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Clinical characteristics and risk assessment of newborns born to mothers with COVID-19

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ABSTRACT

Background: Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) is causing an outbreak of pneumonia in Wuhan, Hubei Province, China, and other international areas.
Objective: Here, we report the clinical characteristics of the newborns delivered by SARS-CoV-2 infected pregnant women.
Methods: We prospectively collected and analyzed the clinical features, laboratory data and outcomes of 7 newborns delivered by SARS-CoV-2 infected pregnant women in Zhongnan Hospital of Wuhan University during January 20 to January 29, 2020.
Results: 4 of the 7 newborns were late preterm with gestational age between 36 weeks and 37 weeks, and the other 3 were full-term infants. The average birth weight was 2096 ± 660 g. All newborns were born without asphyxia. 2 premature infants performed mild grunting after birth, but relieved rapidly with non-invasive continuous positive airway pressure (nCPAP) ventilation. 3 cases had chest X-ray, 1 was normal and 2 who were supported by nCPAP presented mild neonatal respiratory distress syndrome (NRDS). Samples of pharyngeal swab in 6 cases, amniotic fluid and umbilical cord blood in 4 cases were tested by qRT-PCR, and there was no positive result of SARS-CoV-2 nucleic acid in all cases.
Conclusions: The current data show that the infection of SARS-CoV-2 in late pregnant women does not cause adverse outcomes in their newborns, however, it is necessary to separate newborns from mothers immediately to avoid the potential threats.

1. Background

Since December 2019, a newly identified coronavirus (Severe Acute Respiratory Syndrome Coronavirus 2, SARS-CoV-2) is causing an outbreak of coronavirus disease (COVID-19) in Wuhan, Hubei Province and spreads outside of China [1]. On January 30, 2020, the World Health Organization (WHO) declared the outbreak of COVID-19 is a Public Health Emergency of International Concern [2]. National Health Commission of China has updated several versions of the guidelines to deal with the epidemic of COVID-19 [3]. So far as we know, people of all ages are susceptible to SARS-CoV-2. The elderly and those with underlying diseases are more fragile to the virus. To date, hundreds of pediatric cases were documented, including neonatal infection. This situation has drawn public's attention to neonatal infection [4].

Because of the suddenness and high pathogenicity of the virus, little is known about the risk of infection to pregnant women and parturients. Particularly, there is limited report about the influence of COVID-19 pregnant women on their babies [5,6]. Previously, we reported the potential risk of mother-to-child vertical transmission, as well as neonatal infection postpartum exposure to infection source [7]. However it is not clear how COVID-19 mothers affect the physiological status of newborns. Based on this, we summarized the clinical characteristics and potential risk of pregnant women with COVID-19 on their babies, hoping to provide experience for the prevention and treatment of newborns born to mothers infected SARS-CoV-2.

Abbreviations: nCPAP, non-invasive continuous positive airway pressure; NICU, neonatal intensive care unit; WBC, White blood cell count; CRP, C-reactive protein; PCT, Procalcitonin; AST, Aspartate aminotransferase; ALT, Alanine transaminase; CK-MB, Creatine kinase isoenzyme MB; MYO, Myoglobin; DD, D-dimer

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2. Methods

2.1. Objects and data collection

From January 20 to January 29, 2020, 7 newborns delivered by pregnant women infected with SARS-CoV-2 in late pregnancy in Zhongnan Hospital of Wuhan University, were admitted. All of the pregnant women received the cesarean section. 4 cases received cesarean section to prevent the uncertain transmission to newborns when infection symptoms appeared. 2 received emergency cesarean section for hypertension and blurred vision caused by severe preeclampsia. 1 who was asymptomatic at delivery and febrile 2 days later, received cesarean section because of severely elevated aminotransferase. After delivery, 5 newborns were immediately transferred to negative pressure ward (−10 Pa) of neonatal intensive care unit (NICU) for isolation and observation, the other 2 were cared by healthy family members at the request of guardian, separating from their mothers. All 7 newborns were tested for SARS-CoV-2 nucleic acid after birth. Delivery history, neonatal birth status including Apgar score, clinical features, blood tests, as well as nucleic acid detection of amniotic fluid, umbilical cord blood and neonatal pharyngeal swabs were collected. The potential influence of newborns and risk assessment of mother-to-child transmission were analyzed. Data are shown as mean ± standard deviation.

2.2. Procedures

Umbilical cord blood, amniotic fluid and pharyngeal swabs were collected immediately(< 30 min) after delivery in isolation operating room, all the samples were sealed up in sampling bottles, then were sent to the P3 Laboratory in Zhongnan Hospital of Wuhan University for nucleic acid extraction and qRT-PCR test. After given Apgar score, the newborns(5 cases) were either transferred to NICU negative pressure isolation ward for treatment within 10 min or transferred to obstetrical ward for isolation and was cared by healthy family members (2 cases, including 1 case that didn't perform nucleic acid test). The parturients were transferred to the infectious isolation ward for postoperative rehabilitation. The newborns transferred to NICU were further isolated in neonatal incubator and monitored continuously. Blood gas analysis, complete blood count, biochemical profile and coagulation test were performed. During the isolation period, the breathing, heart rate, feeding, response and laboratory results of the newborns were recorded continuously. Antibiotics were not used unless there are signs of bacterial infection during hospitalization.

Pharyngeal swabs were collected for a second SARS-CoV-2 nucleic acid test 2−5 days after birth. Newborns showed 2 consecutive negative results for virus nucleic acid and with good condition in the following 7 days were permitted to be discharged, and continued with home quarantine and telephone follow-up.

2.3. Specimen collection and virus detection

Amniotic fluid, umbilical cord blood and pharyngeal swabs were collected within 5 min after delivery. One of the parturients was diagnosed as COVID-19 two days after delivery, amniotic fluid and umbilical cord blood of the newborn were not obtained. The collection of blood and pharyngeal swabs in newborns in NICU was carried out under the protection of class II. All the blood samples and pharyngeal swabs were placed in the required cell-culture medium and delivered to Laboratory P3 within 30 min. According to the testing guidelines of China Center for Disease Control and prevention [8], SARS-CoV-2 was tested by 2019 novel coronavirus (ORF1ab/N gene) nucleic acid detection kit (BioGerm Medical Technology Company, Shanghai, China).The fluorescence quantitative RT-PCR (qRT-PCR) test was completed according to the instructions of the kit.

2.4. Ethics approval

Informed consents of the routine treatment and specimen's collection were signed by the guardian of newborns and kinsfolk of the pregnant women. This study was approved by the Medical Ethical Committee of Zhongnan Hospital of Wuhan University (clinical ethical approval number 2020004)

3. Results

3.1. General characteristics of SARS-CoV-2 infected pregnant women

A total of 7 pregnant women with SARS-CoV-2 infection in late pregnancy were included in the study. Except case 1, who presented fever 2 days after delivery, the remaining 6 had onset symptoms of infection 1–6 days before delivery. The main clinical manifestations are fever, cough and other respiratory symptoms, followed by abdominal pain, diarrhea and other gastrointestinal symptoms. All seven women delivered by cesarean section, 4 were monitored by the obstetricians before onset of labor, then received cesarean section to prevent the uncertain transmission to newborns when infection symptoms appeared. 2 received emergency cesarean section for hypertension and blurred vision caused by severe preeclampsia to prevent the uncertain transmission to newborns. Among the 7 cases, 6 showed signs of viral pneumonia by chest CT after the symptoms of infection (Fig. 1), and 1 didn't show typical pathological signs in chest CT scan (Table 1).

3.2. Clinical features of newborns delivered by SARS-CoV-2 infected mothers

The 7 newborns delivered by SARS-CoV-2 infected mothers are either late preterm infants with gestational age(GA)between 36 weeks and 37weeks(4 cases) or full term infants (3 cases), with an average birth weight of 2096 ± 660 g (1880−3800 g), without birth asphyxia (Apgar scores of 1 min and 5 min ≥ 8) (Table 2). The appearance of the newborns was normal, with the skin color being ruddy, and with normal limb tension.

Among the 5 neonates admitted to NICU, 2 premature infants performed mild respiratory distress manifestation of grunting after birth, but relieved rapidly with non-invasive continuous positive airway pressure(nCPAP) ventilation. The other 3 cases showed no signs of dyspnea and hypoxia. 3 cases accepted chest X-ray, 1 was normal and 2 who were supported by nCPAP presented mild neonatal respiratory distress syndrome (NRDS). 2 newborns who were not admitted to NICU were taken home by their healthy family members for isolation care at the request of their guradians. Through daily telephone follow-up, we obtained the performance of the newborns and provided families with nursing guidance, and advised that once the infants performed poor reaction or milk rejection, they should return to the NICU immediately.

3.3. Laboratory examination and chest X-ray

Blood test results of 1 h and 48 h are shown in Table 3. The white blood cell count(WBC), neutrophil count ratio(NEU%) and lymphocyte count ratio (LYM%) were normal. As for procalcitonin (PCT), only 1 case increased slightly, while the others were normal or physiologically increased. C-reactive protein (CRP) results were normal for all newborns at birth and the following days. The blood biochemical results showed that the AST increased in 2 cases on the day of birth, and the AST decreased significantly in 1 case after 48 h of reexamination. The other case didn't collect the second blood test due to the discharged from the hospital on the second day after birth at the request of family members. The myocardial globin (MYO) and creatine kinase isoenzyme MB (CK-MB) were increased in 5 neonates, and there was no abnormality in electrocardiograph (ECG) test. As for D-dimer (DD), case 5 and case 7 were in the normal range, the other 3 cases were all increased.

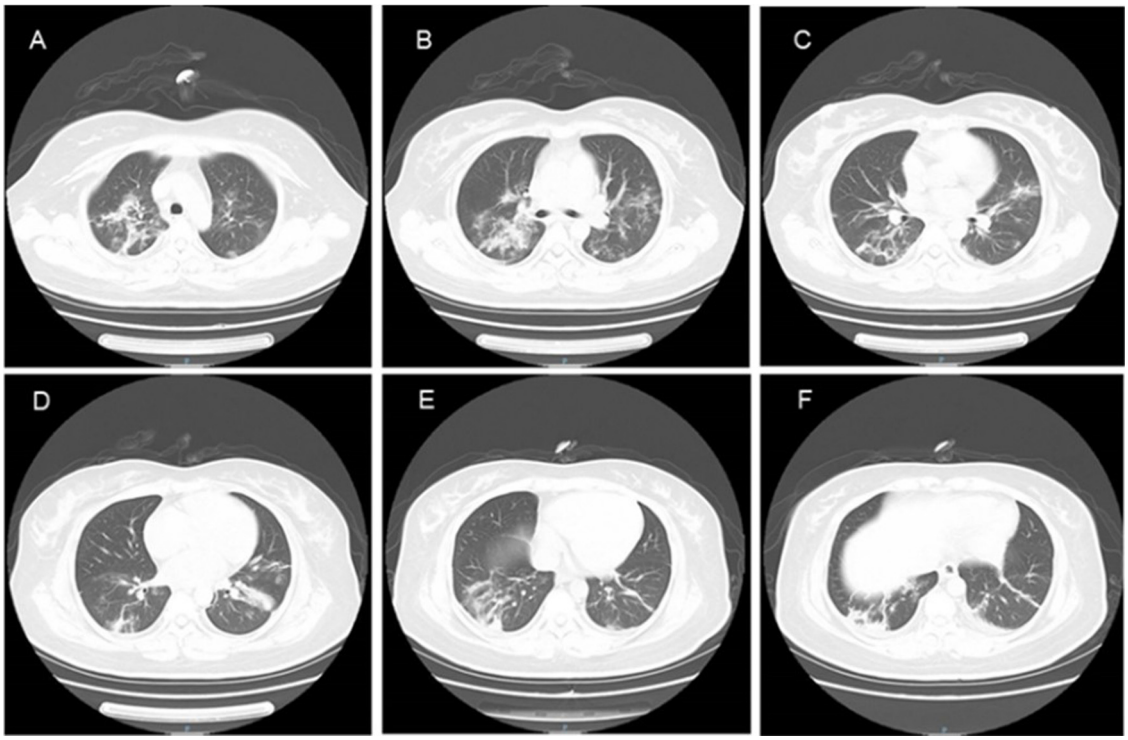


Fig. 1. Chest CT images of SARS-CoV-2 infected pregnant women.
Transverse chest CT images from a 2019-CoV infected pregnant woman showing bilateral ground-glass opacities, stripe opacities and subsegmental areas of consolidation on day 8 after symptom onset (A–F).

And all of the results of blood bacterial cultures were negative.

Three newborns received chest X-ray, one was normal and two presented mild neonatal respiratory distress syndrome (Fig. 2). qRT-PCR results showed that among the 6 neonates, 4 did not detect SARS-CoV-2 nucleic acid fragments in amniotic fluid, cord blood and pharyngeal swabs at birth, and the pharyngeal swabs were also negative within 5 days. Two cases only with pharyngeal swabs detection were also negative.

3.4. Treatment and outcome

Among 5 neonates admitted to the NICU, 2 premature infants were given nCPAP treatment due to signs of mild respiratory distress after birth, 3 did not receive respiratory support or oxygen therapy. 4 newborns were given piperacillin tazobactam for empiric anti-infection treatment, while the others were only given feeding and nursing care. None of the neonates received any antiviral treatment. In final, all of the 7 newborns were discharged without aggravation during hospitalization and isolated at home (including 2 who were not admitted to the NICU), their performance was normal according to telephone follow-up.

4. Discussion

By March 5, 2020, the number of confirmed cases has reached 80552, with 3042 deaths in China [9]. Confirmed cases have also been found in many other countries, the outbreak has rapidly spread to 78 coutries worldwide out of China, and it is predictable that the number of infected people will continue to increase exponentially with the change of diagnostic criteria [10].

As of February 26, 2020, near six hundred cases of infection in children have been reported in China [4].Pregnant women are at high risk of SARS-CoV-2 infection [5,6], and are prone to serious complications after SARS-like virus infection. Accurate data on maternal infection are not available, but the inevitable risk of childbirth and maternal infection poses a serious challenge to medical institutions during the high prevalence season. Therefore, it is imperative to evaluate the risk of infected mothers to their babies.

In this group of data, most pregnant women with SARS-CoV-2 infection showed symptoms of infection before delivery. As little is known to the virus at the early stage of outbreak, most of the newborns were born by planned cesarean delivery to prevent transmission to newborns. Two newborns were separated from their mothers after birth and taken home by healthy family members at their request. 5 newborns were admitted to the NICU, of which 2 newborns developed mild respiratory

Table 1
Clinical data of pregnant women with COVID-19.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Time of onset	22th Jan.	20th Jan.	24th Jan.	23th Jan.	25th Jan.	28th Jan.	27th Jan.
Symptom	Fever	Fever	Fever, diarrhea	Cough	Abdominal pain	Fever	Fever
Time of delivery	22th Jan.	26th Jan.	27th Jan.	27th Jan.	27th Jan.	28th Jan.	29th Jan.
Time of diagnosis	26th Jan.	23th Jan.	27th Jan.	28th Jan.	29th Jan.	29th Jan.	27th Jan.
Chest CT	Viral pneumonia	Viral pneumonia	Viral pneumonia	Viral pneumonia	Viral pneumonia	Normal	Viral pneumonia
Mode of delivery	Cesarean	Cesarean	Cesarean	Cesarean	Cesarean	Cesarean	Cesarean
nCoV-RNA	Positive	Positive	Positive	Positive	Positive	Positive	Positive

Table 2
Clinical features of newborns delivered by pregnant women with COVID-19.

	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6	Case 7
Sex	male	male	female	male	male	female	female
Gestational age	37w + 2	38w + 2	36w + 2	36w + 3	36w	36w + 2	38w
Birthweight, g	2870	3730	1880	3040	3800	2620	2800
1' Apgar score	8	9	8	8	8	9	8
5' Apgar score	9	10	9	9	9	10	9
Symptom	hypoglycemia, vomiting	normal	normal	Moan, spit	Moan	normal	normal
NICU care	yes	no	yes	yes	yes	no	yes
Respiratory support	no	–	no	nCPAP	nCPAP	–	no
nCoV-RNA							
Amniotic fluid	–	negative	negative	negative	negative	–	negative
Umbilical cord blood	–	negative	negative	negative	negative	–	negative
Throat swab (5 min)	–	negative	negative	negative	negative	–	negative
Throat swab (2 − 5d)	negative	–	negative	negative	negative	–	negative

Abbreviations: nCPAP, non-invasive continuous positive airway pressure; NICU, neonatal intensive care unit; -, Not done.

distress after birth, and were given nCPAP-assisted ventilation.3 newborns had stable breathing and didn't require any respiratory support. All newborns were not treated with any antiviral drugs.

The newborns that stayed in NICU had no abnormal signs during the monitoring of breathing, heart rate, and oxygen saturation. There was no abnormal manifestation in digestion, urination, defecation, and mental reactions during hospitalization. Complete blood counts taken on the first and third day of birth did not indicate obvious abnormal, all indicators were consistent with the normal range of newborns of the same gestational age and same day of age. Some newborns' MYO and CK-MB were higher than normal values. Coagulation indexes showed that some neonatal D-dimers were higher than normal values. Although Shek and colleagues have reported that SARS-CoV cannot be transmitted from infected mothers to newborns [11], it can aggravate the clinical outcomes of mothers and newborns. Our observation demonstrated that the condition of infants was not aggravated after their exposure to SARS-CoV-2 infected mothers, and we have also commented that compared to infected adults, the condition of infected children is significantly milder, with faster recovery, shorter virus shedding time and better prognosis [7]. However, one newborn in our department who was born to mother with suspected COVID-19 presented hematochezia recently, so it is still necessary to accumulate more clinical data for further understanding of maternal infection's influence on the newborn.

We understand some limitations in this study. For example, after 5 neonates were admitted to the NICU, no progressive exacerbation was found, so we didn't perform chest X-ray examination for all of them. In addition, the number of cases was limited, and the observation time was short. Despite of this, we should strengthen the monitoring of mother-to-child transmission, and further accumulation and detailed research are still needed.

In summary, the current data demonstrate that late pregnant women with COVID-19 does not cause severe adverse events on their newborns in this small series. In spite of this, newborns are still at high risk of COVID-19 in condition of postnatal infection without rigorous nosocomial infection control. It is necessary to separate newborns from mothers immediately to avoid the potential threats.

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Declaration of Competing Interest

The authors have indicated they have no potential conflicts of interest to disclose.

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Table 3
Blood results of the newborns at 1 h after birth and 48 h after birth.

	Case 1(1 h/48 h)	Case 3(1 h/48 h)	Case 4(1 h/48 h)	Case 5(1 h/48 h)	Case 7(1 h/48 h)
WBC, $\times 10^9$/L	16.62/12.72	7.53/8.39	11.72/12.3	22.5/17.22	14.8/discharged
Neutrophil %	65.2/57.8	50.3/24.3	58.3/71.9	74.2/68	63/-
Lymphocyte %	19.2/32.7	35.9/50.1	28.7/20.3	10.4/17.7	23.7/-
CRP, mg/L	< 5/ < 5	< 5/ < 5	< 5/ < 5	< 5/ < 5	< 5/-
PCT, ng/mL	0.28/5.06	< 0.1/ < 0.1	0.25/14.38	0.24/3.12	1.34/-
AST, U/L	45/46	30/39	39/46	74/46	107/-
ALT, U/L	10/9	< 6/6	7/9	10/8	23/-
CK-MB, ng/mL	8.5/-	4/-	10.5/-	16/-	23.1/-
MYO, ng/mL	170.8/-	113.3/-	203.6/-	248.2/-	580.5/-
DD, ng/mL	2591/808	746/-	611/-	256/-	429/-
Blood culture	Negative/-	Negative/-	Negative/-	Negative/-	Negative/-

Abbreviations: WBC, White blood cell count; CRP, C-reactive protein; PCT, Procalcitonin; AST, Aspartate aminotransferase; ALT, Alanine transaminase; CK-MB, Creatine kinase isoenzyme MB; MYO, Myoglobin; DD, D-dimer; -, Not done.

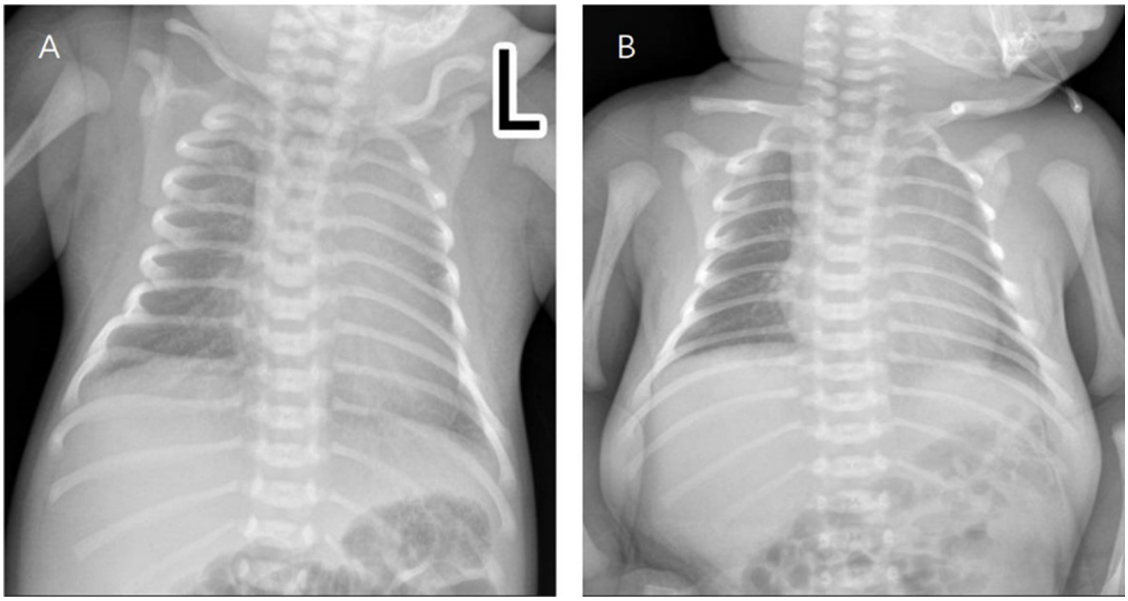


Fig. 2. Chest X-ray images of 2 premature newborns with NRDS/.
Chest X-ray images of 2 premature newborns (A, case 3, B, case 4) who showed mild respiratory distress at birth showing bilateral ground-glass opacities, granular high density shadows.

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