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## Coronavirus disease 2019 infection and hypertensive disorders of pregnancy

**OBJECTIVE:** The possible connection between coronavirus disease 2019 (COVID-19) and hypertensive disorders of pregnancy (HDP) remains unclear.<sup>1</sup> Elucidating these outcomes is important both to better understand COVID-19 pathophysiology and to improve patient care in pregnant patients with COVID-19. Our objectives were to test the hypothesis that COVID-19 infection is associated with an increased risk of HDP and to examine the association

between the gestational age at COVID-19 infection and delivery and HDP risk.

**STUDY DESIGN:** This was a retrospective cohort study at Barnes-Jewish Hospital in St. Louis, which has a universal COVID-19 testing policy on admission to labor and delivery. All women admitted for delivery from June 1, 2020, to November 30, 2020, with a positive severe acute

Characteristic	COVID-19 positive (n=83)	COVID-19 negative (n=166)	P value
Maternal age, y	26 (23-31)	28 (23-32)	.39
Gestational age, wk	39 (37-39)	39 (37—39)	.90
Black maternal race	88 (53.0)	44 (53.0)	matched
Body mass index at delivery, kg/m <sup>2</sup>	32.5±7.6	31.0±7.2	.13
Nulliparity	31 (37)	63 (38)	matched
Chronic hypertension	10 (12.1)	19 (11.5)	1.0
Pregestational diabetes	4 (4.8)	2 (1.2)	.10
Gestational diabetes	2 (2.4)	14 (8.4)	.10
History of hypertensive disorder of pregnancy	14 (16.7)	19 (11.5)	.23
Tobacco use	6 (7.2)	23 (13.9)	.12
Current substance abuse	7 (8.4)	29 (17.5)	.06
COVID-19 severity		_	
Asymptomatic	48 (57.8)		
Moderate	27 (32.5)		
Severe	7 (8.4)	_	
Mode of delivery			.37
Vaginal delivery	57 (68.7)	123 (74.0)	
Cesarean delivery	26 (31.3)	43 (26.0)	
Birthweight, g	3090 (2750-3740)	3065 (2750-3520)	.92
Small for gestational age	6 (7.2)	19 (11.5)	.30
Placental abruption	2 (2.4)	1 (0.6)	.26
Hypertensive disorder of pregnancy			.74
None	59 (71.1)	120 (72.3)	
Gestational hypertension	10 (12.1)	24 (14.5)	
Preeclampsia without severe features	3 (3.6)	7 (4.2)	
Preeclampsia with severe features	11 (13.3)	15 (9.4)	
Any hypertensive disorder of pregnancy	24 (28.9)	46 (27.7)	.84

COVID-19, coronavirus disease 2019; IQR, interquartile range.

Rosenbloom. COVID-19 infection and HDP. Am J Obstet Gynecol 2021.

respiratory syndrome coronavirus 2 (SARS-CoV-2) test result at any time during pregnancy were compared 1:2 with randomly selected controls who had a negative SARS-CoV-2 test result and were matched for race and parity. COVID-19 was diagnosed with nasopharyngeal reverse transcription polymerase chain reaction or rapid antigen testing. HDP was diagnosed using standard criteria. Cox proportional hazards models with left truncation to account for the varying gestational age at COVID-19 diagnosis and random effects (frailty) to account for the matching design and small cluster sizes were used to examine the association between COVID-19 and HDP.<sup>2</sup> Because this was a sensitivity analysis, we also examined early (before 32 weeks' gestation) vs late COVID-19 infection and HDP development. The study was deemed exempt from review by the institutional review board.

**RESULTS:** Of 1856 births, there were 83 women (4.5%) with COVID-19 infection. There was no difference in baseline characteristics between COVID-19 infected women and controls (Table). Patients with COVID-19 infection had almost a 2-fold risk of HDP (hazard ratio [HR], 1.93; 95% confidence interval [CI], 1.13-3.31). However, COVID-19 infection was not associated with severity of HDP, and severity of COVID-19<sup>3</sup> was not associated with HDP development. Among patients with COVID-19 and HDP at delivery, the median interval from COVID-19 diagnosis to delivery was 3.8 weeks (interquartile range, 0.29-11.5). In additional analysis, early, but not late, COVID-19 infection was associated with HDP development (HR for early COVID-19, 2.17 [95% CI, 1.11-4.24]; HR for late COVID-19, 1.68 [95% CI, 0.79-3.57]).

**CONCLUSION:** Early COVID-19 infections are associated with HDP, even when accounting for differential exposure and delivery times, suggesting that COVID-19 infection may alter pregnancy physiology and increase the risk of HDP development over time. Infection closer to term is not associated with HDP, which likely reflects our high proportion of asymptomatic infections found at the time of delivery from a universal testing policy<sup>4</sup> and insufficient time to develop HDP in these cases. Furthermore, emerging evidence suggests that COVID-19 modulates placental angiotensin-converting enzyme 2 expression, which may be related to HDP development.<sup>5</sup> Our study is limited by

sampling in a single institution with a high HDP incidence. However, our results suggest that monitoring of patients with antepartum COVID-19 infection should encompass precautions for HDP development.

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The authors report no conflict of interest.

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## Intracervical balloon catheter for labor induction after rupture of membranes: a systematic review and meta-analysis

**OBJECTIVE:** Although unequivocal benefits to ripening exist in the setting of intact membranes, ripening remains controversial in the setting of prelabor rupture of membranes

(PROM). PROM complicates 8% of term pregnancies, which translates to approximately 270,000 births in the United States annually.<sup>1</sup> We undertook a systematic review and

**<sup>3.</sup>** Berlin DA, Gulick RM, Martinez FJ. Severe Covid-19. N Engl J Med 2020;383:2451–60.