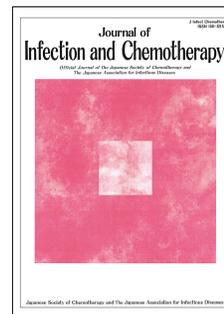


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## **No intrauterine vertical transmission in pregnancy with COVID-19 :a case report**

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### **Abstract**

The coronavirus disease 2019 ( COVID-19 ) has been a worldwide pandemic diseases, nearly 400,000 people died at now. The data of status of pregnant women and neonates after infection of severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) is limited. We report a case of pregnant woman in her third trimester with critical COVID-19, and amniotic fluid, umbilical cord blood, placenta, and neonatal gastric fluid were retained during cesarean section. The SARS-COV-2 nucleic acid test results of these specimens were negative. there is no evidence of intrauterine vertical transmission during delivery in the third trimester, but the data are limited and need to be further explored.

**Keywords**

SARS-COV-2, intrauterine vertical transmission, COVID-19, pregnancy , prognosis

**Introduction**

Since the SARS-COV-2 virus was discovered in China in December 2019, as of June 05, 2020, WHO confirmed 6535354 cases of (SARS-COV-2) infections worldwide, and nearly 400000 deaths were declared <sup>1</sup>. As a special population, pregnant women have attracted much attention, and the presence of intrauterine vertical transmission is critical to the outcome of newborns. Here, we report a pregnant woman with critical COVID-19 to provide some help for the treatment of pregnant women.

**Case report**

A 28-year-old 31-week pregnant woman was admitted to the Fifth People's Hospital of Suzhou on February 6, 2020 for recurrent fever and cough in 2 weeks. Epidemiological history showed that the patient went to Wuhan to visit relatives on January 4, and returned to Suzhou on January 23. She developed fever on January 25, with a maximum body temperature of 38.3°C. She went to the fever clinic of Suzhou Municipal Hospital on February 2. The blood test showed a normal white blood cells, lymphopenia and elevated CRP

(Table). The result of the SARS-COV-2 nucleic acid test was negative, however, given her epidemiological history, the possibility of SARS-COV-2 infection remained to be considered. A chest CT scan on February 4 revealed multiple peripheral ground-glass exudates with partial consolidation in bilateral lungs (Figure). On February 6, after the 4th SARS-COV-2 nucleic acid test returned to be positive, she was transferred to the Fifth People's Hospital of Suzhou for treatment.

Blood test showed  $10.60 \times 10^9/L$  of WBC,  $0.85 \times 10^9/L$  of lymphocytes,  $124.1 \text{ mg / L}$  of CRP,  $0.288 \text{ ng/ml}$  of PCT. ABG analysis showed that  $PO_2$  was  $120.6 \text{ mmHg}$ ,  $PCO_2$  was  $38.2 \text{ mmHg}$ , and  $PO_2/FiO_2$  index was 294. According to the SARS-COV-2 pneumonia protocol (5th edn)<sup>2</sup>, the pregnant woman was classified as critical type of COVID-19. We gave her high flow oxygen, Lopinaviri/Rionavir for antiviral, cefoperazone Tazobactam for anti-infection, dexamethasone for fetal maturation, and symptomatic management. On February 8, the fetal heart rate was 100 beats/min, the patient's ABG analysis showed that PF index was 208, and CT scan indicated pulmonary lesions deteriorated. The cesarean section was performed under lumbosacral combined anesthesia immediately, and a 1830g live-born male infant was delivered successfully. Amniotic fluid, umbilical cord blood, placenta, and neonatal gastric fluid were collected during the operation and tested for the SARS-COV-2 nucleic acid, and the mother and infant were separated after the operation.

On February 9, a blood test showed an increase in PCT of 1.63 ng/ml, linezolid was added to enhance anti-infection. Lopinaviri/Ritonavir was replaced by abidol because of nausea and vomiting. On February 12, CT scan indicated that the lesions absorbed than before and her clinical symptoms improved continually. On February 18, chest CT showed that the lesions almost disappeared. In addition, the sputum SARS-COV-2 nucleic acid test was negative for the fourth time, and the anal swab SARS-COV-2 nucleic acid was also negative. The patient was discharged on February 20.

As for the newborn, his Apgar scores were 8, 8 and 10 at 1, 5, and 10 minutes after birth, with weight of 1830g, blood pressure of 77/48mmHg, and pulse oxygen 95%. He was admitted to the negative pressure isolation ward after birth, NCPAP breathing support, given sulbenicillin sodium, azithromycin for anti-infection treatment. In addition, not only SARS-COV-2 nucleic acid test results were negative in 4 times pharyngeal swabs, but also the anal swab, amniotic fluid, umbilical cord blood, placenta, and neonatal gastric fluid were negative. On March 28, the neonatal weight had grown to 2530g, with no difficulties of breathing and pulse oxygen of 99%, he was discharged.

## **Discussion**

The common syndrome of COVID-19 are fever, dry cough, sore throat, muscle soreness, shortness of breath, occasional diarrhea and other symptoms<sup>3-5</sup>. There was no significant difference in symptoms between

pregnant women and non-pregnant women<sup>6</sup>. It should be noted that this case was diagnosed based on multiple nucleic acid tests. For nucleic acid testing, sputum specimens are recommended because the positive rate of sputum (74.4%~88.9%) is higher than that of the nasopharynx swab (53.6%~73.3%)<sup>7</sup>. In treatment, Lopinavir/Ritonavir has been shown to be safe in HIV-infected pregnant women, but due to adverse reactions, we used arbidol instead, which was proven to be safe and effective.

Another important question is whether there is a possibility of intrauterine vertical transmission. Chen<sup>6</sup> reported the delivery of 9 cases of pregnant women with COVID-19. SARS-CoV-2 tests were performed on amniotic fluid, umbilical cord blood, neonatal throat swabs and breast milk samples from six of these patients. The results were negative. Zhu<sup>8</sup> described 10 neonates in pregnant women with COVID-19, including two cases of vaginal delivery. 9 cases had pharyngeal swab specimens taken 1-9 days after birth for SARS-CoV-2 nucleic acid tests, all of which were negative. Li<sup>9</sup> also reported a 35-week pregnant woman with COVID-19, whose amniotic fluid, cord blood and placenta, breast milk samples as well as neonates swab SARS-CoV-2 nucleic acid were all negative. However, Dong<sup>10</sup> reported a case of a neonate by cesarean, whose SARS-CoV-2 IgG and IgM were positive 2 hours after birth. Before her birth, her mother had been infected SARS-CoV-2 for more than 20 days. It is known that IgM antibodies are not transferred to the fetus via the placenta. It seemed that the elevated IgM in the neonate indirectly

supported the possibility of vertical transmission, but It still needs to be discussed because the mother's vaginal secretions were negative for SARS-CoV-2, and there were no PCR testing of amniotic fluid or placenta to be performed. Also, the infant's repeatedly RT-PCR test of SARS-COV-2 results on nasopharyngeal swabs were negative. Unfortunately, due to the early stage of the SARS-CoV-2 epidemic at that time, the SARS-CoV-2 IgM antibody testing had not been applied in our hospital, and this newborn failed to perform IgM testing.

Placental pathology are of great significance for understanding maternal and fetal outcomes and evaluating intrauterine vertical transmission. Chen<sup>11</sup> analyzed 3 cases of placental pathology of SARS-CoV-2 infection in pregnancy, they found that there were various degrees of fibrin deposition inside and around the villi with local syncytial nodule increases in all three placentas, but no morphological changes of villitis and chorioamnionitis related to infection of SARS-CoV-2 were observed. Unfortunately, this maternal placenta was treated as a potential contaminant and failed to undergo a pathological examination. Based on these results, although clinical samples are small, there is no direct evidence of intrauterine vertical transmission. However, these pregnant women are all in the third trimester. It is uncertain whether there is vertical intrauterine transmission during delivery of COVID-19 pregnant women in the first and second trimester.

Smith V, et al reviewed outcomes of maternal and neonatal in pregnant women with COVID-19 from November 1st, 2019 to March 28th, 2020. There was no indeterminate case of potential vertical transmission, and the proportion of critically ill pregnant women was small<sup>12</sup>. But pregnant women infected with SARS and MERS can easily progress to critical illness with a mortality rate of about 30%<sup>13,14</sup>. Miscarriage, preterm birth, intrauterine distress were common in these women, and most newborns needed to be admitted to ICU. On February 29, 2020, the China-World Health Organization (WHO) Joint Investigation Report on New Coronavirus Pneumonia (COVID-19) was published, and 147 pregnant women were analyzed, of whom 8% were severe and 1% were critical<sup>15</sup>. It seems that the risk of pregnant women with COVID-19 progressing to severe patients is not high, but this still needs further observation.

In a word, pregnant women are a special group in the SARS-COV-2 epidemic. They should be paid more attention because of the safety of pregnant women and their fetuses. In view of the current SARS-COV-2 epidemic in the world, pregnant women with flu symptoms should be tested for SARS-COV-2 nucleic acid as soon as possible, combined with IgM antibody testing if necessary. As of now, there is no sufficient evidence of intrauterine vertical transmission during delivery in the third trimester, but the data are limited and need to be further explored. Newborns are still advised to be

separated from the mother, stopped breastfeeding, and observed for manifestations to rule out SARS-COV-2 infection.

### **Authorship statement**

Yantian Lv and Xiao Xu were responsible for the organization and coordination of the clinical case. Xinghua Shen was the chief investigator and responsible for the data analysis. Yantian Lv, Binbin Gu, Siming Hu, Ying Chen, Ting Ruan, Jian Ding and Guopeng Xu collected clinical data. All authors contributed to the writing of the final manuscript, and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All authors meet the ICMJE authorship criteria.

### **Ethics approval**

Informed consent was obtained from the patient for publication of this case report. No potentially identifiable human images or data is presented in this study. The studies involving human participants were reviewed and approved by Ethics Committee of Suzhou Municipal Hospital.

### **Funding**

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### **Conflict of Interest Statement**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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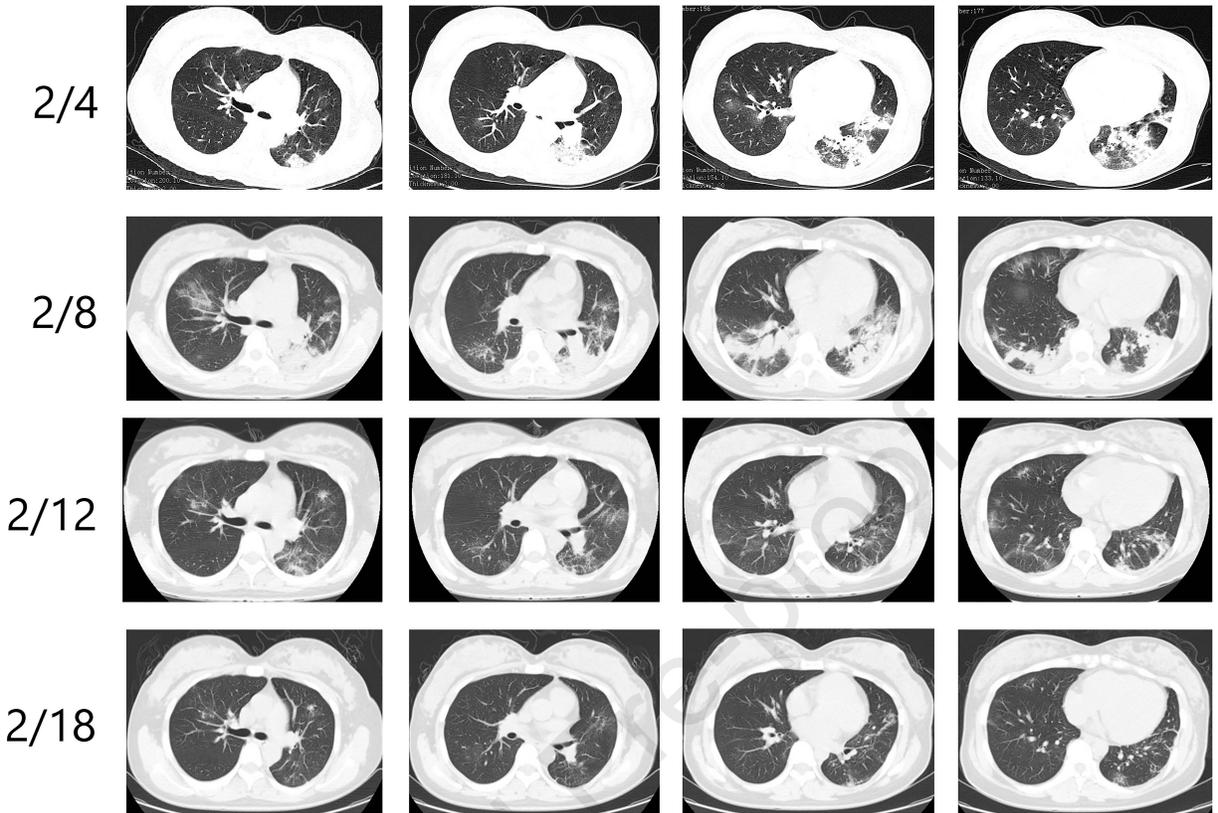
### **Figure legends**

Chest CT scans of a case of COVID-19 pregnant woman. 2/4 Multiple ground-glass shadows and consolidation in bilateral lungs, prominent in the lower left lung. 2/8 The exudation and consolidation of both lungs deteriorated. 2/12 Multiple cloudy patches and cord-like shadows in bilateral lungs, absorbed than before. 2/18 Ground-glass speckle and cord-like shadows in bilateral lungs, almost absorbed.

Table 1: Clinical, laboratory characteristics and medicine of a pregnant woman with COVID-19

Date	WBC ( $\times 10^9/L$ )	LYM ( $\times 10^9/L$ )	PT (s)	D-dimer (mg/L)	N-proBNP (pg/ml)	cTn (ng/ml)	AST (U/L)	Cre ( $\mu\text{mol/L}$ )	CRP (mg/L)	PCT (ng/ml)	PF index	Medicine
2/2	8.76	1.06					24	39	60.00	0.03		Ose
2/6	10.60	0.86	11.70	0.84	318	0.02	33	25.70	124.10	0.29	294	Lop/Rit Cef
2/8	8.66	1.06	11.10	0.99	162	0.04	34	33.80	47.90	0.20	208	Lop/Rit Cef, Lin
2/9	21.41	1.62	10.90	2.14	822	0.02	34	33.80	19.06	1.63	219	Arb, Cef, Lin
2/10	13.62	2.18	11.00	5.90	355	0.03	42	37.00	14.70	0.09	252	Arb, Cef, Lin
2/11	13.66	1.61	11.10	2.01	92	0.01	38	30.90	43.10	0.07	303	Arb, Cef, Lin
2/12	12.39	1.65	11.20	1.67	18	0.01	18	32.00	49.00	0.04	401	Arb, Cef, Lin
2/13	11.12	1.52	11.30	2.14	54	0.00	17	33.60	31.30	0.03		Arb, Cef, Lin
2/14	9.78	1.50	11.40	2.76	43	0.00	17	31.00	44.80	0.04	409	Arb, Cef, Lin
2/17	8.69	1.84	17.10	2.52	68	0.00	39	34.40	15.90	0.05	484	Arb, Cef, Lin

Abbreviations: WBC: White Blood Cell; LYM: Lymphocyte; PT: Prothrombin time; cTn: Cardiac troponin; AST: Aspartate aminotransferase; Cre: Creatinine; CRP:C-reactive protein; PCT: Procalcitonin; PF index:  $PO_2/FiO_2$  index; Ose: Oseltamivir; Arb: Arbidol; Lop/Rit :Lopinaviri/Ritonavir; Cef :Cefoperazone Tazobactam; Lin: Linezolid.



Journal

## Detailed Response to Reviewers

Dear editors and reviewers:

Thank you very much for giving us an opportunity to revise our manuscript. We appreciate the editor and reviewers very much for their constructive comments and suggestions on our manuscript entitled "No intrauterine vertical transmission in pregnancy with COVID-19 : a case report". Those comments are very helpful for revising and improving our paper. We have studied the comments carefully and made corrections which we hope meet with approval. The main corrections are in the manuscript and the responds to the reviewers' comments are as follows (the replies are highlighted in blue).

Kind regards.

Yantian Lv.

### **Replies to the reviewers' comments:**

#### **Reviewer #1:**

1. I think it is a very valuable case report.

This data is useful for treating and controlling COVID-19 infections in pregnant women.

**Response:** Thank you very much for your approval of my article. By reading the literature, some new content has been added to the manuscript, and I hope to get your review again.

#### **Reviewer #2:**

1. The presence of specific anti-SARS-CoV-2 IgM antibodies suggests intrauterine infection. Dong et al reported that the cases of vertical COVID-19

transmission based on positive IgM antibodies in cord blood samples collected at the time of delivery (JAMA, 2020). The authors should cite this paper and discuss this point. Did the authors investigate anti-SARS-CoV-2 IgM in umbilical cord blood?

**Response:** I have studied the article you recommended carefully, and I think the finding of SARS-COV-2 IgM positivity in newborns is of great significance for intrauterine transmission. Unfortunately, due to the early stage of the SARS-CoV-2 epidemic at that time, the SARS-CoV-2 IgM antibody testing had not been applied in our hospital, and this newborn failed to perform IgM testing. But it still needs to be discussed because the mother's vaginal secretions were negative for SARS-CoV-2, and there were no PCR tests of amniotic fluid or placenta to be performed. Also, the infant's repeated RT-PCR test of SARS-COV-2 results on nasopharyngeal swabs were negative.

2. How about the histopathological findings of the placenta? Frequent abnormal findings in placental pathology have been reported among COVID-19-positive mothers such as malperfusion. The authors should discuss the histopathological findings of the placenta. And it would be helpful if the authors showed the histopathological findings of the placenta.

**Response:** Placental pathology are of great significance for understanding maternal and fetal outcomes and evaluating intrauterine vertical transmission. I studied an article of placental pathology of pregnant women with COVID-19, Chen analyzed 3 cases of placental pathology of SARS-CoV-2 infection in pregnancy, they found that there were various degrees of fibrin deposition inside and around the villi with local syncytial nodule increases in all three placentas, but no morphological changes of villitis and chorioamnionitis related to infection of SARS-CoV-2 were observed. Unfortunately, this maternal placenta was treated as a potential contaminant at that time and failed to

undergo a pathological examination.

3. It would be helpful if the authors could indicate more details about the neonatal health status including APGAR score.

**Response:** According to your kind suggestions, supplemental neonatal vital signs and Apgar scores and conditions at discharge are shown in the manuscript. As for the newborn, his Apgar scores were 8, 8 and 10 at 1, 5, and 10 minutes after birth, with weight of 1830g, blood pressure of 77/48mmHg, and pulse oxygen 95%. On March 28, the neonatal weight had grown to 2530g, with no difficulties of breathing and pulse oxygen of 99%, he was discharged.

4. Abbreviations must be defined at their first of the text.

**Response:** According to your kind suggestions, the abbreviations of the coronavirus disease 2019(COVID) and severe acute respiratory syndrome coronavirus 2 (SARS-COV-2) has been defined at their first of the text

5. I am afraid that Lopinaviri/Tonavir should be Lopinavir/Ritonavir.

**Response:** Thanks very much for your correction, the right word "Lopinavir/Ritonavir" has been corrected in the manuscript.