverse obstetrical or newborn outcomes between women with and without SARS-CoV-2. However, our cohort was limited by small sample size, and more subtle difference may be highlighted by larger cohorts. Our reported findings are important as they will contribute to future meta-analyses, which will provide a better understanding of the population effect of SARS-CoV-2 during pregnancy. Until further data become available, heightened surveillance for pregnancies affected by SARS-CoV-2 remains warranted.

References

1. Ellington S, Strid P, Tong VT, et al. Characteristics of Women of Reproductive Age with Laboratory-Confirmed SARS-CoV-2 Infection by Pregnancy Status—United States, January 22–June 7, 2020. MMWR Morb Mortal Wkly Rep. 2020;69:769–75. DOI: http://dx.doi.org/10.15585/mmwr.mm6925a1external icon.
2. Elwood C, Raeside A, Boucoiran I, et al. Committee Opinion No. 400: COVID-19 and Pregnancy. March 13, 2020. Updated July 27, 2020. Accessible at: https://www.sogc.org/common/Uploaded%20files/Media%20Updates/EN_Statement-COVID_Pregnancy.pdf.
3. Thomas P, Alexander PE, Ahmed U, et al. Vertical transmission risk of SARS-CoV-2 infection in the third trimester: a systematic scoping review. J Matern Fetal Neonatal Med. 2020:1-8.
4. Elshafeey F, Magdi R, Hindi N, et al. A systematic scoping review of COVID-19 during pregnancy and childbirth. Int J Gynecol Obstet. 2020;150:47-52.
5. Della Gatta A, Rizzo R, Pilu G, et al. Coronavirus Disease 2019 during Pregnancy: A Systematic Review of Reported Cases. Am J Obstet Gynecol. 2020 Jul; 223(1):36-41.
6. Lisonkova S, Hutcheon JA, Joseph KS. Temporal trends in neonatal outcomes following iatrogenic preterm delivery. BMC Pregnancy Childbirth. 2011;11:39.
7. World Health Organization. Clinical Management of COVID-19: Interim Guidance. May 27, 2020. Accessible at: https://www.who.int/publications/i/item/clinical-management-of-covid-19.
8. Delahoy MJ, Whitaker M, O'Halloran A, et al. Characteristics and Maternal and Birth Outcomes of Hospitalized Pregnant Women with Laboratory-Confirmed COVID-19—COVID-NET, 13 States, March 1-August 22, 2020. MMWR Morb Mortal Wkly Rep. 2020;69:1347-54.
9. Schwartz DA, Graham AL. Potential Maternal and Infant Outcomes from Coronavirus 2019-nCoV (SARS-CoV-2) Infecting Pregnant Women: Lessons from SARS, MERS, and Other Human Coronavirus Infections. Viruses. 2020 Feb;12(2):194,
10. Trahan MJ, Malhame I, Mitric C, et al. Management of severe and critical COVID-19 in pregnancy. *AJOG*. 2021; Supplement to 2021 Feb: S236.

Table 1: Maternal Characteristics of Patients with SARS-CoV-2 during Pregnancy

	Group; no (%)	
	Patients who tested positive for SARS-CoV-2 during pregnancy; n = 45	Patients who did not test positive for SARS-CoV-2 during pregnancy; n = 225
Delivery hospital		
A	37 (82)	185 (82)
B	8 (18)	40 (18)
Maternal age (years)		
<25	9 (20)	19 (8)
25-34	20 (44)	119 (53)
35+	16 (36)	87 (39)
Ethnicity		
White	29 (64)	114 (51)
Asian	4 (9)	27 (12)
Black	8 (18)	31 (14)
Hispanic	2 (4)	12 (5)
Biracial/multiracial	1 (2)	5 (2)
First Nations	0 (0)	6 (3)
Not reported	1 (2)	30 (13)
Parity		
0	15 (33)	85 (38)
1	12 (27)	62 (28)
2+	18 (40)	78 (35)
Twin pregnancy	2 (4)	2 (1)
Underlying medical conditions		

Asthma	3 (7)	10 (4)
Diabetes mellitus	0 (0)	5 (2)
Chronic hypertension	2 (4)	8 (4)
Cardiac condition	3 (7)	0 (0)
Obesity (pre-pregnancy BMI≥30 kg/m^2)	4 (9)	5 (2)
Pregnancy-associated conditions		
Gestational diabetes	1 (2)	24 (11)
Gestational hypertension or preeclampsia	3 (7)	17 (8)
IUGR	1 (2)	7 (3)
Severe COVID-19	8 (18)	—
Mechanical ventilation	1 (2)	—
ECMO	0 (0)	—

BMI: body mass index; ECMO: extracorporeal membranous oxygenation; IUGR: intra-uterine growth restriction.

Table 2: Pregnancy Outcomes and Mode of Delivery among Patients with SARS-CoV-2 during Pregnancy

	Group; no (%)[a]		*P* value
	Patients who tested positive for SARS-CoV-2 during pregnancy; n = 45	Patients who did not test positive for SARS-CoV-2 during pregnancy; n = 225	
Obstetrical outcomes			
GA at delivery, wk, mean ± SD	38.9 ± 2.2	38.8 ± 2.5	0.74
GA at delivery, wk, median (IQR)	39.3 (37.7-40.4)	39.1 (38.3-40.1)	
Preterm delivery <37 weeks	7 (16)	21 (9)	0.28
Preterm delivery <34 weeks	2 (4)	10 (5)	1.0
PPROM	2 (4)	9 (4)	1.0
Intrapartum complications			
Major intrapartum FHRT abnormalities requiring intervention	13/40 (33)	39/192 (20)	0.09
Mode of delivery			
Instrumental vaginal delivery	4/40 (10)	12/192 (6)	0.73
Cesarean delivery (overall)	13 (29)	76 (34)	0.45
Emergency cesarean delivery	8/40 (20)	43/192 (22)	0.74
Newborn outcomes			
Birthweight, g, median (IQR)	3250 (2780-3530)	3340 (3025-3665)	0.08
Low birthweight	5/47 (11)	22/227 (10)	0.79
Very low birthweight	0/47 (0)	5/227 (2)	-
NICU admission	6/47 (13)	22/227 (10)	0.60

[a] Unless otherwise secified.

FHRT: fetal heart rate tracing; GA: gestational age; IQR: interquartile range; NICU: neonatal intensive care unit; PPROM: preterm premature rupture of membranes.

Appendix: Pregnancy Outcomes and Mode of Delivery among Patients with Severe COVID-19 during Pregnancy

	Patients with severe COVID-19 during pregnancy (n=4)
GA at delivery, wk, mean ± SD	34.8 ± 3.9
GA at delivery, wk, median (IQR)	34.5 (31.3-38.5)
Preterm delivery <37 weeks	2 (50)
Preterm delivery <34 weeks	2 (50)
PPROM	1 (25)
Major intrapartum FHRT abnormalities requiring intervention	2 (50)
Instrumental vaginal delivery	0 (0)
Cesarean delivery (overall)	2 (50)
Emergency cesarean delivery	2 (50)
Birthweight, g, median (IQR)	1945 (1748-3458)
Low birthweight	4/6 (67)
Very low birthweight	0/6 (0)
NICU admission	4/6 (67)

FHRT: fetal heart rate tracing; GA: gestational age; IQR: interquartile range; NICU: neonatal intensive care unit; PPROM: preterm premature rupture of membranes.