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Published in:
International Journal of Gynecology & Obstetrics

DOI:
10.1002/ijgo.14405

Publication date:
2022

Document Version
Publisher's PDF, also known as Version of record

Received: 8 April 2022 | Revised: 22 July 2022 | Accepted: 10 August 2022

DOI: 10.1002/ijgo.14405

BRIEF COMMUNICATION

International Journal of Gynecology & Obstetrics FIGO WILEY

Effects of severe acute respiratory syndrome coronavirus 2 infection on obstetric outcomes: Results from a prospective cohort in the Netherlands

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Keywords birth weight, COVID-19, gestational age, obstetric outcomes, SARS-CoV-2 infection

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection during pregnancy has been associated with adverse obstetric outcomes.[1] Most studies included symptomatic or hospitalized patients or patients infected in the third trimester or lacked appropriate control groups. Three studies identified patients infected in early pregnancy based on antibody status and reported no increased risk of adverse outcomes.[2,3] These results suggest that severity and timing are important determinants of adverse outcomes of SARS-CoV-2 infection during pregnancy. We assessed whether SARS-CoV-2 infection before 28 weeks of gestation is associated with selected obstetric outcomes.

We analyzed data from 1031 participants in a prospective pregnancy cohort in the Netherlands (Brabant study, previously described and approved by the medical ethical committee of the Máxima Medical Center Veldhoven [#NL64091.015.17]).[4] Recruitment started in 2018 prepandemic and continued through November 1, 2021. Demographic, laboratory, and obstetric characteristics were collected at 12, 20, and 28 weeks of gestation and 8 weeks postpartum and did not differ from the main cohort. Past SARS-CoV-2 infection was assessed using repeated serological testing for IgG antibodies to the SARS-CoV-2 nucleocapsid (N) protein and self-reported results from coronavirus disease 2019 (COVID-19) tests. Linear and logistic regression models of each obstetric outcome were adjusted using stepwise procedures for potential covariates in SPSS software version 28.0 (IBM).

A total of 77 of 1031 participants (7.5%) were infected with SARS-CoV-2 before 28 weeks of gestation (41 [4%] during pregnancy, 14 [1.4%] before pregnancy, and 22 [2%] unknown timing). Participants with evidence of SARS-CoV-2 infection were younger (t[999], 1.99; $P = 0.047$, $d = 0.24$) and more often nulliparous (X^2 [1, $N = 1031$], 5.69; $P = 0.017$, $V = 0.076$) compared with uninfected participants. After adjustment, we found no association of SARS-CoV-2 infection before 28 weeks of gestation with selected obstetric outcomes (Table 1). A sensitivity analysis restricted to infections during pregnancy ($n = 41$) also showed no association (results not shown).

We did not find an association between SARS-CoV-2 infection before 28 weeks of gestation and adverse obstetric outcomes. Our results are consistent with three studies showing a similar rate of pregnancy complications among participants infected with SARS-CoV-2 in early to mid-pregnancy compared with noninfected pregnant women.[2,3] A key strength of this study, inherent to the prospective design, is the unbiased sample of pregnant

TABLE 1 Association between SARS-CoV-2 infection and selected obstetric outcomes

Outcome	Cases: SARS-CoV-2 (*n* = 77)	Controls: No SARS-CoV-2 (*n* = 954)	Unadjusted ß	95% CI	*P* Value	Adjusted ß[a]	95% CI	*P* Value
Gestational age at birth (week, d), SD (in d)	39, 1 (15)	39, 3 (11)	−0.318	−0.72 to 0.08	0.116	−0.28	−0.68 to 0.12	0.173
Birth weight (g), SD (g)	3396.55 (523.96)	3422.82 (517.67)	−22.7	−150 to 104.6	0.726	3.94	−119.29 to 127.18	0.950
Outcome			**Unadjusted OR**	**95% CI**	***P* Value**	**Adjusted OR[a]**	**95% CI**	***P* Value**
Preterm birth, *n* (%)	8 (10.4)	59 (6.2)	1.8	0.81–3.8	0.155	1.7	0.75–3.72	0.214
SGA, *n* (%)	7 (9.1)	60 (6.3)	1.5	0.66–3.38	0.34	1.4	0.6–3.23	0.441
LGA, *n* (%)	12 (15.6)	105 (11)	1.5	0.78–2.86	0.226	1.4	0.7–2.98	0.325

Note: Obstetric outcomes gestational age, birth weight, preterm birth (PTB), small for gestational age (SGA), and large for gestational age (LGA) were compared between cases (77 pregnant participants with evidence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection before pregnancy or during pregnancy before 28 weeks of gestation) and controls (954 pregnant participants with no evidence of SARS-CoV-2 infection). Linear and logistic regression analyses were performed for each obstetric outcome separately. Two linear regression analyses were performed with gestational age at birth and birth weight as the dependent variable and SARS-CoV-2 infection as the exposure variable. Three logistic regression analyses were performed with PTB, SGA, and LGA as the dependent variable and SARS-CoV-2 infection as the exposure variable. Analyses were adjusted for covariates listed below. We found no significant association between SARS-CoV-2 infection and obstetric outcomes in unadjusted and adjusted linear and logistic regression analyses.

Abbreviations: CI, confidence interval; OR, odds ratio; SD, standard deviation.

[a]Adjusted for maternal age, prepregnancy body mass index, alcohol/smoking during pregnancy, previous miscarriage, parity, autoimmune disease, and vaccination status.

women regardless of symptom and illness severity. A limitation is the low case rate (comparable to the general population in the Netherlands in 2020–2021), limited information on exact timing and severity of infection, and homogeneity of the cohort; results may not be generalizable to other populations or those with severe infection.

AUTHOR CONTRIBUTIONS

FG, VP, and LdW conceptualized the study. FG computed the analyses. FG and LdW wrote the initial draft. FG, MB, ASR, SD, VP, VB, and LdW critically revised the manuscript. VP, VB, and LdW supervised the project. ASR, SD, VP, VB, and LdW acquired funding. All authors approved the final submission.

ACKNOWLEDGMENTS

The authors would like to thank several members of the US Centers for Disease Control (CDC) who contributed to the interpretation of the data and have provided their feedback on the manuscript: Margaret C. Snead, Sascha R. Ellington, Romeo R. Galang, and Lauren B. Zapata. The authors also thank the laboratory of the Máxima Medical Center (The Netherlands) and especially Dr Maarten Broeren for analyzing the laboratory parameters. In addition, the authors thank all colleagues from the Department of Obstetrics, Gynecology and Reproductive Science, Icahn School of Medicine at Mount Sinai, New York City, NY, who contributed to the conceptualization of the manuscript and especially Whitney Lieb, Rebecca H. Jessel, Teresa Janevic, Joanne Stone, and Elizabeth A. Howell.

FUNDING INFORMATION

This analysis was partially funded from the CDC, which also provided technical assistance related to analysis and interpretation of data and writing the report (contract 75D30120C08186). The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the CDC.

CONFLICT OF INTEREST

The authors have no conflicts of interest.

DATA AVAILABILITY STATEMENT

Research data are not shared.

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How to cite this article: Gigase FAJ, Boekhorst MGB, Rommel A-S, et al. Effects of severe acute respiratory syndrome coronavirus 2 infection on obstetric outcomes: Results from a prospective cohort in the Netherlands. *Int J Gynecol Obstet*. 2022;00:1-3. doi: 10.1002/ijgo.14405