

LETTER TO THE EDITOR

Perinatal outcomes of pregnancies affected by COVID-19 in Singapore: A cohort study

Dear Editor,

Pregnant women and infants were not spared from the coronavirus disease 2019 (COVID-19) after it was first identified in December 2019.^{1,2} In the beginning of the pandemic, a lack of data on transmission risks and outcomes of pregnancies affected by SARS-CoV-2, impacted perinatal clinical decision-making.^{1,3} We report the perinatal outcomes of pregnancies affected by COVID-19 in Singapore, covering the period from initial virus identification to the emergence of the Omicron variant in late 2021. We investigated the impact of COVID-19 vaccination and the Omicron variant on the perinatal outcomes of infected pregnant women and their newborns.

We conducted a cohort study of mother-infant pairs from pregnancies with laboratory-confirmed COVID-19 from 3 tertiary-level public hospitals in Singapore—KK Women's and Children's Hospital, Singapore General Hospital and National University Hospital—from December 2019 to February 2022. During the study period, pregnant women with COVID-19 preferentially received care in these hospitals as per prevailing government policy.³ Symptomatic COVID-19 was defined according to the World Health Organization classification.⁴ Based on reports in Singapore on circulating SARS-CoV-2 variants, the following periods were used to delineate the likely infecting variants—wild-type variant (December 2019–November 2020); Alpha variant (December 2020–April 2021); Delta variant (April 2021–November 2021); and Omicron variant (November 2021–February 2022).⁵ COVID-19 vaccination for pregnant women in Singapore started from June 2021.⁶

Differences in proportions between categories were tested using chi-squared test or Fisher's Exact test and Mann-Whitney U-test for continuous variables. All tests were two-sided, and $P < 0.05$ was considered statistically significant. Analyses were performed using SPSS version 25.0 (IBM Corp, Armonk, NY, US). The study received ethics approval with waiver of informed consent from SingHealth Centralised Institutional Review Board (Reference no. 2020/2094).

A total of 371 women were admitted to participating hospitals with antenatal SARS-CoV-2 infection: 8 (2.2%) wild-type variant, 3 (0.8%) Alpha variant, 67 (18.1%) Delta variant and 293 (79.9%) Omicron variant. Affected pregnant

women had a median age of 31.0 years (interquartile range [IQR] 28.0–35.0, 135 (36.4%) primigravida, 70 (18.9%) had gestational diabetes and 16 (4.3%) had pregnancy-induced hypertension. Forty-three women (11.6%) were infected in the first/second trimester, 280 (75.5%) in the third trimester, and 48 (12.9%) with infection period unknown. The majority (298, 94.9%) of infected women had mild COVID-19 symptoms and 10 (4.6%) women required intensive care unit (ICU) admission. Twenty-three women (6.2%) received steroids, 2 (0.5%) received remdesivir and 2 (0.5%) received tocilizumab.

Of 353 women with reported COVID-19 vaccination status, 278 (78.8%) received ≥ 1 dose before or during the current pregnancy. There were significantly higher incidence of moderate/severe disease (8.0% versus 1.8%, $P = 0.01$) and ICU admission (8.0% vs 1.4%, $P = 0.008$) among unvaccinated women compared with vaccinated ones. Of note, 1 unvaccinated woman required extracorporeal membrane oxygenation support during her illness.

A total of 371 infants were born to women with COVID-19 during pregnancy (Table 1). Thirty-eight (10.2%) were admitted to the neonatal ICU, while 16 (4.3%) needed admission to Special Care Nursery. Eleven (3.0%) required mechanical ventilation, and 6 (1.6%) required continuous positive airway pressure. Four infants (1.1%) were diagnosed with COVID-19 after birth, of which 3 (1.1%) were from mothers with COVID-19 vaccination compared to 1 infant (1.3%) without. None of the infants received antiviral therapy for SARS-CoV-2. The sole mortality was a SARS-CoV-2 negative premature infant born at 32 weeks gestation who died of pulmonary hypoplasia, which was determined to be unrelated to maternal COVID-19.

We compared the characteristics and outcomes of 293 pregnancies affected by the Omicron variant against 78 pregnancies affected by non-Omicron variants (Table 1). Women infected by Omicron variant were less likely to have moderate/severe disease (1.7% vs 7.7%, $P = 0.006$), less ICU admissions (1.0% vs 9.0%, $P < 0.001$) and less mechanical ventilation (0.3% vs 3.8%, $P = 0.008$) compared with non-Omicron. Infants born to women infected with the Omicron variant were less likely to have ICU admissions (14.1% vs 3.8%, $P = 0.001$) and more likely to be allowed to room-in with their mothers (73.3% vs 52.9%, $P = 0.004$).

Table 1. Maternal and infant clinical characteristics and outcomes with antenatal exposure to Omicron and non-Omicron SARS-CoV-2 variants.

Variables	Vaccinated n=278	Not vaccinated n=75	P value	Omicron n=293	Not Omicron n=78	P value
Median maternal age, years (IQR)	31.3 (28.0–35.0)	31.0 (27.5–35.0)	0.7	31 (28.0–35.0)	32.3 (29.0–36.0)	0.09
Primigravida, no. (%)	96 (34.5)	32 (42.7)	0.2	102 (34.9)	33 (42.3)	0.2
Vaginal delivery, no. (%)	192 (69.1)	53 (70.7)	0.5	210 (71.9)	46 (59.7)	0.04
Gestational age at birth <37 weeks, no. (%)	21 (7.5)	8 (10.7)	0.3	13 (4.4)	11 (14.1)	0.002
Maternal symptomatic disease, no. (%)	239 (85.9)	60 (80.0)	0.2	249 (85.0)	65 (83.3)	0.7
Moderate to severe, no. (%)	5 (1.8)	6 (8.0)	0.01	5 (1.7)	6 (7.7)	0.006
Maternal ICU admission, no. (%)	4 (1.4)	6 (8.0)	0.008	3 (1.0)	7 (9.0)	<0.001
Maternal respiratory support supplemental oxygen, no. (%)	6 (2.2)	0	0.2	6 (2.0)	0	0.2
Ventilated, no. (%)	2 (0.7)	2 (2.7)	0.2	1 (0.3)	3 (3.8)	0.008
ECMO, no. (%)	0	1 (1.3)	0.2	0	1 (1.3)	0.2
Male infant, no. (%)	141 (50.7)	35 (46.7)	0.4	149 (50.9)	37 (47.4)	0.6
5 minutes Apgar score <7, no. (%)	1 (0.4)	1 (1.3)	0.4	1 (0.3)	2 (2.6)	0.1
Infant respiratory support mechanical ventilation, no. (%)	5 (1.8)	1 (1.3)	0.6	4 (1.4)	2 (2.6)	0.5
CPAP, no. (%)	5 (1.8)	1 (1.3)	0.6	7 (2.4)	9 (11.5)	0.002
No support, no. (%)	262 (95.3)	72 (96.0)	0.4	282 (96.2)	67 (85.9)	0.001
Rooming-in with mother, no. (%)	177 (63.7)	34 (45.3)	0.006	192 (73.3)	27 (52.9)	0.004
Initial mode of feeding						
Breastmilk/PDHM, no. (%)	44 (15.8)	20 (26.7)	0.04	45 (15.5)	22 (28.6)	0.008
Mixed feeding, no. (%)	202 (72.8)	42 (56.0)	0.008	211 (72.5)	42 (54.5)	0.002
Formula only, no. (%)	32 (11.5)	13 (17.3)	0.25	35 (12.0)	13 (16.9)	0.3
Cleansing of infant skin after delivery, no. (%)	20 (7.1.9)	49 (65.3)	<0.001	53 (18.2)	18 (23.1)	0.3

CPAP: continuous positive airway pressure; ECMO: extracorporeal membrane oxygenation; ICU: intensive care unit; IQR: interquartile range; PDHM: pasteurised donor human milk

We describe the maternal-infant outcomes of pregnancies affected by COVID-19 in Singapore from the beginning of the pandemic to the emergence of the Omicron variant. Through the study period, 2.9% of pregnant women had moderate to severe disease and 2.6% required mechanical ventilation. This is lower than the 9.9% severe disease with 7.3% requiring advanced oxygen support reported in the largest cohort study to our knowledge.⁷ Higher (78.8%) uptake of vaccination in our cohort might have contributed to the difference. The incidence of vertical COVID-19 transmission was 1.1%, which was comparable to previous reports (0.3–2.9%).^{7–9} Of note, the incidence of preterm births (<37 weeks) was 6.5%, which is lower than the expected incidence of around 10% in the general population.⁹

Consistent with previous studies,^{7,9} SARS-CoV-2-infected mothers who had received COVID-19 vaccination before or during the pregnancy had milder symptoms and were less likely to require ICU admission. Maternal COVID-19 vaccinations, however, did not influence neonatal outcomes with regard to ICU admissions or need for mechanical ventilation.⁷ Based on the reported timelines of circulating variants in Singapore, we found trends of lower severity of maternal and infant illness with the Omicron variant compared with non-Omicron variants. There were significantly lower rates of moderate to severe disease, ICU admission and mechanical ventilation. These findings are consistent with other epidemiological studies in adults comparing different variants.^{2,10}

Our study is limited by several factors. Lists intended for infection control purposes were used to identify all eligible women, which may have resulted in missing or incomplete data. However, given the challenges during the pandemic, this method was deemed to be a pragmatic way of collecting such data. Our study also did not include infected women who were admitted to private hospitals. In addition, we used published Singapore reports on circulating SARS-CoV-2 variants to determine the infecting SARS-CoV-2 variant instead of genotyping the virus, which may not be an accurate determination of the actual variant.¹⁰ Future studies could include virus genotyping.

We conclude that vertical SARS-CoV-2 transmission appears to be rare in our cohort. The Omicron variant appears to have lower pathogenicity among pregnant women compared to other variants. Risks of poor maternal outcomes, including ICU admissions, can be mitigated by the administration of maternal COVID-19 vaccination and should be encouraged.

Availability of data and materials

The datasets generated and analysed are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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