

Letters

RESEARCH LETTER

Association Between Mode of Delivery Among Pregnant Women With COVID-19 and Maternal and Neonatal Outcomes in Spain

Data from China found severe complications in 8% of pregnant women with coronavirus disease 2019 (COVID-19).¹ However, the high rate of cesarean deliveries (>90%) in Chinese reports is concerning,² and whether mode of delivery is associated with maternal complications or neonatal transmission is unknown.³ We assessed births to women with COVID-19 by mode of delivery.

Methods | Women with singleton pregnancies and a positive reverse transcriptase-polymerase chain reaction (RT-PCR) test result for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) between March 12 and April 6, 2020, and who delivered within the next 14 days at 96 level 2 or level 3 maternity hospitals throughout Spain were included.

The study was approved by the national ethics committee. Oral informed consent was obtained.

Pregnant women were tested if they presented with symptoms compatible with COVID-19 or a history of potential exposure; additionally, universal screening was started in some hospitals in April. Newborns had a nasopharyngeal swab obtained for RT-PCR within 6 hours of life.

Mothers were stratified by symptom severity at admission as asymptomatic, mild, or severe (need for advanced oxygen support: high-flow nasal cannula, noninvasive ventilation, or mechanical ventilation).

Maternal outcomes were defined as severe if mothers required advanced oxygen support or admission to the intensive care unit (ICU) or had signs of sepsis with hypoperfusion/

organ dysfunction. Clinical deterioration was defined by an increased need for oxygen supplementation after delivery.

Neonatal outcomes considered were neonatal ICU (NICU) admission and rates of SARS-CoV-2 perinatal transmission.

Multivariable logistic regression was performed assessing the association between mode of delivery and maternal and neonatal outcomes among patients with mild symptoms, adjusting for maternal age, body mass index, comorbidities, need for oxygen supplementation at admission, abnormal chest x-ray findings at admission, nulliparity, smoking, and prematurity. Stata version 14 (StataCorp) was used. A 2-tailed $P < .05$ defined statistical significance.

Results | Of 82 pregnant patients included, 4 presented with severe COVID-19 symptoms, including 1 with concomitant preeclampsia; all 4 underwent cesarean delivery and required ICU admission.

Seventy-eight patients presented with no or mild COVID-19 symptoms, including 11 patients requiring oxygen supplementation. Forty-one (53%) delivered vaginally and 37 (47%) by cesarean delivery, 29 for obstetrical indications and 8 for COVID-19 symptoms without other obstetrical indications. Women with cesarean deliveries were more likely to be multiparous, be obese, require oxygen at admission, and have abnormal chest x-ray findings than those delivering vaginally (Table 1). No patients with a vaginal delivery developed severe adverse outcomes, while 5 (13.5%) with cesarean delivery required ICU admission. Two patients (4.9%) with a vaginal delivery had clinical deterioration after birth vs 8 (21.6%) with cesarean delivery. After adjustment for potential confounding factors, cesarean birth was significantly associated with clinical deterioration (adjusted odds ratio, 13.4; 95% CI, 1.5-121.9; $P = .02$) (Table 2).

Table 1. Maternal Characteristics, Clinical Presentation, and Obstetrical Management

Characteristics	Asymptomatic/mild COVID-19 symptoms		Severe COVID-19 symptoms and cesarean delivery (n = 4)
	Vaginal delivery (n = 41)	Cesarean delivery (n = 37)	
Maternal characteristics			
Age			
Median (range), y	35 (19-43)	33 (19-48)	36 (22-47)
>35, No. (%)	21 (51.2)	18 (48.7)	2 (50.0)
Parity, No. (%)			
Nulliparous	16 (39.0)	9 (24.3)	1 (25.0)
Multiparous >3	3 (7.3)	5 (13.5)	0
Comorbidities, No. (%)			
Any ^a	14 (34.1)	11 (30.6)	1 (25.0)
Gestational diabetes	1 (2.4)	0	0
Preeclampsia	1 (2.4)	2 (5.6)	1 (25.0)
Asthma	3 (7.3)	3 (8.3)	0
Smoking, No. (%)	3 (7.3)	3 (8.3)	0
BMI			
Median (range)	23 (17-35)	26 (19-38)	23 (22-30)
>30, No. (%)	3 (8.8)	15 (36.6)	1 (25.0)

(continued)

Table 1. Maternal Characteristics, Clinical Presentation, and Obstetrical Management (continued)

Characteristics	Asymptomatic/mild COVID-19 symptoms		Severe COVID-19 symptoms and cesarean delivery (n = 4)
	Vaginal delivery (n = 41)	Cesarean delivery (n = 37)	
COVID-19 history and prepartum clinical presentation			
Signs and symptoms at presentation, No. (%)			
Asymptomatic	13 (31.7)	9 (25.0)	NA
Oxygen supplementation at admission	4 (9.8)	7 (18.9)	4 (100.0) ^b
Diagnostic tests, No. (%)			
Abnormal chest x-ray	8 (19.5)	12 (32.4)	3 (75.0)
Abnormal ALT/AST	5 (12.2)	0	0
Lymphopenia (<1.0 × 10 ⁹ /L), No. (%)	4 (9.8)	2 (5.6)	1 (25.0)
Delivery management			
Time from onset of symptoms to delivery, median (range), d	2 (0-14)	1 (0-10)	4 (1-6)
Gestational age at delivery			
Median (range)	39 wk 1 d (27 wk 3 d-41 wk 3 d)	38 wk 3 d (25 wk 0 d-41 wk 4 d)	29 wk 6 d (28 wk 0 d-34 wk 0 d)
Preterm birth, No. (%)			
34 wk to <37 wk	4 (9.8)	10 (27.0)	1 (25.0)
iatrogenic preterm birth	1 (25) ^c	4 (40.0) ^c	1 (100.0) ^d
<34 wk	3 (7.3)	4 (10.8)	3 (75.0)
iatrogenic preterm birth	0	3 (75.0) ^e	3 (100.0) ^d
Premature rupture of membranes, No. (%)	9 (22.0)	9 (24.3)	0
Preterm premature rupture of membranes, No. (%)	3 (7.3)	4 (10.8)	0
Obstetrical management, No. (%)			
Prelabor cesarean delivery	NA	13 (35.1)	4 (100.0)
Induction of labor	8 (19.5)	8 (21.6)	0
Spontaneous onset of labor	33 (80.5)	16 (43.2)	0
In-labor cesarean delivery	NA	24 (64.9)	0
Instrumental delivery	12 (29.3)	NA	NA
Anesthesia, No. (%)			
Locoregional analgesia	32 (78.0)	32 (86.5)	2 (50.0)
General anesthesia	NA	5 (13.5)	2 (50.0)

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); COVID-19, coronavirus disease 2019; NA, not applicable.

^a In the vaginal delivery group, other maternal complications included hypothyroidism (n=3), epilepsy (n=1), Subek muscular dystrophy (n=1), myopathy (n=1), heterozygous factor V mutation (n=1), psychiatric disorders (n=3), unspecified autoimmune disease (n=1), hyperprolactinemia (n=1), gastritis (n=1), vitiligo (n=1), and chronic hepatitis C infection (n=1). In the cesarean delivery group, other maternal complications included hypothyroidism (n=2), homocysteine mutation (n=1), anti-Kell alloimmunization (n=1), concomitant pyelonephritis (n=1), myomatosis (n=1), mutation of methylenetetrahydrofolate reductase (*MTHFR*) (n=1), ischemic cardiomyopathy (n=1), and depressive disorders (n=1).

^b These patients required advanced oxygen support (eg, high-flow nasal cannula or continuous positive airway pressure).

^c Indications for iatrogenic preterm birth at ≥34 weeks' gestation included maternal COVID-19 symptoms without other obstetrical reasons in 4 (1 vaginal delivery after induction of labor and 3 prelabor cesarean deliveries) and preeclampsia in 1 (cesarean delivery after failure of induction).

^d All iatrogenic preterm births were performed in relation to COVID-19 in the mother without other obstetrical indications.

^e Indication for iatrogenic preterm birth at <34 weeks' gestation included 2 patients with COVID-19 symptoms without any other obstetrical indications for delivery (prelabor cesarean deliveries) and 1 patient with abnormal findings on fetal cardiac monitoring and suspected fetal asphyxia leading to prelabor cesarean delivery.

Eight newborns (19.5%) delivered vaginally and 11 (29.7%) born by cesarean delivery were admitted to the NICU. After adjustment for confounding factors, cesarean birth was significantly associated with an increased risk of NICU admission (adjusted odds ratio, 6.9; 95% CI, 1.3-37.1; *P* = .02).

Three (4.2%) of 72 newborns tested within 6 hours after birth had a positive SARS-CoV-2 RT-PCR result. Repeat testing at 48 hours was negative. None developed COVID-19 symptoms within 10 days.

Two other newborns, both cesarean deliveries at term, developed COVID-19 symptoms within 10 days. Though initial testing at birth was negative, repeat testing was positive. Both newborns were in contact with their parents immediately after birth. Symptoms resolved within 48 hours.

Discussion | In this cohort of pregnant women in Spain, severe adverse maternal outcomes occurred in 11% (9/82),

4 of whom presented with severe and 5 with mild COVID-19 symptoms.

Among patients with mild symptoms at presentation, all patients with a vaginal birth had excellent outcomes. In contrast, 13.5% of women undergoing cesarean delivery had severe maternal outcomes and 21.6% had clinical deterioration. Women undergoing cesarean delivery may have been at higher risk of adverse outcomes, but after adjusting for confounding factors, cesarean birth remained independently associated with an increased risk of clinical deterioration. The physiological stress induced by surgery is known to increase postpartum maternal complications.^{4,5} Cesarean delivery was also associated with an increased risk of NICU admission.

Limitations include a lack of sufficient information on newborns to determine vertical transmission. Also, the 95% CIs around the odds ratios for cesarean birth were wide and the estimates fragile.

Table 2. Maternal and Neonatal Outcomes^a

Outcomes	Asymptomatic/mild COVID-19 symptoms			Adjusted odds ratio (95% CI)	Severe COVID-19 symptoms and cesarean delivery, No. (%) (n = 4)
	Vaginal delivery, No. (%) (n = 41)	Cesarean delivery, No. (%) (n = 37)	Odds ratio (95% CI)		
Maternal outcomes					
Severe adverse outcomes	0	5 (13.5)	NA	NA	4 (100.0)
Severe pneumonia	0	3 (8.1)			2 (50.0)
Sepsis	0	0			1 (25.0)
Postnatal intensive care unit admission	0	5 (13.5)			4 (100.0)
Length of stay, median (range), d	NA	10 (2-18)			4 (1-13)
Mechanical ventilation	0	4 (10.8)			2 (50.0)
Clinical deterioration	2 (4.9)	8 (21.6)	5.4 (1.0-54.6)	13.4 (1.5-121.9)	2 (50.0)
Neonatal outcomes					
Neonatal intensive care unit admission	8 (19.5)	11 (29.7)	8.3 (1.6-80.5)	6.9 (1.3-37.1)	3 (75.0)
SARS-CoV-2 perinatal transmission rates					
Total with tests at birth	41 (100)	30 (81.1)			1 (25.0)
Suspected ^b	2 (4.9)	1 (3.3)	0.7 (0.0-13.6)	NA	0
Confirmed ^c	0	2 (5.4)	NA	NA	0
Secondary outcomes					
Apgar score <5 at 5 min	0	3 (8.1)			0
Arterial umbilical pH <7.10	3 (7.3)	3 (8.1)			0
Birth weight, median (range), g	3060 (940-4750)	3210 (910-4510)			1450 (1110-1580)
<10th percentile	1 (2.4)	0			0
Breastfeeding	23 (56.1)	19 (51.4)			0

Abbreviations: COVID-19, coronavirus disease 2019; NA, not applicable; RT-PCR, reverse transcriptase-polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

^a Odds ratios and 95% CIs are based on multivariate logistic regression analysis assessing risk of severe maternal outcomes, clinical deterioration, neonatal intensive care unit admission, and perinatal transmission associated with mode of delivery among patients with mild symptoms. Estimates were adjusted for confounding factors and heterogeneity between the 2 groups (maternal age >35 years, body mass index >30, maternal comorbidities, need for oxygen supplementation at admission, abnormal chest x-ray findings at admission, nulliparity, smoking, and prematurity).

^b Positive RT-PCR result at birth. Two were preterm births in which testing was performed after initial resuscitation; the other newborn had contact with his mother immediately after birth.

^c Repeat positive RT-PCR result and compatible symptoms.

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Accepted for Publication: May 26, 2020.

Published Online: June 8, 2020. doi:10.1001/jama.2020.10125

Author Contributions: Drs Martínez-Perez and Vouga had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Drs Martínez-Perez and Vouga contributed equally. *Concept and design:* Martínez-Perez, Vouga, Cruz Melguizo, Panchaud.

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Obtained funding: Martínez-Perez.

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Conflict of Interest Disclosures: None reported.

Additional Contributions: We thank the Emergencia Obstetrica España Group for participation in the study. We also thank Tirso Perez Medina, MD, PhD, Obstetrics and Gynaecology Department, Puerta de Hierro University Hospital, Autonoma University, Madrid, Spain, for his contribution to the design of the study and data collection. He received no compensation for his participation.

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