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CASE REPORT



# No evidence for vertical transmission of SARS-CoV-2 in two neonates with mothers infected in the second trimester

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## ABSTRACT

**Background:** COVID-19 reported in pregnant women has occurred in late pregnancy, while there are no reports of infection in the first and second trimester. We report two neonates born to mothers with COVID-19 during the second trimester.

**Case presentation:** Two pregnant women had symptomatic COVID-19 in the second trimester. Throat swabs at delivery for SARS-COV-2 RNA were negative for both women and their newborns. The first woman had positive serum IgM and IgG antibodies to SARS-COV-2 before delivery. Her newborn had negative IgM antibody to SARS-COV-2 but IgG was positive on the 7th day after birth. The second woman had negative serum IgM antibody to SARS-COV-2 but IgG was positive before delivery. Her newborn had negative serum IgM antibody to SARS-COV-2 but IgG was positive at 48 h after birth. None of the neonates developed clinical symptoms of COVID-19.

**Conclusion:** SARS-COV-2 is unlikely to be vertically transmitted in utero as evidenced by the specific antibodies in the serum of the two women and their newborns. The two women with SARS-COV-2 infection in the second trimester did not develop serious complications at delivery and outcomes of the neonates were good.

## KEYWORDS

The second trimester  
COVID-19  
SARS-CoV-2  
IgM  
IgG

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## Introduction

Since December 2019, the coronavirus disease (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread rapidly in China and worldwide [1]. People of all ages are susceptible to SARS-CoV-2 [2]. Reported cases of maternal infection have occurred in late pregnancy. The earliest time of diagnosis was in the 31st week of pregnancy, and most were diagnosed in the 37th week [3]. No cases of maternal infection in the first and second trimester of pregnancy have been reported. This case report describes two mothers infected with COVID-19 in the second trimester of pregnancy and their neonates.

## Case presentation

### Mothers

The first woman was 34 years old and had gestational diabetes treated with insulin without regular monitoring of blood sugar. On 23 January 2020, (24 weeks and 3 days of gestation) she developed fever, shortness of breath and dyspnoea and was admitted to a COVID-19 designated hospital in Wuhan. Chest computed tomography (CT) showed ground glass opacities in the right upper and lower lung lobes. She received empirical treatment with ceftriaxone and oseltamivir. Fever and respiratory symptoms disappeared after 2 days and she was discharged one week later. On April 28 (37 weeks and 6 days of gestation), she was admitted to the obstetrics department of Wuhan No.1 Hospital due to premature rupture of membranes since five hours. She developed no clinical symptoms such as fever or shortness of breath. On April 28 and 29, PCR for SARS-CoV-2 RNA was negative in throat swabs. However, she had positive serum IgM and IgG antibodies to SARS-CoV-2 (Table 1). Chest CT showed scattered patchy lesions in both lungs and a small amount of left-sided pleural effusion. On April 28, she delivered a full-term baby girl by caesarean section. Placental tissue taken postpartum showed no microscopic abnormality.

The second woman was 28 years old and had no concomitant disease during pregnancy. On 28 January 2020 (27 weeks and 3 days of gestation), she and her husband developed fever and were admitted to a COVID-19 designated hospital in Wuhan. On January 30, the husband's chest CT showed multiple blotchy shadows in the lungs. His symptoms subsided after 6 days of outpatient infusion treatment. He had negative PCR in throat swabs on Feb. 8, 10, and 15 and still negative on

**Table 1.** Clinical and laboratory characteristics of mothers.

	Mother 1	Mother 2
Age, years	34	28
Maternal history	G1P1	G1P1
Comorbidity	Gestational diabetes	No
Signs and symptoms		
Fever	Yes	Yes
Cough	No	No
Fatigue	No	No
Headache	No	No
Mulligrubs	No	No
Dyspnoea	Yes	No
Laboratory tests		
White blood cell count, $\times 10^9/L$	8.86	6.26
Lymphocyte count, $\times 10^9/L$	0.94	0.98
C-reactive Protein, mg/L	123.7	24.12
Chest radiograph	Abnormal	Normal
SARS-CoV-2 RNA(throat swab)	Negative	Negative
SARS-CoV-2 IgM	positive	Negative
SARS-CoV-2 IgG	Positive	Positive

Reference ranges for blood parameters of adults: white blood cell count,  $3.50\text{--}9.50 \times 10^9/L$ ; lymphocyte count,  $1.10\text{--}3.20 \times 10^9/L$ ; C-reactive Protein,  $0.00\text{--}5.00$  mg/L.

April 28 when serum IgM antibody to SARS-CoV-2 was negative, and IgG positive. Since the wife had only mild symptoms and due to low availability of PCR tests, throat swabs for SARS-CoV-2 RNA were not taken. On 21 April 2020, her throat swab was negative for SARS-CoV-2 RNA, serum IgM antibody to SARS-CoV-2 was negative and IgG positive (Table 1). Chest CT was normal. Considering that she had no obvious symptoms, no special treatment was given. On May 2, a full-term baby girl was delivered vaginally.

### Neonates

The first neonate was a girl born at 37 weeks and 6 days gestation by caesarean section. Her birth weight was 4,000 g and Apgar scores were 9 at 1 min and 10 at 5 min. She was isolated from her mother immediately after birth and received formula feeding. She had yellowish skin on the second day after birth and was transferred to the Neonatology department with bilirubin 11.3 mg/dL. No fever, dyspnoea or other symptoms occurred. SARS-CoV-2 RNA test was negative in throat swabs taken immediately after birth, on the 3rd and the 7th day. Serum IgM antibody to SARS-CoV-2 was negative and IgG was positive on the 7th day after birth (Table 2). No chest radiograph or CT scan was done. The newborn was discharged after 5 days of phototherapy and partial blood exchange.

The second baby girl was born at 40 weeks and 5 days gestation by vaginal delivery. Her birth weight was 3,850 g and Apgar scores were 9 at 1 min and 10 at 5 min. She was isolated from her mother immediately

**Table 2.** Clinical and laboratory characteristics of neonates.

	Neonate 1	Neonate 2
Gender	Female	Female
Gestational age, weeks	37 <sup>+6</sup>	40 <sup>+5</sup>
Birth weight, g	4,000	3,850
Apgar score (1,5min)	8.9	8.9
Delivery mode	Caesarean section	Vaginal delivery
Laboratory tests		
White blood cell count, $\times 10^9/L$	17.04	15.05
Lymphocyte count, $\times 10^9/L$	4.69	3.44
Neutrophil count, $\times 10^9/L$	9.23	10.36
Hematocrit, %	63.8	48.7
Hemoglobin, g/L	218	168
Erythrocyte antibody release test	positive	positive
Total bilirubin, mmol/L	227.4	228.7
Alanine aminotransferase, U/L	22	6
C-reactive Protein, mg/L	<4.5	25.5
SARS-CoV-2 RNA (throat swab)	negative	negative
SARS-CoV-2 RNA (anal swab)	negative	negative
SARS-CoV-2 IgM	negative	negative
SARS-CoV-2 IgG	positive	positive
Signs and symptoms		
Fever	No	No
Dyspnoea	No	No
Heart rate	Normal	Normal
Blood pressure	Normal	Normal
Jaundice	Yes	Yes

Reference ranges for blood parameters of neonates: white blood cell count,  $5.0\text{--}14.5 \times 10^9/L$ ; lymphocyte count,  $2.0\text{--}5.0 \times 10^9/L$ ; Neutrophil count,  $2.0\text{--}7.0 \times 10^9/L$  C-reactive Protein, <16 mg/L.

after birth and received formula feeding. Due to neonatal jaundice with bilirubin 14 mg/dL on the second day after birth, she was transferred to the Neonatology department. No fever, dyspnoea or other symptoms occurred. At 48 h after birth, throat and anal swabs tested negative for SARS-CoV-2 RNA, IgM antibody to SARS-CoV-2 was negative and IgG was positive (Table 2). No chest radiograph or CT scan was done. She was discharged after 5 days of phototherapy.

## Discussion

Controversy exists regarding whether SARS-CoV-2 can be transmitted vertically. The presence of SARS-CoV-2 in placental tissue, amniotic fluid, umbilical cord blood, and neonatal nasopharyngeal swab samples can be used to assess intrauterine transmission [4]. Using reverse transcription polymerase chain reaction (RT-PCR), no direct evidence of intrauterine infection has been found in published studies [4–11]. Two recent case reports proposed the possibility of vertical intrauterine transmission by assessing neonatal serum specific antibodies [12,13]. Specific antibodies are gradually produced 3–5 days after infection. IgM antibodies appear first, and then IgG. Positive IgM antibody indicates recent acute infection, while positive IgG antibody indicates earlier infection [14]. Since maternal IgM antibodies are too large to cross the placenta, elevated IgM

antibody levels in neonates are presumed to be produced by the neonate [13].

In our report, SARS-CoV-2 RNA was negative in both pregnant women before delivery. However, the first woman had positive IgM and IgG antibody to SARS-CoV-2. Combined with her clinical features and imaging abnormalities, this suggests that she was recently infected with SARS-CoV-2 and was in the recovery stage. The virus had been cleared, but the IgM level had not decrease below the limit of detection. Alternatively, the nucleic acid test results were falsely negative and she was still in an active stage of infection [14]. Her newborn had no symptoms of COVID-19 and had three negative tests for SARS-CoV-2 RNA and two negative tests for IgM antibody. This suggests that the newborn had no acute infection, and the IgG was most likely transmitted from the mother. The second woman tested negative for IgM antibody to SARS-CoV-2 and positive for IgG at 12 days before delivery. These results indicate that she was infected earlier and the virus had been cleared. IgG antibodies remain in the blood for a long time [14]. Her newborn showed no symptoms of infection. The baby had negative SARS-CoV-2 RNA and IgM antibody and IgG antibody was positive. IgG was most likely transmitted from the mother. However, due to the short follow-up time, the titres of IgM and IgG antibodies to SARS-CoV-2 need to be dynamically monitored to confirm this conclusion.

Similar to reported maternal outcomes of SARS-CoV-2 infection in the third trimester [3], the two women with infection in the second trimester in our report did not experience serious complications perinatally. Both the infants and their mothers remain healthy at follow-up so far.

A limitation of this report, obviously, is that only two cases are described. Additionally, umbilical cord blood, amniotic fluid and breast milk were not tested for SARS-CoV-2 nucleic acid. Studies of dynamic changes in maternal and infant antibody titres and out-comes at long-term follow-up are warranted.

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## Consent for publication

Written informed consent for publication of the clinical details was obtained from the patients.

## Disclosure statement

No potential conflict of interest was reported by the author(s).

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