An Analysis of 38 Pregnant Women With COVID-19, Their Newborn Infants, and Maternal-Fetal Transmission of SARS-CoV-2

Maternal Coronavirus Infections and Pregnancy Outcomes

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• The emergence of a novel coronavirus, termed SARS-CoV-2, and the potentially life-threatening respiratory disease that it can produce, COVID-19, has rapidly spread across the globe, creating a massive public health problem. Previous epidemics of many emerging viral infections have typically resulted in poor obstetric outcomes including maternal morbidity and mortality, maternal-fetal transmission of the virus, and perinatal infections and death. This article reviews the effects of 2 previous coronavirus infections—severe acute respiratory syndrome (SARS) caused by SARS-CoV and Middle East respiratory syndrome (MERS) caused by MERS-CoV—on pregnancy outcomes. In addition, it analyzes literature describing 38 pregnant women with COVID-19 and their newborns in China to assess the effects of SARS-CoV-2 on the mothers and infants, including clinical, laboratory, and virologic data, and the transmissibility of the virus from mother to fetus. This analysis reveals that unlike coronavirus infections of pregnant women caused by SARS and MERS, in these 38 pregnant women COVID-19 did not lead to maternal deaths. Importantly, and similar to pregnancies with SARS and MERS, there were no confirmed cases of intrauterine transmission of SARS-CoV-2 from mothers with COVID-19 to their fetuses. All neonatal specimens tested, including placentas in some cases, were negative by RT-PCR for SARS-CoV-2. At this point in the global pandemic of COVID-19 infection there is no evidence that SARS-CoV-2 undergoes intrauterine or transplacental transmission from infected pregnant women to their fetuses. Analysis of additional cases is necessary to determine if this remains true.

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The emergence of the novel coronavirus infection that occurred in China in December 2019 has resulted in an epidemic that has rapidly expanded to become one of the most significant public health threats in recent times.[1–5] This newly emergent coronavirus was isolated in China in early January 2020, initially referred to as 2019-nCoV and subsequently termed SARS-CoV-2—the disease it produces has been termed COVID-19.[6] Since then it has become an increasingly widespread and important cause of respiratory infection that can progress to severe pneumonia and, in a small percentage of cases, death. Since its initial identification in Wuhan, Hubei province, China, COVID-19 has now been reported from all continents except for Antarctica, affecting 167,515 persons in 151 countries and territories, and resulting in 6606 deaths as of March 16, 2020.[7] COVID-19 was declared a pandemic by the World Health Organization on March 11, 2020.[8]

There has been a rapid increase in knowledge of the genetic, virologic, epidemiologic, and clinical aspects of this emerging agent—the seventh coronavirus identified to cause human infection.[9] Recently, the initial description of the pulmonary pathology that occurs from fatal COVID-19 has been described.[10]

An important question that remains unanswered is whether SARS-CoV-2 can be transmitted from a pregnant woman to her fetus, a process termed *vertical transmission*, and to determine the mechanism(s) if it does occur.[9,11–17] Not only is this a significant public health issue, but it also represents an obstetric management issue in determining the care received by pregnant women. The question is especially relevant given the recent history of maternal-fetal transmission of such emerging viral infections as the Zika virus, Ebola virus, Marburg virus, and other agents that can threaten the health and survival of an infected mother and fetus.[18–21]

PREVIOUS EXPERIENCES WITH CORONAVIRUS INFECTIONS DURING PREGNANCY

Pregnancy increases the risk of adverse obstetric and neonatal outcomes from many respiratory viral infections. The physiologic and immunologic changes that occur as a normal component of pregnancy can have systemic effects that increase the risk for complications from respiratory

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Table 1. Characteristics of 7 Pregnant Women With COVID-19 and Their Infants (after Chen et al[13])

	Chen[13]						
First Author and Case	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Maternal age, y	33	27	40	26	26	26	29
Gestational age at delivery	37 wk 2 d	38 wk 3 d	36 wk	36 wk 2 d	38 wk 1 d	36 wk 3 d	36 wk 2 d
Comorbid events	Influenza	None	Gestational hypertension	Preeclampsia	Fetal distress	None	PROM
Maternal RT-PCR for SARS-CoV-2	Positive	Positive	Positive	Positive	Positive	Positive	Positive
Symptom-to-delivery interval	1 d	6 d	4 d	3 d	1 d	4 d	2 d
C-s or vaginal	C-s	C-s	C-s	C-s	C-s	C-s	C-s
Birth weight, g	2870	3730	3820	1880	2970	3040	2460
Apgar score at 1 and 5 min	8, 9	9, 10	9, 10	8, 9	9, 10	9, 10	9, 10
Neonatal outcome	Normal	Normal	Normal	SGA	Normal	Normal	Normal
Neonatal RT-PCR for SARS-CoV-2	According to Chen et al,[13] 6 of 9 neonates were tested for SARS-CoV-2 and all 6 were found to be negative by RT-PCR, but which 6 neonates were tested was not specified.						

Abbreviations: C-s, C-section; PROM, premature rupture of membranes; RT-PCR, reverse transcription–polymerase chain reaction; SARS, severe acute respiratory syndrome; SGA, small for gestational age.

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infections. Changes in the maternal cardiovascular and respiratory systems, including increased heart rate, stroke volume, oxygen consumption, and decreased lung capacity, as well as the development of immunologic adaptations that allow a mother to tolerate an antigenically distinctive fetus, increase the risk for pregnant women to develop severe respiratory disease.[22] Outcomes data from multiple studies of influenza have demonstrated an increased risk of maternal morbidity and mortality when compared with nonpregnant women.[22,23] This association has also been previously demonstrated to occur when pregnant women develop either of 2 pathogenic coronavirus infections: severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS).[9]

Severe Acute Respiratory Syndrome

The SARS epidemic occurred from November 2002 to July 2003, affecting greater than 8000 persons in 26 countries and resulting in 774 fatalities.[24] The causative agent, a coronavirus termed SARS-CoV, was transmitted through close person-to-person contact, respiratory droplets, environmental contamination, and potentially sewage.[9,25] There were 12 reports of pregnant women who developed SARS during the epidemic, of whom 3 died during pregnancy (case fatality rate of 25%).[9] Miscarriages during the first trimester occurred in 4 of 7 women. Two of 5 women in the second and third trimester had a neonate with intrauterine growth restriction. In addition, 4 of 5 pregnancies resulted in preterm birth: 1 spontaneous and 3 induction deliveries that were performed for maternal conditions.[26] Vertical transmission of the SARS-CoV virus did not occur in any of the infants; however, the clinical outcomes of pregnant women with SARS were worse than those of infected women who were not pregnant.[9,26–29]

Middle East Respiratory Syndrome

MERS is another coronavirus infection that causes potentially severe respiratory disease. It was first reported from Saudi Arabia in 2012, after which it spread to more than 27 countries both within and outside of the Arabian Peninsula.[9,30] MERS-CoV has been identified in camels, which have been suggested as the primary source of human infections, as well as in bats, but more research is needed to understand the role that these and other animals may play in transmission. MERS-CoV is characterized by sporadic zoonotic transmission events as well as spread between infected patients and close contacts (ie, intrafamilial transmission). Outbreaks of MERS in health care settings are characteristic and result from poor infection control and preventative measures.[30,31]

MERS-CoV infection has been reported from 11 pregnant women, where it has been associated with a variety of adverse clinical outcomes among 10 (91%) of them. These outcomes have included maternal deaths, premature delivery, intensive care treatment for newborns, and perinatal death. There have been no confirmed cases of vertical transmission of MERS-CoV.[9]

CURRENT CLINICAL FEATURES AND OBSTETRIC OUTCOMES OF PREGNANT WOMEN WITH COVID-19

Reports have been published on a total of 38 pregnant women with COVID-19 originating from the epicenter of the pandemic in China.[13–17] All women were in the third trimester of pregnancy and included 37 women whose SARS-CoV-2 positivity was confirmed by reverse transcription–polymerase chain reaction (RT-PCR). These pregnancies resulted in 39 infants (1 set of twins); detailed clinical information, obstetric outcomes, and SARS-CoV-2 status were available for 29 neonates.

Zhongnan Hospital of Wuhan University, Wuhan, China

The condition of 9 pregnant women with COVID-19 has been described in a retrospective review of medical records by Chen et al[13] (Table 1). The women were tested for SARS-CoV-2 with RT-PCR kits recommended by the Chinese Center for Disease Control and Prevention (BioGerm, Shanghai, China). Samples were tested simultaneously using RT-PCR at the Clinical Laboratory of Zhongnan Hospital and State Key Laboratory of Virology/Institute of Medical Virology, School of Basic Medical Sciences, Wuhan University. Positive confirmatory cases of SARS-CoV-2 infection were reported when a positive test result from either laboratory was obtained. The mothers' ages varied between 26 and 40 years of age; they had documented exposure to the novel coronavirus and were in the third trimester of pregnancy when they developed COVID-19 infection. Although none of the women had a preexisting chronic condition such as diabetes, cardiovascular disease,

Table 2. Characteristics of Additional 7 Pregnant Women With COVID-19 and Their Infants (after Chen et al,[13] Liu et al,[14] and Zhu et al[15])

	Chen[13]		Liu[14]			Zhu[15]	
First Author and Case	Case 8	Case 9	Case 1	Case 2	Case 3	Case 1	Case 2
Maternal age, y	28	34	34	34	30	25	35
Gestational age at delivery	38 wk	39 wk 4 d	40 wk	38 wk 4 d	39 wk 5 d	38 wk 4 d	33 w 6 d
Comorbid events	Fetal distress	PROM	Hypothyroid	Placenta acreta	Gestational diabetes	Fetal distress, oligo	Scarred uterus
Maternal RT-PCR for SARS-CoV-2	Positive	Positive	Positive	Positive	Positive	Positive	Positive
Symptom-to-delivery interval	2 d	7 d	~1 d	~7 d	~13 d	<1 d	<1 d
C-s or vaginal	C-s	C-s	C-s	C-s	Vaginal	C-s	C-s
Birth weight, g	2800	3530	3250	3250	3670	2450	2050
Apgar scores at 1 and 5 min	9, 10	8, 10	8, 9	8, 9	8, 9	9, 10	9, 10
Neonatal outcome	Normal	Normal	Normal	Normal	Normal	SGA	SOB
Neonatal RT-PCR for SARS-CoV-2	See Table 1	See Table 1	Negative	Negative	Negative	Negative	Negative

Abbreviations: C-s, C-section; oligo, oligohydramnios; PROM, premature rupture of membranes; RT-PCR, reverse transcription–polymerase chain reaction; SARS, severe acute respiratory syndrome; SGA, small for gestational age; SOB, shortness of breath.

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or hypertension, 3 women had comorbid conditions that developed during their pregnancy: influenza (case 1), gestational hypertension occurring since 27 weeks' gestation (case 3), and preeclampsia developing at 31 weeks' gestation (case 4). Seven women were febrile upon admission; additional findings included cough (4 of 9), myalgia (3 of 9), sore throat (2 of 9), malaise (2 of 9), gastrointestinal symptoms (1 of 9), and shortness of breath (1 of 9). Laboratory findings included elevated C-reactive protein (6 of 9), lymphopenia (5 of 9), and increased alanine aminotransferase and aspartate aminotransferase (3 of 9). Chest computed tomography (CT) scans showed abnormalities for 8 of the 9 women, demonstrating lungs with patchy ground-glass shadows. Four women had preterm labor, but none occurring before 36 weeks' gestation. Cases 5 and 8 had fetal distress, and cases 7 and 9 had premature rupture of membranes. None of the women developed severe pneumonia, and there were no maternal deaths.

All 9 women underwent cesarean deliveries. Two of the 4 preterm infants were delivered at 36 weeks 2 days and weighed less than 2500 g (cases 4 and 7)—one of the newborn infants (case 4) had a birth weight of 1880 g and was delivered to a mother with preeclampsia. All of the infants had good Apgar scores.

The presence of SARS-CoV-2 was evaluated in 6 of the 9 cases from amniotic fluid, breastmilk, umbilical cord blood, and neonatal throat swabs; all test results were negative. The specific cases tested were not specified. All of the 6 neonatal samples tested were negative for SARS-CoV-2.

Tongji Hospital of Tongji Medical College, Huazhong University, Wuhan, China

Liu et al[14] reported on 3 pregnant women from the Tongji Hospital who became infected with SARS-CoV-2 during the third trimester. These 3 women were among a total of 17 pregnant women admitted to the obstetrics ward during the study period—a COVID-19 prevalence of approximately 18%. The women's ages ranged from 30 to 34 years (Table 2). COVID-19 testing was performed by using the RT-PCR assay with a SARS-CoV-2 ORF1ab/N gene detection kit (Shanghai Huirui Biotechnology Co, Ltd, Shanghai, China), a product based on the recommendation of the National Institute for Viral Disease Control and Prevention, Chinese Center for Disease Control and Prevention.

Case 1 involved a 34-year-old woman with hypothyroidism who was febrile before her hospital admission. Her chest CT showed progressively worsening bilateral pulmonary infiltrates. The mother had positive RT-PCR test results for SARS-CoV-2 from an oropharyngeal swab and feces; testing of breast milk, vaginal mucus, and placenta was negative. Her 3250-g infant was delivered at 40 weeks' gestational age by cesarean birth with chronic fetal distress, chorioamnionitis, meconium-stained membranes, but with good Apgar scores. Specimens from the infant including whole blood, plasma serum, umbilical cord blood, and an oropharyngeal swab were negative for SARS-CoV-2 by RT-PCR.

Case 2 involved a 34-year-old woman with no significant obstetric history or comorbid conditions. She developed a fever at 37 weeks of gestation, and a CT scan of the chest revealed bilateral ground-glass opacities and pulmonary consolidation, nodules in the left lower lobe, and patchy consolidation in the right middle lobe. An oropharyngeal swab taken 1 day before delivery was positive for SARS-CoV-2 by RT-PCR. A 3250-g infant was delivered by cesarean birth at 38 weeks 4 days' gestation with good Apgar scores. The newborn had slightly decreased muscle tone and responsiveness that had improved the day after delivery. Testing for SARS-CoV-2 from whole blood, serum, oropharyngeal swabs, urine, and feces by RT-PCR yielded all negative results for the novel coronavirus.

Case 3 involved a 30-year-old woman who had developed gestational hypertension during her first pregnancy. She developed cough at 37 weeks' gestation, and upon admission to the hospital had a chest CT scan that demonstrated ground-glass opacities, subsolid patch, and linear fibrosis in the left lung and enlarged mediastinal lymph nodes. An RT-PCR test finding for SARS-CoV-2 performed on an oropharyngeal swab was positive; follow-up testing of an anal swab, vaginal mucus, and breast milk yielded all negative results. She delivered a 3670-g infant by vaginal delivery at 39 weeks 5 days' gestation with good Apgar scores. Two RT-PCR tests for SARS-CoV-2 were performed on successive days with whole blood, plasma, oropharyngeal swabs, urine, and feces, and all yielded negative results.

The mothers in this report all presented with either fever or cough accompanied by CT abnormalities during the

course of their COVID-19 disease. None of the women developed severe pneumonia or died, and all 3 had successful perinatal outcomes with no evidence of intrauterine transmission of SARS-CoV-2.

Maternal and Child Health Hospital of Hubei Province, Union Hospital, Renmin Hospital, Tianmen First People's Hospital, Jingzhou Municipal Hospital and Child Health Hospital, and Pediatric Hospital Affiliated With Fudan University, China

Zhu et al[15] described in detail the pregnancies of 9 women with COVID-19 and their 10 infants (including 1 set of twins) from 5 hospitals in Hubei Province (Tables 2 and 3). The women's ages ranged from 25 to 35 years, and they had a 1- to 6-day interval between the onset of symptoms and delivery. All of the women had a chest CT revealing ground-glass opacities, patchy pulmonary consolidation, and blurred borders typical of viral pneumonia. Viral testing for SARS-CoV-2 nucleic acid was performed on throat swab specimens from the 9 women, and results were positive for all patients except the mother of the twins—her test finding was negative. She had typical clinical symptoms of COVID-19 and viral interstitial pneumonia by chest CT scan, and other diseases that could cause fever and lung infection were excluded. The local CDC then registered her as a confirmed 2019-nCoV case, and she was included in the current study.

The initial symptoms among these women were fever and/or cough. Prenatal conditions included fetal distress in 6 cases, premature rupture of membranes in 3 cases (5 to 7 hours before the onset of labor), oligohydramnios and polyhydramnios in 1 case each, umbilical cord abnormalities in 2 cases, and placenta previa in 1 case. Third-trimester obstetrical ultrasound findings were all normal. Seven of the mothers underwent cesarean deliveries, and 2 had vaginal deliveries. There were no cases of severe pneumonia or maternal death among the 9 women.

There were 8 singletons and 1 set of twins delivered to the mothers with COVID-19: 4 were full-term and 6 were premature. Two newborns were small for gestational age and 1 was large for gestational age. The infants were evaluated for well-being with the Pediatric Critical Illness Score (PCIS), the most widely used pediatric critical illness scoring method in China. Six of the newborns had a PCIS of less than 90—6 infants had shortness of breath, 2 were febrile, and 1 had a rapid heart rate. Gastrointestinal symptoms were present in 4 infants; these included gastric bleeding, refusal of milk, bloating, and feeding intolerance. Chest radiographs revealed that 7 newborns had abnormalities at the time of admission that included infection in 4, neonatal respiratory distress syndrome in 2, and pneumothorax in 1 infant. Two infants had the onset of thrombocytopenia associated with liver dysfunction. One premature infant developed shortness of breath and fluctuations of oxygenation with a decrease in platelets treated with respiratory support and transfusions. There was 1 neonatal fatality among the cohort (case 4)—a premature newborn developed shortness of breath, refractory shock, multiple organ failure, and disseminated intravascular coagulation and died on the ninth day of life. Four neonates remained hospitalized at the time of submission of the report. Pharyngeal swab specimens were collected from 9 of the neonates between 1 and 9 days following delivery and tested for SARS-CoV-2, and all were negative.

Table 3. Characteristics of Additional 7 Pregnant Women With COVID-19 and Their Infants Including 1 Set of Twins (after Zhu et al[15])

First Author and Case	Zhu[15]							
	Case 3	Case 4	Case 5	Case 6	Case 7	Case 8	Case 9	Case 10
Maternal age, y	35	30	30	30	30	29		34
Gestational age at delivery	34 w 2 d	34 wk 5 d	39 w	37 w	34 w 6 d	31 w		39 w
Comorbid events	Fetal distress	Vaginal bleeding, fetal distress	Cholecystitis	Placenta previa, fetal distress poly	Fetal distress	Twins, fetal distress, viral pneumonia c/w COVID-19		None
Maternal RT-PCR for SARS-CoV-2	Positive	Positive	Positive	Positive	Positive	Negative		Positive
Symptom-to-delivery interval	2 d after delivery	3 d after delivery	6 d before delivery	4 d before delivery	4 d before delivery	3 d before delivery		1 d after delivery
C-s or vaginal	Vaginal	C-s	C-s	C-s	C-s	Vaginal twin		C-s
Birth weight, g	2350	2200	3030	3800	2300	1520	1720	2810
Apgar scores at 1 and 5 min	8, 9	8, 8	8, 9	7, 8	9, 10	9, 10	9, 10	10, 10
Neonatal outcome	SOB	Multiple organ failure, shock, gastric bleeding, DIC, death	Diffuse scattered rashes, edema, facial skin lesions	LGA, in hospital	SOB, fever, GI bleeding DIC	SOB, in hospital	SOB, in hospital	SGA, SOB, cyanosis, in hospital
Neonatal RT-PCR for SARS-CoV-2	Negative	Negative	Not performed	Negative	Negative	Negative	Negative	Negative

Abbreviations: C-s, C-section; c/w, consistent with; DIC, disseminated intravascular coagulation; GI, gastrointestinal; LGA, large for gestational age; poly, polyhydramnios; RT-PCR, reverse transcription–polymerase chain reaction; SARS, severe acute respiratory syndrome; SGA, small for gestational age; SOB, shortness of breath.

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Table 4. Characteristics of an Additional 17 Pregnant Women With COVID-19 and Their Infants (after Wang et al 2020[16] and Zhang et al 2020[17])

Case and First Author	Case 1, Wang[16]	Cases 1 to 16, Zhang[17]
Maternal age, y	28	Varies from 24 to 34 y with mean of 29.3 ± 2.9 y
Gestational age at delivery	31 wk	Varies from 35 wk 5 d up to 41 wk with mean of 38.7 ± 1.4
Comorbid events	Fetal distress	Gestational diabetes (3), PROM (3), preterm delivery (3), uterine scarring (2), B-Lynch/compression suture procedure (2), severe preeclampsia (1), fetal distress (1), fetal asphyxia (1), meconium staining (1), COVID-19 pneumonia (1)
Maternal RT-PCR for SARS-CoV-2	Positive	Positive in all 16 women
Symptom-to-delivery interval	13 d before delivery	Not stated
C-s or vaginal	C-s	C-s in all 16 women
Birth weight	1830 g	Varies from 2300 to 3750 g with mean of 3139 ± 437 g
Apgar scores at 1 and 5 min	9, 10	Not stated
Neonatal outcome	Normal	Bacterial pneumonia in 3 neonates, 1 preterm infant
Neonatal RT-PCR for SARS-CoV-2	Negative	Viral testing results available for 10 of 16 neonates, all of whom were negative for infection

Abbreviations: C-s, C-section; PROM, premature rupture of membranes; RT-PCR, reverse transcription–polymerase chain reaction; SARS, severe acute respiratory syndrome.

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The Second Affiliated Hospital and The Affiliated Infectious Hospital of Soochow University, Suzhou, China

In a case report Wang et al[16] described the condition of a 28-year-old pregnant woman who presented to the hospital with a fever of 1-week duration (Table 4). She was at 30 weeks' gestation at the time of her admission and 2 throat swabs tested negative for SARS-CoV-2 by RT-PCR. Chest CT examination 2 days later showed left-sided subpleural patchy consolidation and right-sided ground-glass opacities. A repeated RT-PCR examination of sputum performed 4 days after admission showed positivity for SARS-CoV-2. She was transferred to the intensive care unit where she was placed in isolation. Obstetric ultrasonography revealed a normal fetus of 30 weeks' gestation. On hospital day 3, decreased fetal movement was observed with absent variability of the fetal heart rate, and an emergency cesarean delivery was performed. A preterm male infant was delivered that weighed 1830 g and with Apgar scores of 9 and 10 at 1 and 5 minutes, respectively. Samples were taken of placenta, amniotic fluid, umbilical cord blood, gastric juice, and throat swabs of the infant; all tested negative for SARS-CoV-2 by RT-PCR. Three days following delivery RT-PCR test results of the neonatal throat swab and stool samples were negative. Seven and 9 days after birth throat swab and RT-PCR test findings from the mother and the infant remained negative for the novel coronavirus.

Renmin Hospital of Wuhan University, Wuhan and the Central Hospital of Qianjiang City, Qianjiang, China

Zhang and colleagues[17] retrospectively examined medical records of 16 pregnant women with RT-PCR–confirmed COVID-19 and their newborn infants, and compared these results with a cohort of 45 pregnant women who were not infected (translated from Simplified Chinese by DAS); this constituted the first comparison study between women with and without SARS-CoV-2 infection during pregnancy. Throughout this study testing for SARS-CoV-2 was performed by using the New Coronavirus (2019) Nucleic Acid Detection Kit (Dual Fluorescence PCR) provided by Jiangsu Shuo Shi Biotechnology Co, Ltd (Taizhou City, China). All women were in their third trimester of pregnancy. Diagnosis of COVID-19 was based on the diagnostic criteria of the New Coronavirus Infected Pneumonia Diagnosis and Treatment Plan (Trial Fifth Edition) issued by the National Health and Health Commission.

In the COVID-19 cohort the women's ages varied from 24 to 34 years; they had previously been pregnant between 1 and 4 times and had parity varying from 0 to 1 (Table 4). The gestational age at the time of delivery varied between 35 weeks 5 days and up to 41 weeks, averaging 38.7 weeks. In the cohort of women who were not infected with SARS-CoV-2 the maternal ages varied between 24 and 40 years; they had 1 to 5 previous pregnancies and parity of 0 or 1, and delivered their infants between 35 weeks 2 days and 41 weeks with an average of 37.9 weeks. The women with COVID-19 had infants weighing between 2300 and 3750 g (average, 3139 g), and the women without COVID-19 had infants weighing between 2180 and 4100 g (average, 3260 g). There were no significant differences between the 2 cohorts in gravidity, parity, gestational age at delivery, birth weight, or intraoperative blood loss. The maternal ages were significantly different: mothers in the COVID-19 cohort were younger than those in the non–COVID-19 cohort ($P = .01$).

Among the 16 women with COVID-19 there were several mothers with comorbid obstetric conditions: 3 women had gestational diabetes, 3 had premature rupture of membranes, 3 had preterm deliveries, 2 had scarred uterus, and 2 required B-Lynch suture procedure (a form of compression suture used in obstetrics to mechanically compress an atonic uterus in the clinical setting of severe postpartum hemorrhage). There was 1 incident of severe preeclampsia, meconium-stained amniotic fluid, fetal distress, and fetal asphyxia. Three of 16 women with COVID-19 had cough, chest tightness, shortness of breath, and diarrhea that did not improve significantly with treatment. One of these mothers had COVID-19 pneumonia; she was 35 weeks 6 days' gestation with oxygen saturation of 93% accompanied by chest tightness and shortness of breath, and with decreased fetal movement and abnormal fetal heart monitoring. All of the women with COVID-19 underwent cesarean deliveries.

There were no significant differences between the groups of pregnant women with and without COVID-19 in occurrence of severe preeclampsia, gestational diabetes, premature rupture of membranes, fetal distress, meconium-

stained amniotic fluid, premature delivery, neonatal asphyxia, B-Lynch suture procedure or other compression sutures. The proportion of uterine scarring in the non–COVID-19 group was statistically higher than that in COVID-19 group ($P = .03$); this abnormality predated the development of COVID-19.

Among the cohort of 16 mothers with COVID-19 there were 10 infants for whom SARS-CoV-2 infection status was known; all findings were negative by RT-PCR analysis of throat swabs. Nine of these newborns were full-term and 1 was preterm (36 weeks 2 days). Three of the neonates had bacterial pneumonia as based on their symptoms, laboratory testing, sputum culture, and imaging results; all of them recovered after treatment. After discharge of the newborns from the hospital, follow-up examinations demonstrated no neonatal illness or deaths.

DISCUSSION

Intrauterine transmission is one of the most serious complications of viral diseases occurring during pregnancy. It can occur with maternal infection by congenitally transmitted TORCH agents (acronym for **T**oxoplasma, **o**ther, **r**ubella, **c**ytomegalovirus, **h**erpes) that also include Zika virus and Ebola virus.[32] Maternal-fetal transmission of viral diseases (with the exception of herpes virus) is usually through the hematogenous route in which the virus circulating in the maternal blood stream enters the placenta, reaches the chorionic villous tree and fetal blood vessels, and is transmitted to the fetus. Fortunately, this mechanism of transmission has been shown not to occur with infection of pregnant women with 2 other pathogenic coronaviruses—SARS-CoV and MERS-CoV—although the clinical infections caused by these coronaviruses has resulted in severe maternal pneumonia, maternal deaths, and early pregnancy losses.[12]

In this analysis of the detailed published reports of 38 pregnant women with COVID-19, of whom 37 had RT-PCR–confirmed SARS-CoV-2 infection, there were no cases of either severe pneumonia or maternal deaths. Although there were comorbid conditions present in some of the women, some of which were obstetric in etiology, they did not result in life-threatening maternal SARS-CoV-2 disease. It is significant that these comorbid maternal conditions, which included preeclampsia, pregnancy-induced hypertension, uterine scarring, gestational diabetes, and uterine atony, did not appear to be risk factors for intrauterine transmission of SARS-CoV-2 to the fetus.

Among the 29 neonates delivered to these women who underwent testing, there were no cases of RT-PCR–confirmed SARS-CoV-2 infection, despite the existence of perinatal complications in some of the infants. An interesting observation is that in those cases where placentas were tested for SARS-CoV-2, the results were negative. This lack of maternal-fetal transmission of SARS-CoV-2 is consistent with past experiences with other coronavirus infections—SARS and MERS—occurring in pregnant women.

Early in the epidemic there were 2 reported cases of neonatal SARS-CoV-19 infection. One involved an infant diagnosed at 17 days of life with a history of close contact with 2 confirmed cases of SARS-CoV-2 infection (mother and nanny), and the other was a neonate who was found to be infected 36 hours following delivery. For both infants there was no direct evidence for vertical transmission, and because viral testing was delayed, a postpartum neonatal infection acquired through an infected contact could not be eliminated.[11,12]

A joint mission by the World Health Organization, consisting of 25 national and international experts, travelled to the affected regions of China between February 16 and 24, 2020.[33] They investigated 147 pregnant women (64 confirmed, 82 suspected, and 1 asymptomatic with COVID-19). Among these women 8% had severe disease and 1% had critical conditions. The joint mission concluded that pregnant women were not at higher risk for developing severe disease due to COVID-19. This report did not examine vertical transmission or neonatal outcomes.

As this global epidemic continues to expand there will be additional information available on the effects of COVID-19 on pregnant women and their infants. In the unfortunate event of mortality resulting from SARS-CoV-2 infection among pregnant women or neonates, pathologic evaluation of tissues together with molecular characterization of the virus would be useful in determining the pathogenesis of the disease as it has in many cases of emerging infections.[34] There are currently updated recommendations available on the obstetric management of SARS-CoV-2 infection in pregnant women.[35] In addition, it must be remembered that as vaccine development proceeds for COVID-19, pregnant women should be considered for inclusion in the clinical trials, as well as the eventual distribution of the vaccine, unless the risks outweigh the potential benefits.[36]

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