Effects of Severe Acute Respiratory Syndrome Coronavirus 2 Infection on Pregnant Women and Their Infants

A Retrospective Study in Wuhan, China

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• ***Context.***—**The pandemic of a novel coronavirus, termed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has created an unprecedented global health burden.**

Objective.—**To investigate the effect of the SARS-CoV-2 infection on maternal, fetal, and neonatal morbidity and other poor obstetrical outcomes.**

Design.—**All suspected cases of pregnant women with coronavirus disease 2019 (COVID-19) admitted into one center in Wuhan from January 20 to March 19, 2020, were included. Detailed clinical data of those pregnancies with COVID-19 were retrospectively collected and analyzed.**

Results.—**Twenty-seven pregnant women (4 early pregnancies included) with laboratory or clinically confirmed SARS-CoV-2 infection and 24 neonates born to the 23 women in late pregnancy were analyzed. On admission, 46.2% (13 of 27) of the patients had symptoms, including fever (11 of 27), cough (9 of 27), and vomiting (1 of 27). Decreased total lymphocytes count was observed in 81.5% (22 of 27) of patients. Twenty-six patients showed typical viral pneumonia by chest computed tomography scan, whereas 1 patient confirmed with COVID-19 infection showed no abnormality on chest computed tomography. One mother developed severe pneumonia 3 days after her delivery. No maternal or perinatal death occurred. Moreover, 1 early preterm newborn born to a mother with the complication of premature rupture of fetal membranes, highly suspected to have SARS-CoV-2 infection, was SARS-CoV-2 negative after repeated real-time reverse transcriptase polymerase chain reaction testing. Statistical differences were observed between the groups of women in early and late pregnancy with COVID-19 in the occurrence of lymphopenia and thrombocytopenia.**

Conclusions.—**No major complications were reported among the studied cohort, though 1 serious case and 1 perinatal infection were observed. Much effort should be made to reduce the pathogenic effect of COVID-19 infection in pregnancies.**

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In December 2019, a series of pneumonia cases of unknown cause was reported in Wuhan, Hubei, China.[1] Soon after the report, deep sequencing analysis indicated that a novel betacoronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was the pathogen, and the disease caused by SARS-CoV-2 was termed coronavirus disease 2019 (COVID-19).[2,3] Although the strictest preventive measures were taken in Wuhan, in a short span of time COVID-19 was reported in China and other countries around the world. A severe public health problem was caused by SARS-CoV-2. On March 11, 2020, COVID-19 was declared a pandemic by the World Health Organization.[4]

With the global outbreak of COVID-19, increasing evidence has enriched our knowledge of the genetic, virologic, epidemiologic, and clinical aspects of this pandemic novel coronavirus infection pneumonia.[5–7]

Pregnant women experience changes in their bodies that may increase their risk of pneumonia infection.[8] There are more and more reports of pregnant women with COVID-19 infection.[9,10] However, many issues in this special population with COVID-19 are still largely undefined. An

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important question that remains unanswered is whether SARS-CoV-2 can be transmitted from a pregnant woman to her fetus. Large, continuous investigation on pregnant women with COVID-19 and their newborns remains merited.

In this study, we report the clinical characteristics and obstetric outcomes of 27 pregnant women with COVID-19 (4 early pregnancies included) and follow-up information on 24 newborns (including 1 set of twins) born to 23 women in late pregnancy at a center in Wuhan, China, from January 20 to March 19, 2020. We include all hospitalized pregnant women confirmed or clinically diagnosed with COVID-19 infection in the studied center in Wuhan during this epidemic. The focus of the study is to investigate whether pregnant women with COVID-19 are more likely to have serious illness, the possibility of maternal-fetal transmission of the virus, and perinatal infections and death.

METHODS

Study Design and Patients

This is a retrospective study conducted at Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology in Wuhan, China. The study was approved by the institutional ethics board of the studied hospital (No. 202041). Eligible participants were hospitalized pregnant patients with suspected or probable SARS-CoV-2 infection admitted to the studied center from January 20 to March 19, 2020; cases were diagnosed based on the updated new coronavirus pneumonia prevention and control program published by the National Health Commission of China.[11] On February 2, clinical diagnosis was proposed for the first time in the 5th edition of guidance for diagnosis and treatment of COVID-19.[12] A laboratory-confirmed case with COVID-19 was defined as a positive result of a real-time reverse transcriptase polymerase chain reaction (RT-PCR) assay for nasal and pharyngeal swab specimens and/or antibody testing of SARS-CoV-2. Patients who presented with fever and respiratory symptoms were clinically confirmed. Further laboratory and chest radiographic testing also demonstrated typical findings of COVID-19 while pathogen detection of SARS-CoV-2 was negative.

Data Collection

Clinical records, laboratory results, and chest CT scans from all the pregnant patients suspected with SARS-CoV-2 infections were retrospectively reviewed. The data were reviewed and collected by the ordering physicians from electronic medical records. Information recorded included demographic data, medical history, exposure history, underlying comorbidities, symptoms, signs, laboratory findings, chest CT scans, and treatment measures (ie, antiviral therapy, corticosteroid therapy, respiratory support, etc). The date of disease onset was defined as the day a symptom was noticed. The clinical outcomes (ie, discharges, maternal and neonatal morbidity and mortality) were monitored up to March 29, 2020, the final date of follow-up.

Laboratory Confirmation

Repeated tests of RT-PCR for SARS-CoV-2 were done in the suspected cases. All samples were processed and analyzed at the Department of Clinical Laboratory of Wuhan Central Hospital. The combination of nucleic acid and immunologic detection of antibodies of SARS-CoV-2 was recommended at that time by medical experts and scientists.

RNA was extracted from the collected swab samples. The RT-PCR assay was performed using a fluorescence-based quantitative polymerase chain reaction kit with the Chinese Center for Disease Control and Prevention recommendation. The assay was conducted in accordance with the protocol established by the World Health Organization.[13]

The commercial SARS-CoV-2 IgM/IgG Antibodies Rapid Test kit (Innovita Biological Technology Co Ltd) was used to detect antibodies of SARS-CoV-2 in the blood samples of suspected patients according to the manufacturer's protocol (available since March 4, 2020). Another 7 common respiratory viruses (influenza virus A and B, parainfluenza virus 1, 2, and 3, respiratory syncytial virus, and adenovirus) were also tested for in those suspected cases by immunofluorescence assay.

Statistical Analysis

Categorical variables are described as frequency rates and percentages, and continuous variables are described using mean, median, and interquartile range values. Differences in continuous variables were analyzed with independent group t tests when the data were normally distributed; otherwise, the Mann-Whitney test was used. Differences in the categorical variables within the 2 groups were compared by χ^2 test or Fisher exact test as appropriate. All statistical analyses were performed using SPSS version 18.0 software. All statistical tests were 2-sided, and statistical significance was set at $P < .05$.

RESULTS

Clinical Features and Obstetrical Outcomes of Pregnant Women With COVID-19

Nineteen confirmed and 8 clinically diagnosed COVID-19–infected pregnant women were included in the current study. All 8 clinically diagnosed cases had typical clinical symptoms of COVID-19 and had viral interstitial pneumonia by chest CT scan, although pathogen detection for SARS-CoV-2 and the other 7 common respiratory viruses was negative. Among this studied cohort of pregnant women, 3 cases were admitted to the hospital in January, 18 cases in February, and 6 cases in March. Four pregnant women were in their first trimester; the other 23 pregnant women were all in their third trimester, with gestational weeks ranging from 30 to 40.

The age distribution of the studied patients was 22 to 39 years. Three patients had underlying diseases: 2 patients had hepatitis B infection and the other had schistosomiasis. Further, 7 patients had at least 1 complication of pregnancy, including gestational diabetes mellitus (3 cases), dysfunction of blood coagulation (3 cases), gestational hypertension (2 cases), hypothyroidism (2 cases), severe preeclampsia (1 case), and hypoproteinemia (1 case).

All patients were given oxygen support (nasal cannula) and antibiotic treatment (orally and intravenously). Nineteen patients were administered antiviral therapy (Arbidol orally and/or ribavirin intravenously). Corticosteroid therapy was given in 1 patient with severe pneumonia. Additionally, all 4 hospitalized early pregnant women voluntarily choose an induction abortion on admission because of COVID-19 infection, though a stable condition was maintained during their pregnancy and no presage abortion were reported. As of March 29, 2020, all the 27 infected pregnant women were discharged after treatment and quarantine isolation.

On admission, 46.2% (13 of 27) of the pregnant women had symptoms, including fever (11 of 27) and/or cough (9 of 27) and vomiting (1 of 27). Patients' body temperatures fluctuated within a range of 36.3°C to 38.6°C, with 2 patients exceeding 38.2°C. During hospitalization, 1 patient with hepatitis B infection and dysfunction of blood coagulation during her pregnancy developed severe pneumonia (arterial oxygen saturation <90%) 3 days after the delivery.

Of the 23 women in the third trimester, 18 underwent cesarean section and 5 had vaginal delivery. Most mothers

Table 1. Characteristics of 23 Women in Late Pregnancy With COVID-19 and Their Infants				
Cases	All Patients in the Third Trimester (N = 23)	Case 21 (Severe Case)	Case 22 (Twin Gestation)	Case 23 (pPROM)
Maternal age, y	Mean, 29.91 ± 3.61 (range, 21–40)	28	26	39
Gestational age at delivery	Median, 38.0 wk (range, 30 wk 6 d–40 wk; IQR, 37.3–39.1 wk)	38 wk 5 d	37 wk 2 d	30 wk 6 d
Comorbid disease	Virus hepatitis (2 cases), schistosomiasis (1 case)	Virus hepatitis	None	None
Complications in gestation	Gestational diabetes (3 cases), dysfunction of blood coagulation (3 cases), hypothyroid (2 cases), gestational hypertension (2 cases), severe preeclampsia (1 case), hypoproteinemia (1 case)	Dysfunction of blood coagulation	None	Gestational diabetes
Initial symptom(s)	Fever (11 cases), cough (9 cases), vomiting (1 case)	None	Fever	Fever, cough
Symptom to delivery interval, d	1–20	2	2	7
Maternal nucleic acid test (RT-PCR) for SARS-CoV-2	Positive (11), negative (12)	Positive	Positive	Negative
Maternal serologic testing for SARS-CoV-2	IgG positive (6 cases), not tested (17 cases)	Not tested	Not tested	IgG positive
Delivery mode	Cesarean section (18 cases); vaginal (5 cases)	Vaginal	Cesarean section	Cesarean section
Birth weight, g	Mean, 3290 ± 297 (range, 1500–3750)	3370	2350/2620	1500
Apgar scores				
1 min	9	10	10	4
5 min	10	10	10	7
Neonatal outcome	Premature delivery (1 case), low birth weight (<2500 g) (2 cases), severe neonatal asphyxia (1 case)	Normal	Low birth weight	Severe neonatal asphyxia
Neonatal nucleic acid test (RT-PCR) for SARS-CoV-2	Negative (23 cases), positive (0 case), not tested (1 case)	Negative	Negative	Negative
Neonatal serologic testing for SARS-CoV-2	IgG and IgM positive (1 case), not tested (23 cases)	Not tested	Not tested	IgG and IgM positive

Abbreviations: Ig, immunoglobulin; IQR, interquartile range; pPROM, preterm premature rupture of fetal membranes; RT-PCR, reverse transcriptase polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

(19 of 23) delivered on the first or second day of their admission. Specifically, 1 pregnancy presented to the hospital at 35 weeks 4 days' gestation with a fever of 1-week duration. Then, she had a term delivery by cesarean section in the 37th week of gestation. Additionally, 3 patients had premature rupture of fetal membranes (PROM), including 1 mother with preterm PROM (pPROM) at the 30th gestational week. The mother with pPROM had an emergency caesarean section at 30 weeks 6 days' gestation. The other 22 patients had mature delivery. The prenatal problems included abnormal umbilical cord (n = 4), intrauterine distress (n = 3), and abnormal amniotic fluid (n = 1) (Table 1).

Radiologic and Laboratory Findings of Pregnant Women With COVID-19 at Presentation

All patients had a chest CT scan; 26 showed typical viral pneumonia—multiple patchy ground-glass shadows in lungs. Nineteen patients presented with bilateral pulmonary lesions, and 7 showed with unilateral pulmonary lesions. One patient showed no abnormality on chest CT, whereas both her nucleic acid test and serologic testing results for SARS-CoV-2 were positive.

No significant difference in CT scan presentation was observed between the confirmed and clinically diagnosed patients. Specifically, 78.9% (15 of 19) confirmed-infection women showed bilateral pulmonary lesions, in contrast to 62.5% (5 of 8) clinically diagnosed women.

The routine blood testing of patients on admission showed that 14 of the 27 pregnant women had a decreased total lymphocyte count ($<1.5 \times 10^9$ cells/L), with 1 patient presenting with leukopenia (white blood cell count $<4 \times 10^9$/L). Additionally, 9 patients had an increased total white blood cell count ($>10 \times 10^9$ cells/L) on admission. Data from laboratory testing also showed that many patients had increased serum levels of D-dimer, C-reactive protein, and procalcitonin on admission.

During hospitalization, more patients showed abnormal white blood cell count and elevated C-reactive protein. Moreover, more prominent laboratory testing abnormalities (ie, leukopenia, lymphopenia, thrombocytopenia) were observed in the case with severe pneumonia (data not shown).

No significant differences in laboratory findings were observed between the confirmed and clinically diagnosed patients. However, there was a statistical difference between the groups of early-pregnancy and late-pregnancy groups in occurrence of laboratory testing abnormalities. Particularly, more patients in late pregnancy showed lymphopenia and thrombocytopenia compared with those in early pregnancy ($P < .05$; Table 2).

Table 2. Radiologic and Laboratory Findings of Pregnant Women With COVID-19

		Confirmed Versus Suspected Cases			Early Versus Late Pregnancy		
	All Patients (n = 27)	Confirmed Cases (n = 19)	Clinically Diagnosed Cases (n = 8)	*P*	Patients in the First Trimester (n = 4)	Patients in the Third Trimester (n = 23)	*P*
Radiologic findings							
Abnormalities on chest CT, No./total (%)	26/27 (96.3)	18/19 (94.7)	8/8 (100)	>.99	4/4 (100)	22/23 (95.7)	>.99
Bilateral patchy shadowing, No./total (%)	19/27 (70.4)	14/19 (73.7)	5/8 (62.5)	.66	2/4 (50.0)	17/23 (73.9)	.29
Unilateral patchy shadowing, No./total (%)	7/27 (25.9)	4/19 (21.1)	3/8 (37.5)		2/4 (50.0)	5/23 (21.7)	
Laboratory findings							
White blood cell count, $\times 10^9$ cells/L	9.52 (6.2–11.22)	10.24 (4.69–11.7)	8.41 (6.63–10.97)	.83	5.2 (3.28–12.19)	10.23 (6.58–11.22)	.20
<4, No./total (%)	4/27 (14.8)	4/19 (21.1)	0/8 (0)	.61	2/4 (50.0)	2/23 (8.7)	.12
>10, No./total (%)	14/27 (51.9)	10/19 (52.6)	3/8 (37.5)		1/4 (25.0)	13/23 (56.5)	
Lymphocyte count, $\times 10^9$/L	1.19 (0.86–1.46)	1.13 (0.79–1.44)	1.35 (1.17–1.58)	.22	1.83 (1.25–2.16)	1.18 (0.82–1.42)	.03
≥1 to <1.5, No./total (%)	14/27 (51.9)	9/19 (47.4)	5/8 (62.5)	.62	1/4 (25.0)	13/23 (56.5)	.01
<1, No./total (%)	8/27 (29.6))	7/19 (36.8)	1/8 (12.5)		0/4 (0)	8/23 (34.8)	
Platelet count ≤150× 10^9/L, No./total (%)	3/4 (75.0)	1/2 (50.0)	2/2 (100.0)	>.99	NA	3/4 (75.0)	NA
D-dimer, mg/L	2.74 (0.21–4.99)	2.85 (1.30–6.81)	2.74 (1.59–3.62)	.74	0.80 (0.23–1.17)	3.62 (1.88–3.63)	.003
≥0.5 to <1, No./total (%)	2/23 (8.7)	1/19 (5.3)	1/8 (12.5)	.86	2/4 (50.0)	0/19 (0)	.002
≥1 to <3, No./total (%)	10/23 (43.5)	6/19 (31.6)	4/8 (50.0)		1/4 (25.0)	9/19 (47.4)	
≥3, No./total (%)	10/23 (43.5)	8/19 (42.1)	2/8 (25.0)		0/4 (0)	10/19 (52.6)	
C-reactive protein concentration, mg/L	20.3 (8.1–52.7)	2.40 (0.99–5.27)	1.38 (0.42–4.71)	.40	9.8 (2.55–13.97)	24.0 (8.13–53.35)	.08
≥10, No./total (%)	19/26 (73.1)	14/18 (77.8)	5/8 (62.5)	.64	2/4 (50.0)	17/22 (77.3)	.29
Procalcitonin level, ng/mL	0.07 (0.05–0.17)	0.06 (0.05–0.16)	0.08 (0.06–0.28)	.35	0.04 (0.04–0.04)	0.12 (0.05–0.18)	.05
≥0.1 to <0.5, No./total (%)	9/21 (42.9)	6/15 (40.0)	3/6 (50.0)	.66	0/2 (0)	9/19 (47.4)	.21
≥0.5, No./total (%)	2/21 (9.5)	1/15 (6.7)	1/6 (16.7)		0/2 (0)	2/19 (10.5)	
Lactose dehydrogenase ≥250 U/L, No./total (%)	4/23 (17.4)	3/16 (18.8)	1/7 (14.3)	>.99	1/3 (33.3)	3/20 (15.0)	.45
Aspartate aminotransferase >40 U/L, No./total (%)	2/27 (7.4)	2/19 (10.5)	0/8 (0)	>.99	0/4 (0)	2/23 (8.7)	>.99
Alanine aminotransferase >40 U/L, No./total (%)	2/27 (7.4)	2/19 (10.5)	0/8 (0)	>.99	0/4 (0)	2/23 (8.7)	>.99
Creatinine ≥133 μmol/L, No./total (%)	0/19 (0)	0/19 (0)	0/8 (0)	>.99	0/4 (0)	0/23 (0)	>.99

Abbreviations: CT, computed tomography; NA, not available.

Information About Neonates Born to Infected Mothers

Twenty-four live births (including 1 set of twins) were delivered to the 23 women in late pregnancy with COVID-19. Among these newborns, 23 were full term with a good Apgar score, and 1 preterm infant had Apgar scores of 4 at 1 minute and 7 at 10 minutes. In addition, 1 of the twin newborns had a birth weight lower than 2500 g, with a birth weight of 2350 g.

Twenty-three of the 24 newborns had SARS-CoV-2 testing of throat swab samples, and all showed negative on RT-PCR testing for SARS-CoV-2. Among these, 1 preterm newborn, born to a mother with pPROM, showed elevated immunoglobulin (Ig) G and IgM levels for SARS-CoV-2 two hours after the birth, but tested negative for SARS-CoV-2 on repeated RT-PCR testing (twice) of the swab samples (one collected immediately after birth and the other collected along with the blood draw for serum antibody test of SARS-CoV-2). Additionally, besides the newborn highly suspected to have SARS-CoV-2 infection, another 3 infants with a chest x-ray after birth showed slight inflammatory changes.

After their discharge, a telephone follow-up was conducted on the 23 newborns with unavailable testing results or negative results for pathogen detection of SARS-CoV-2. No infants showed signs of infection, and all have remained healthy until the date of submission of this paper.

DISCUSSION

As of April 16, coronavirus cases have surpassed 2 million around the world (Johns Hopkins University and Medicine in Baltimore, Maryland, Coronavirus Resource Center), though cases in mainland China are beginning to decrease. Pregnant women bear a high risk of developing severe pneumonia because of the physiologic and immunologic changes during pregnancy.[8] This has been evident historically during previous epidemics of viruses from the same family of COVID-19—severe acute respiratory syndrome, Middle East respiratory syndrome, and other viral respiratory infections.[14]

The majority of mothers in this study had no serious illness, although comorbid conditions and obstetrical complications such as preeclampsia, gestational diabetes, hypothyroidism, dysfunction of blood coagulation, etc, presented in some of the women. One pregnant woman with COVID-19 showed severe pneumonia. All mothers were discharged without major complications. Up to now, there has been one case of maternal intensive care unit admission and no maternal deaths have been reported in China.[10,15] The clinical manifestations, complications, and treatments in this study were similar to those in earlier published studies in the same population.[16–18] The clinical observations were further validated by the recent study by Thevarajan et al[19] of the immune responses of a female patient with mild to moderate COVID-19, which indicated that the immune responses to the newly emerged virus SARS-CoV-2 was similar to those of the avian H7N9 disease. Early adaptive immune responses might correlate with better clinical outcomes.[19]

Notably, our study has revealed that pregnant women with COVID-19 infection in the third trimester more easily presented with laboratory testing abnormalities than those infected with COVID-19 in their first trimester. Studies in nonpregnant adult patients with COVID-19 have showed that more prominent abnormal laboratory results were found in severe cases and were important risk indicators for the clinical outcome.[1,20,21] Whether women in late pregnancy were at a higher risk for developing severe disease than those in early pregnancy is not possible to conclude because of limited information on pregnant patients at earlier stages of gestation. Future studies are needed to address this subject.

One newborn, born to the mother with pPROM, was clinically diagnosed with SARS-CoV-2 infection, though repeated RT-PCR testing for SARS-COV-2 was negative. The newborn was delivered by urgent cesarean at 30 weeks 6 days' gestation in our hospital (March 19, 2020). She had shortness of breath at birth and SARS-CoV-2 infection was suspected. The newborn was isolated without physical contact with the mother after her birth. Then, she was transferred to Wuhan Women and Children Health Hospital (designated medical center for COVID-19 pregnant women and their newborns) immediately and was reported to have an elevated IgM level of SARS-CoV-2 two hours after her birth. Her mother was still hospitalized in our hospital after the delivery. The mother presented with bilateral pulmonary lesions and elevated IgG and IgM levels of SARS-CoV-2, though RT-PCR testing on her nasopharyngeal swab was negative (tested twice). Particularly, the mother had PROM at 30 weeks' gestation, 7 days before the delivery, which indicated that the fetus has been exposed for 7 days without the protection of the amniotic membrane. One can easily assume that the intrauterine COVID-19 infection in this particular case most probably occurred in the period between membrane rupture and birth. In cases of pPROM, the medical decision of delivery is more complicated. It is not clear if intervening early is better than waiting for birth to occur spontaneously. Fortunately, the infected newborn was discharged without major complications 29 days after her birth (April 17, 2020), with antibody testing for SARS-CoV-2 turning negative. Nonetheless, our observation has suggested that more efforts should be taken to reduce the occurrence of serious pathologic events in these particular patients.

Intrauterine transmission is one of the most serious complications of viral diseases occurring during pregnancy. There was no case of vertical transmission identified among pregnant women infected with other coronavirus infections—severe acute respiratory syndrome and Middle East respiratory syndrome—during epidemics.[14] Early in the SARS-CoV-2 epidemic, 3 cases of neonatal infection were reported.[22,23] On March 26, 2 articles[24,25] in *JAMA* from separate research teams in China reported neonatal infection: they presented 3 newborns with elevated IgM antibody values in blood drawn following birth, which suggested possible vertical transmission of SARS-CoV-2. However, similarly to our study, repeated nucleic acid tests of SARS-CoV-2 on nasopharyngeal samples from the 3 infants were negative. Whether SARS-CoV-2 can be transmitted from a pregnant woman to her fetus warrants more evidence, and the mechanism(s) merits further study.

Except for this particular case, no serious case or neonatal death was observed among our studied cohort of neonates. However, Zaigham and Andersson[10] analyzed the perinatal outcome of 108 infected pregnancies among the available literature, and 1 case of intrauterine fetal death and 1 case of neonatal death were found. In light of these findings, severe perinatal morbidity as a result of a mother with COVID-19 cannot be ruled out.

CONCLUSIONS

We acknowledge that this study has some limitations due to the retrospective method used. One limitation is that no direct testing of intrauterine tissue samples such as amniotic fluid, cord blood, or placenta was done to confirm the intrauterine transmission of COVID-19 infection in the neonate.

Collectively, data addressed in our study will improve our understanding of the effects of this newly emerged coronavirus on pregnant women and their infants. No maternal or neonatal death occurred. Perinatal infection was observed in 1 infant born to a mother with COVID-19. It remains to be seen which factors may modulate maternal and perinatal outcomes during the global COVID-19 epidemic. Additional research on the immune response in relation to the clinical characteristics, as well as the mechanisms of vertical transmission, is necessary.

References

1. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395(10223):497–506. doi:10.1016/S0140-6736(20)30183-5

2. Lu R, Zhao X, Li J, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet*. 2020;395(10224):565–574. doi:10.1016/S0140-6736(20)30251-8

3. World Health Organization. Naming the coronavirus disease (COVID-2019) and the virus that causes it. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it. Accessed February 23, 2020.

4. World Health Organization. WHO Director-General's opening remarks at the media briefing on COVID-19—11 March 2020. https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19—11-march-2020. Accessed March 11, 2020.

5. Xie M, Chen Q. Insight into 2019 novel coronavirus—an updated interim review and lessons from SARS-CoV and MERS-CoV. *Int J Infect Dis*. 2020;94:119–124. doi:10.1016/j.ijid.2020.03.071

6. Shereen MA, Khan S, Kazmi A, Bashir N, Siddique R. COVID-19 infection: origin, transmission, and characteristics of human coronaviruses. *J Adv Res*. 2020;24:91–98. doi:10.1016/j.jare.2020.03.005

7. Kolifarhood G, Aghaali M, Mozafar Saadati H, et al. Epidemiological and clinical aspects of COVID-19; a narrative review. *Arch Acad Emerg Med*. 2020; 8(1):e41.

8. Goodnight WH, Soper DE. Pneumonia in pregnancy. *Crit Care Med*. 2005; 33(10 suppl):S390–S397.

9. Schwartz DA. 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 [published online March 17, 2020]. *Arch Pathol Lab Med*. doi:10.5858/arpa.2020-0901-SA

10. Zaigham M, Andersson O. Maternal and perinatal outcomes with COVID-19: a systematic review of 108 pregnancies [published online April 7, 2020]. *Acta Obstet Gynecol Scand*. doi:10.1111/aogs.13867

11. National Health Commission of China. Guideline of diagnosis and treatment of the pneumonia caused by the novel coronavirus. http://www.nhc.gov.cn/yzygj/s7653p/202003/46c9294a7dfe4cef80dc7f5912eb1989.shtml. Accessed March 4, 2020.

12. National Health Commission of the People's Republic of China. Novel coronavirus pneumonia diagnosis and treatment protocol (5th edition, trial). http://www.nhc.gov.cn/yzygj/s7653p/202002/3b09b894ac9b4204a79db5b8912d4440.shtml. Accessed 2 February, 2020.

13. World Health Organization. Laboratory diagnostics for novel coronavirus. https://www.who.int/health-topics/coronavirus/laboratory-diagnostics-for-novel-coronavirus. Accessed February 6, 2020.

14. Schwartz DA, Graham AL. Potential maternal and infant outcomes from coronavirus 2019-nCoV (SARS-CoV-2) infecting pregnant women: lessons from SARS, MERS, and other human coronavirus infections. *Viruses*. 2020;12:194.

15. Liu Y, Chen H, Tang K, Guo Y. Clinical manifestations and outcome of SARS-CoV-2 infection during pregnancy [published online March 4, 2020]. *J Infect*. doi:10.1016/j.jinf.2020.02.028

16. Chen H, Guo J, Wang C, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet*. 2020;395(10226):809–815. doi: 10.1016/S0140-6736(20)30360-3

17. Li N, Han L, Peng M, et al. Maternal and neonatal outcomes of pregnant women with COVID-19 pneumonia: a case-control study [published online March 30, 2020]. *Clin Infect Dis*. doi:10.1093/cid/ciaa352.

18. Zhu H, Wang L, Fang C, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *Transl Pediatr*. 2020;9(1):51–60. doi:10.21037/tp.2020.02.06

19. Thevarajan I, Nguyen THO, Koutsakos M, et al. Breadth of concomitant immune responses prior to patient recovery: a case report of non-severe COVID-19. *Nat Med*. 2020;26(4):453–455. doi:10.1038/s41591-020-0819-2

20. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of 2019 novel coronavirus infection in China. *N Engl J Med*. 2020;382(18):1708–1720. doi:10.1056/NEJMoa2002032

21. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*. 2020;323(11):1061–1069. doi:10.1001/jama.2020.1585

22. Qiao J. What are the risks of COVID-19 infection in pregnant women? *Lancet*. 2020;395(10226):760–762. doi:10.1016/S0140-6736(20)30365-2

23. Wang S, Guo L, Chen L, et al. A case report of neonatal COVID-19 infection in China [published online March 12, 2020]. *Clin Infect Dis*. doi:10.1093/cid/ciaa225

24. Dong L, Tian J, He S, et al. Possible vertical transmission of SARS-CoV-2 from an infected mother to her newborn [published online March 26, 2020]. *JAMA*. doi:10.1001/jama.2020.4621

25. Zeng H, Xu C, Fan J, et al. Antibodies in infants born to mothers with COVID-19 Pneumonia [published online March 26, 2020]. *JAMA*. doi:10.1001/jama.2020.4861