

# Severe Acute Respiratory Syndrome Coronavirus 2(SARS-CoV-2) infection during late pregnancy: A Report of 18 patients from Wuhan, China

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## Research article

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# Abstract

Background Compared with Severe Acute Respiratory Syndrome(SARS) and Middle East Respiratory Syndrome(MESR), Corona Virus Disease 2019(COVID-19) spread more rapidly and widely. The population was generally susceptible. However, reports on pregnant women infected with SARS-CoV-2 were very limited. By sharing the clinical characteristics, treatments and outcomes of 18 patients with COVID-19 during late pregnancy, we hoped to provide some references for obstetric treatment and management.

Methods: A total of 18 patients with COVID-19 treated in Renmin Hospital of Wuhan University were collected. The epidemiological characteristics, clinical manifestations, laboratory tests, chest CT and pregnancy outcomes were performed for analysis.

Results: 1.18 cases of late pregnancy infected with SARS-CoV-2 pneumonia were delivered at 35 + 5 weeks to 41 weeks. According to the clinical classification of COVID-19, 1 case was mild type, 16 cases were ordinary type, and 1 case was severe type. 2 . According to Imaging examinations: 15 (83%) cases showed unilateral or bilateral pneumonia, 2 (11%) cases had pulmonary infection with pleural effusion, and 1(6%) case had no abnormal imaging changes. 3. Among the 18 newborns, there were 3 (17%) premature infants, 1 (6%) case of mild asphyxia, 5 (28%) cases of bacterial pneumonia, 1 (6%) case of gastrointestinal bleeding, 1 (6%) case of necrotizing enteritis, 2 (11%) cases of hyperbilirubinemia and 1 (6%) case of diarrhea. All the newborns were negative for the first throat swab test of SARS-CoV-2 after birth. 4. Follow-up to Mar 7, 2020, no maternal and neonatal deaths occurred.

Conclusions: The majority of patients in late term pregnancy with COVID-19 were of ordinary type, and they less likely developed into critical pneumonia after early isolation and antiviral treatment. Vertical transmission of SARS-CoV-2 was not detected, but the proportion of neonatal bacterial pneumonia was higher than other neonatal diseases in newborns.

## Background

On Jan 30, 2020, the World Health Organization (WHO) listed the new coronavirus pneumonia epidemic as a public health emergency of international concern [1]. The WHO named the new coronavirus-infected disease as "Corona Virus Disease 2019(COVID-19)", and the International Virus Classification Commission named the new coronavirus as "Severe Acute Respiratory Syndrome Coronavirus 2(SARS-CoV-2)". The epidemic had been spread across China and the world rapidly, posing a continuing threat to global health. Fever, cough, chest tightness, and dyspnea may appear in patients with COVID-19, however, acute respiratory distress syndrome and septic shock could lead to death [2–3]. Great changes were taken placed in the respiratory system during pregnancy due to changes in hormones and physiological structure [4–5]. The immune system has been tolerant to the paternal antigen from the fetus, and certain cell-mediated immunity has been suppressed, which could make pregnant women more prone to critical illness after infected with the virus. [6–7]. At present, there are few reports about pregnant women with COVID-19 worldwide. Renmin Hospital of Wuhan University is one of the first batch of maternal health

and critical illness designated in Wuhan, China. From Jan 30, 2020, pregnant women with COVID-19 had been admitted to the hospital. The purpose of this article is to analyze the clinical characteristics and outcomes of 18 patients with late term pregnancy infected with COVID-19 retrospectively.

## Methods

**Patients** From Jan 30, 2020 to Mar 1, 2020, a total of 18 patients with COVID-19 in the 3rd trimester were clinically confirmed or diagnosed and hospitalized in Renmin Hospital of Wuhan University. Statistical analysis were performed on the age of women, gestational week of labor, source of infection, symptoms, blood tests, chest CT, throat swab tests of SARS-CoV-2, obstetric complications and neonatal outcomes. This study was approved by the institutional ethics board of Renmin Hospital of Wuhan University and the need for informed consent was waived (No. WDRY2020-K097).

**Diagnostic criteria** Reference to the “Notice on printing and distributing the diagnosis and treatment plan of pneumonia with new coronavirus infection (trial version 5)” issued by National Health Committee [8].

**Laboratory confirmation** of 2019-nCoV New Coronavirus (2019) Nucleic Acid Detection Kit (Dual Fluorescence PCR) was provided by bioPerfectus technologies.

**Clinical treatment** After admission, all pregnant women with COVID-19 in this study group were given with low-flow oxygen inhalation and finger oxygen saturation monitoring, oral oseltamivir / abidol and Lianhuaqingwen Capsules (Chinese medicine), and IFN- $\alpha$  nebulized inhalation selectively. Pregnant women with bacterial infections should use antibacterial drugs in combination with antiviral treatment as soon as possible, such as azithromycin, cephalosporin, moxifloxacin, etc. Breastfeeding should be suspended for 2 weeks after cesarean section or vaginal birth and antiviral therapy could be enhanced, such as ribavirin. Glucocorticoids and immunoglobulins that used in a short term could be considered based on the symptom of dyspnea and chest imaging progress.

**Statistical analysis** Using SPSS17.0 software, measurement data of normal distribution was expressed as mean  $\pm$  standard deviation. All counts and measurement data were descriptive statistics, and the results were expressed as percentages.

## Results

1. General information and clinical characteristics in patients of COVID-19 in the 3rd trimester (Table 1).

Table 1  
General information and clinical characteristics in 18 patients of  
COVID-19 in the 3rd trimester

<b>Age(year)</b>	
Mean(SD)	29.11(2.78)
Range	24–34
Gestational age at illness(weeks)	
Mean(SD)	38.40(1.56)
Range	(35.71-41)
Source of infection	
Hospital visit	2(11%)
Household infected with SARS-CoV-2 pneumonia	3(17%)
Colleague infected with SARS-CoV-2 pneumonia	1(6%)
Occupational exposure	2(11%)
Unknown	10(55%)
Signs and symptoms of COVID-19 at admission	
Fever	5(28%)
Cough	3(17%)
Sore throat	1(6%)
Fatigue	2(11%)
Shortness of breath and chest tightness	2(11%)
Diarrhea	1(6%)
Runny nose and nasal congestion	1(6%)
Clinical typing	
Mild	1(6%)
Ordinary	16(88%)
Severe	1(6%)
Critical	0(0%)

18 patients with late term pregnancy, aged 24–34 years, delivered at 35<sup>+</sup> 5 weeks to 41 weeks. There were 2 (11%) cases infected followed by hospital visits, 3 (17%) cases by family members infected with COVID-19, 1 (6%) case by colleague infected with COVID-19, and 2 (11%) cases were occupational exposures due to medical staff. Another 10 (56%) cases without clear history of infection exposure had a clinical diagnosis of COVID-19 after admission. Most pregnant women had fever, cough, sore throat, fatigue, chest tightness or shortness of breath, diarrhea, and runny nose (Table1). According to the clinical classification of the 5th edition of the guidelines [8], 1 (6%) patient was mild type, 16 (88%) patients were ordinary type, 1(6%) patient was severe type, but no critically ill patients. All the patients were cured and discharged.

2. Blood test results at admission in patients of COVID-19 in the 3rd trimester (Table 2).

Table 2  
Blood test results at admission in 18 patients of COVID-19 in the 3rd  
trimester

<b>Leucocytes (<math>\times 10^9</math> /L; normal range 3.5–9.5)</b>	<b>9.51(3.66)</b>
Increased	7(39%)
Neutrophils (%; normal range 40–75)	79.92(6.86)
Increased	14(78%)
Lymphocytes ( $\times 10^9$ /L; normal range 1.1–3.2)	1.20(0.29)
Decreased	8(44%)
Hemoglobin (g/L; normal range 115–150)	124.89(12.81)
Decreased	4(22%)
Procalcitonin (ng/mL; normal range < 0.1)	0.13(0.14)
Increased	5(28%)
C-reactive protein (mg/L; normal range 0–10)*	19.01(20.48)
Increased	10(56%)
Alanine aminotransferase (U/L; normal range 7–40)	17.94(13.17)
Increased	2(11%)
Aspartate aminotransferase (U/L; normal range 13–35)	23.12(9.92)
Increased	3(17%)
Serum creatinine ( $\mu$ mol/L; normal range 41–73)	45.29(7.74)
normal range	18(100%)
Blood urea (mmol/L; normal range 2.6–7.5)	3.23(0.68)
normal range	18(100%)
Lactate dehydrogenase (U/L; normal range 120–250)	217.80(38.65)
Increased	5(28%)
Creatine kinase (U/L; normal range 40–200)	48.30(31.75)
Normal range	18(100%)

Blood routing test: Leucocytes was increased in 7 (39%) cases, neutrophils was increased in 14 (78%) cases, lymphocyte count was decreased in 8 (44%) cases, hemoglobin was decreased in 4 (22%) cases. C-reactive protein (CRP) was increased in 10 (56%) cases, and procalcitonin (PCT) was increased in 5

(28%) cases. Biochemical examination: Alanine aminotransferase (ALT) was above the normal range in 2 (11%) cases, aspartate aminotransferase (AST) was above the normal range in 3 (17%) cases, lactate dehydrogenase was above the normal range in 5 (28%) cases, serum creatinine, urea and creatine kinase were in the normal range.

3. Chest CT and the nucleic acid test of SARS-CoV-2 in patients of COVID-19 in the 3rd trimester (Table 3).

**Table 3**  
Chest CT and new coronavirus nucleic acid tests in 18 patients of COVID-19 in the 3rd trimester

<b>Chest CT</b>	
Unilateral pneumonia	9(50%)
Bilateral pneumonia	6(33%)
Pneumonia with pleural effusion	2(11%)
No abnormal imaging changes	1(6%)
<b>Nucleic acid test of SARS-CoV-2 for pregnancy women</b>	
Positive	8(44%)
Negative	10(56%)

18 patients in this study had completed chest CT before admission. The results of CT revealed 9 (50%) cases of Unilateral pneumonia, 6 (33%) cases of bilateral pneumonia, 2 (11%) cases of pulmonary infection adjoint of pleural effusion. No abnormal imaging changes was found in 1 (6%) case (the nucleic acid test of SARS-CoV-2 was positive). The chest CT of 17 pregnant women were mostly in line with the imaging characteristics of typical COVID-19 patients: multiple lamellar, patchy, segmental ground glass shadows in the single or double lungs, mainly distributed outside the band. Eight (44%) patients were positive and ten (56%) patients were negative for throat swab tests of SARS-CoV-2.

4. Pregnancy outcomes in patients of COVID-19 in the 3rd trimester (Table 4).

Table 4  
Pregnancy outcomes in 18 patients of COVID-19 in the 3rd trimester

<b>Pregnancy complications</b>	
Premature rupture of membranes	4(22%)
Scar uterus	2(11%)
Severe preeclampsia	1(6%)
Gestational diabetes	3(17%)
Fetal distress	1(6%)
Meconium-stained amniotic fluid	2(11%)
B-Lynch or other compression sutures	2(11%)
Postpartum hemorrhage	1(6%)
Delivery method	
Vaginal delivery	1(6%)
Cesarean section	17(94%)
Neonatal outcomes	
Premature birth	3(17%)
Full term birth	15(83%)
Birth weight	
Mean(SD)	3181.11(448.63)
Range(gram)	2300–3910
The first nucleic acid test of SARS-CoV-2 for neonates	
Negative	18(100%)
Positive	0(0%)
Mild neonatal asphyxia	1(6%)
Chest radiograph and blood test results suggest bacterial pneumonia	5(28%)
Neonatal gastrointestinal bleeding	1(6%)
Neonatal necrotizing enteritis	1(6%)
Neonatal hyperbilirubinemia	2(11%)
Neonatal diarrhea	1(6%)

Of the 18 pregnant women, 17 (94%) patients were delivered by cesarean section, and 1 (6%) patient was vaginal delivery. There were 4 (22%) cases of premature rupture of membranes, 2 (11%) cases of scarred uterus, 1 (6%) case of severe preeclampsia, 3 (17%) cases of gestational diabetes, 1 (6%) case of fetal distress, and 2 (11%) cases of meconium-stained amniotic fluid. There were 2 (11%) cases of B-Lynch or other compression sutures due to uterine contraction fatigue during operations, and 1 (6%) case of postpartum hemorrhage. In 18 newborns, the first nucleic acid test of SARS-CoV-2 were negative within 24 hours and the weight range was 2300–3910 g. There were 3 (17%) cases of premature infants, 1 (6%) case of mild neonatal asphyxia, 5 (28%) cases of bacterial pneumonia, 1 (6%) case of neonatal gastrointestinal bleeding, 1 (6%) case of necrotizing enteritis, 2 (11%) cases of hyperbilirubinemia, and 1 (6%) case of newborn diarrhea. Followed up to Mar 7, 2020, no neonatal death occurred.

## Discussion

Among the pregnant women admitted to our hospital in late pregnancy, 1 case was mild type, 16 cases were ordinary type, and 1 case was severe type. The clinical manifestations included fever, cough, sputum, fatigue, chest tightness, shortness of breath, and diarrhea. According to epidemiological statistics, 6 cases had a history of contact with patients of COVID-19, 2 cases of hospital visits, and the remaining 10 patients was not clear about the source of the infection. The peripheral blood leukocytes of these pregnant women could be normal, but it elevated during bacterial infection. Lymphocytes might decrease. ALT, AST, and LDH were increased in some patients. But serum creatinine, urea, and creatine kinase were within normal range in all the patients. Chest CT of patients with COVID-19 had certain characteristics, and early manifestations were multiple flaky ground-glass shadows [9]. Most patients in this study had typical CT manifestations similar to the general population: multiple flaky, patchy, segmental ground glass shadows in one or both lungs, mainly distributed outside the band. Two patients had pleural effusion in addition to typical CT findings. One patient had occasional cough and denied a history of exposure to COVID-19. There was no abnormal radiographic change in CT examination, but the nucleic acid test of SARS-CoV-2 was positive. Therefore, in the areas with a high incidence of epidemics, patients with highly suspected of COVID-19 had no characteristic changes in CT imaging, further testing for coronavirus throat swabs was still needed. A normal CT result cannot be used as an exclusion criterion for COVID-19.

In this study, 18 patients terminated pregnancy during the 3rd trimester, and the gestational age was from 35<sup>+</sup> 5 to 41 weeks. 13 cases were terminated by cesarean section because of labor onset, premature rupture of membranes, severe preeclampsia, scar uterus, and fetal distress. 3 cases of pneumonia did not improve significantly after antiviral therapy, and thus terminated by cesarean Sect. 1 case required for caesarean section at 39<sup>+</sup> 5 weeks due to psychosocial factors. In addition, 1 case was vaginal delivery. Under strict isolation and active treatment, all the patients had been cured and discharged. We considered that the indications for termination of pregnancy with COVID-19 should still be based on obstetric management principles. For the patients of mild or ordinary pneumonia, the gestational age could be prolonged properly under monitoring of changes in pneumonia and fetal. If the treatment of pneumonia

was not ideal or the condition was critical, and the fetus had a certain survival rate during this gestational age, the choice for termination of pregnancy was feasible. Cesarean section was preferred for termination of pregnancy if vaginal delivery couldn't be finished in a few hours, which could reduce the load of cardiopulmonary during labor and control the disease towards critical illness.

SARS-CoV-2 was a new coronavirus that is pathogenic to humans. Roujian Lu et al. found that SARS-CoV-2 had a similar structure of receptor binding domain as SARS-CoV-1, which indicated that SARS-CoV-2 infection might have a similar pathogenesis as SARS-CoV-1 infection [10–11]. Some scholars speculated that the risk of vertical transmission of SARS-CoV-2 might be as low as SARS-CoV-1 [12]. The clinical data of 9 pregnant women were analyzed by Zhongnan Hospital of Wuhan University. The nucleic acid test for SARS-CoV-2 were negative in the amniotic fluid, umbilical cord blood, neonatal pharynx, and breast milk of 6 patients. They believed that the vertical transmission of the SARS-CoV-2 was relatively low [13]. Also, some researchers performed pathological analysis of placenta in 3 pregnant women infected with SARS-CoV-2 in late pregnancy. Histopathological analysis of the placenta revealed 1 case with chorionic hemangioma and another with massive placental infarction. In all 3 cases, various degrees of fibrin deposition inside and around the villi with local syncytia nodules increased was observed. Both of placental tissue and neonatal throat swabs tested for SARS-CoV-2 were negative. They considered that there was no pathological evidence of intrauterine vertical transmission of SARS-CoV-2 [14]. A study of various types of cells at the maternal-fetal interface found that the angiotensin-converting enzyme 2(ACE2) which was the receptor of SARS-CoV-2 expressed at low levels. Furthermore, it suggested that the maternal-fetal interface might not have a potential subgroup of susceptible cells of SARS-CoV-2, and SARS-CoV-2 infection during pregnancy did not cause intrauterine infection through vertical transmission of the placenta [15].

The results of this study was consistent with previous reports, and no vertical transmission of the SARS-CoV-2 was found. However, this study had certain limitations. We only performed swab nucleic acid testing in 18 neonates. No nucleic acid tests were performed on breast milk, placenta, amniotic fluid, and cord blood of pregnant women. Therefore, it is very important to collect evidence for the vertical transmission in the later stage. Meanwhile, evaluate the risk of the vertical transmission based on the data of multiple hospitals is more valuable.

The outcomes of 18 neonates were as follows: 3 cases of premature infants, 1 case of mild neonatal asphyxia, 5 cases of bacterial pneumonia, 1 case of neonatal gastrointestinal bleeding, 1 case of necrotizing enteritis, 2 cases of hyperbilirubinemia, 1 case of neonatal diarrhea. The chest radiographs of these 5 neonates showed pneumonia lesion absorption after antibiotic treatment, and they had been cured. The occurrence of perinatal neonatal pneumonia was related to premature rupture of membranes, maternal infection and premature birth [16]. This study found that the incidence of neonatal bacterial pneumonia was higher than other neonatal diseases significantly when mother infected with COVID-19 in the state of inflammatory stress or fever.

## Conclusions

Twelve pregnant women were infected with SARS in 2003, and three of them died of respiratory failure or infection. Spontaneous abortion occurred in 4 of the 7 early pregnancy patients. In the second or third trimester of pregnancy, 3 of the 5 patients gave birth at 26–32 weeks, and 2 gave birth at 33 weeks and term [17, 18]. Sarah H [19] summarized the cases of pregnant women with MERS-CoV in the MEDLINE database from 2012 to 2016, and 2 cases of them were reported from her. Of all 11 patients, 6 patients were admitted to the ICU, 3 patients died during hospitalization, and the infant mortality rate was 27%. The mortality rate of 11 MERS-CoV infected pregnant women was not statistically different from the 35% total mortality rate.

Compared with previous reports of SARS and MESR, the number of pregnancy women with COVID-19 was much more in our research, but the maternal and infant outcomes were relatively better. The clinical classification of patients was mostly ordinary type, and the possibility of progress to severe pneumonia had been reduced after early isolation and drug treatments. However, we should still be vigilant and pay more attention to the monitoring and treatment of pregnant women infected with SARS-CoV-2 pneumonia, and control the disease towards severe infection, ARDS and multiple organ failure which endanger the lives of mothers and fetus.

There are still some limitations in this study, and a comparative study of clinical data with larger samples is needed in future. By observing the pregnancy process of patients with COVID-19 in the early, middle and late stages and long-term follow-up of infants, we will fully understand the risks of pregnancy associated with COVID-19.

## **Abbreviations**

SARS-CoV-2: Severe Acute Respiratory Syndrome Coronavirus 2; SARS: Severe Acute Respiratory Syndrome; WHO: World Health Organization; MESR: Middle East Respiratory Syndrome; COVID-19: Corona Virus Disease 2019; ACE2: Angiotensin-Converting Enzyme 2.

## **Declarations**

### **Ethics approval and consent to participate**

This study was approved by the institutional ethics board of Renmin Hospital of Wuhan University (No. WDRY2020-K097). As an observational study retrospectively, which didn't not interfere with the patient or involve the personal privacy and commercial interests, also, which didn't cause any harm or risk to the patient. Therefore, the study obtained an informed consent waiver application from the Ethics Committee.

### **Consent for publication**

Not applicable.

### **Availability of data and materials**

Data and materials in the current study is available from the authors upon reasonable request.

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## **Role of the Funder**

The funders had no role in the design, collection, management, analysis, interpretation of the data and conduct of the study; preparation, review, approval of the manuscript or decision to submit the manuscript for publication.

**Competing interests** We declare no competing interests.

## **Authors' contributions**

ZL, DL, LJ collected the epidemiological and clinical data. HRh, ZL, LJ took responsibility of the accuracy of the data analysis. ZL and DL contributed to writing the manuscript. ZL, DL, WM, ML and YJ revised the final manuscript. All authors contributed to data acquisition, data analysis, and reviewed and approved the final version.

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