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Short Communication

Clinical presentations and outcomes of SARS-CoV-2 infected pneumonia in pregnant women and health status of their neonates

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The outbreak of COVID-19 has affected the world greatly. While much remains unknown, the severity of the illness is quite alarming. The disease outbreak is still ongoing with a rapidly growing number of patients. With confirmed human-to-human transmission, this disease has put pregnant women at risk, endangering the lives of infected mothers and their babies. However, current data so far have been mainly focused on general population but not for these patients, and we were not sure if SARS-COV-2 can be vertical transmitted from mothers to their babies. Here, we report the clinical, laboratory, radiological profiles and treatment outcomes of these five COVID-19 pregnant women and provide clinical information of their neonates.

For this retrospective study, five pregnant women were admitted from Jan 21, 2020 to Feb 9, 2020 by Wuhan Union Hospital. All pregnant patients were >34 week pregnancy with fever or respiratory symptoms and all of them were laboratory-confirmed SARS-CoV-2 positive by real-time reverse-transcription PCR (RT-PCR). Laboratory confirmation of SARS-CoV-2 infection was done using real time RT-PCR to amplify ORF1ab gene and N gene (two genes recommended by Chinese Center for Disease Control and Prevention) [2] following the manufacturer's instructions (BioGerm, Shanghai, China). The tests were performed on a Roche Cobas z480 Automated PCR Analyzer. The sequences for ORF1ab gene amplification and

detection were: forward primer 5′-CCCTGTGGGTTTTACACTTAA-3′, reverse primer 5′-ACGATTGTGCATCAGCTGA-3′, fluorescence probe 5′-FAM-CCGTCTGCGGTATGTGGAAAGGTTATGC-BHQ1-3′; The sequences for N gene amplification and detection were: forward primer 5′-GGGGAACTTCTCCTGCTAGAAT-3′, reverse primer 5′-CAGACATTTTGCTCTCAAGCTG-3′, fluorescence probe 5′-FAM-TTGCTGCTGCTTGACAGATT-TAMRA-3′. A cycle threshold value less than 35 (or above 35 but less than 38 for twice) was defined as positive.

The clinical features, laboratory and radiological findings, therapeutic methods and outcomes for all the five patients and their neonates were obtained, recorded and carefully analyzed. All data were checked by three researchers. This study was approved by Wuhan Union Hospital Ethics Committee and informed consent was obtained.

Between Jan 21, 2020 and Feb 9, 2020, five pregnant women were admitted with laboratory-confirmed SARS-CoV-2-infection (Tables 1 and S1 online). None of them had Huanan seafood market exposure (Table 1) and all the patients were residents of Wuhan. According to patients' records, only Patient 4's family member was confirmed with SARS-CoV-2 before onset of her symptoms, and the others did not have close contact with COVID-19 patients within 14 days before symptoms' onset. These patients were aged between 23 and 34 years (average 29 years) (Table 1), all of their fetuses were healthy and had normal development during pregnancy. Patient 1 was initially admitted due to obstetric reasons, while Patients 2–5 were admitted due to pneumonia-like symptoms such as fever and dry cough (Table 1). During clinical course

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Table 1

Clinical features of the pregnant women with COVID-19 pneumonia.

	Patient 1		Patient 2		Patient 3		Patient 4		Patient 5	
Age (year)	34		25		23		34		28	
Sex	Female		Female		Female		Female		Female	
Gestational age at admission (weeks + days)	38 weeks + 6 days		34 weeks + 4 days		37 weeks + 3 days		36 weeks + 4 days		37 weeks	
Pregnancy/birth	1/0		1/0		2/0		5/1		1/0	
Huanan seafood market exposure	No		No		No		No		No	
Reasons for hospitalization	Wait for parturition, abdominal pain		Pregnancy with viral pneumonia		Pregnancy with viral pneumonia		Pregnancy with viral pneumonia		Fever, colporrhagia	
Chronic illness	No		No		No		No		No	
Initial symptoms	Fever		Fever		Fever		Fever		Fever, cough	
Severity of pneumonia	Mild		Mild		Mild		Mild		Mild	
24 h before to 72 h after onset of parturition	Antepartum 24 h	Postpartum 72 h	Antepartum 24 h	Postpartum 72 h	Antepartum 24 h	Postpartum 72 h	Antepartum 24 h	Postpartum 72 h	Antepartum 24 h	Postpartum 72 h
Fever	No	Yes	No	No	No	Yes	No	No	Yes	Yes
Highest temperature (°C)	36.5	37.6	NA	36.8	38.7	38.5	36.4	36.8	38.1	39.3
Chest distress	No	Yes	No	No	Yes	No	No	No	No	No
Myalgia	No	No	No	No	No	No	No	No	No	No
Nasal congestion	No	No	No	No	No	No	No	No	No	No
Cough	No	No	No	No	Yes	Yes	No	No	Yes	Yes
Sore throat	No	No	No	No	No	No	No	No	No	No
Sputum Production	No	No	No	No	No	No	No	No	Yes	Yes
Dyspnea	No	No	No	No	Yes	No	No	No	No	Yes
Hemoptysis	No	No	No	No	No	No	No	No	No	No
Other	Abdominal, anorexia	No	No	No	No	No	No	No	Abdominal	No
Lowest SpO$_2$ (%)	93%–96%	93% with oxygen inhalation	99%	99%	ND	ND	94%	94%	ND	94% with oxygen inhalation
Oxygen support	No	Nasal cannula (3 L/min)	Nasal cannula (2 L/min)	Nasal cannula (2 L/min)	No	Nasal cannula (3 L/min–5 L/min)	No	Nasal cannula (3 L/min)	No	Nasal cannula (10 L/min)
Duration of fever (day)	7		2		11		8		11	
Days from illness onset to dyspnoea	None		None		4		None		None	
Diagnosis method	Real-time PCR		Real-time PCR		Real-time PCR		Real-time PCR		Real-time PCR	
Days from admission to SARS-CoV-2 detection	5		0		5		1 day before admission		3	
Surgical indications	39 weeks pregnant, abdominal pain		Viral pneumonia		Viral pneumonia		Viral pneumonia		Eutocia	
Delivery mode	Cesarean section		Cesarean section		Cesarean section		Cesarean section		Eutocia	
Time between symptom onset and neonate delivery (day)	6		11		5		10		8	
Antiviral therapy	Yes		Yes		Yes		Yes		Yes	
Antibiotic therapy	Yes		Yes		Yes		Yes		Yes	
Corticosteroid	No		Yes		No		Yes		Yes	

ND: not detected; NA: not available.

of COVID-19 infection, the other symptoms included fatigue and dyspnea (Table 1). Fever was the most common symptom, and could be intermittent, lasting for a median duration of 8 days (range 2–11 days) (Table 1). Dry cough was significant, often aggravated by supine position.

According to the definition of illness severity by WHO interim guideline for COVID-19 [3], all the patients developed mild pneumonia and gave birth to babies during hospitalization (Table 1). The time from the onset of symptoms to delivery for these patients was 6, 10, 5, 10 and 8 days, respectively. Their indicators for baby delivery were: Patient 1 (39 weeks) received C-section due to abdominal pain; Patient 2 (34 weeks + 4 days), Patient 3 (37 weeks + 3 days) and 4 (36 weeks + 4 days) were physiologically ready for parturition through C-section; Patient 5 (37 weeks) had natural laboring due to colporrhagia. None of them had pregnancy terminated due to uncorrectable hypoxemia.

Lymphopenia (<1.1 × 10^9/L) and eosinopenia (<0.02 × 10^9/L) were noted in all the patients at the onset of fever. The timing of eosinopenia largely matched that of lymphopenia. Lymphopenia and eosinopenia could persist until patients' illness clinically and radiographically improved after antiviral/antibacterial treatment. In contrast, leukopenia was observed in only one patient (Patient 1). Moreover, Patients 2 and 3 had anemia (Table S1 online). All the patients had decreased albumin, and increased CRP and D-dimer levels (Table S1 online), and all the patients were tested negative for other common respiratory infection pathogens (influenza A and B, respiratory syncytial virus, adenoviruses, coxsackie virus, chlamydia pneumonia, and mycoplasma pneumonia) (Table S1 online).

All five patients were subjected to chest CT examination 2–7 days (median 6 days) after the onset of fever (Fig. S1 online), and plumbic suits were covered on their abdomens to protect the fetuses. The CT imaging showed bilateral pneumonia in all five patients with characteristic flake-like or regional ground-glass opacity in segments or lobes (Fig. S1 online, Table S1 online). The opacity was often associated with peripheral lung with no clear subpleural sparing. The CT findings were consistent with early reports [5,6].

We recorded and analyzed the treatment of five patients (Table S2 online). Notably, Patients 1–5 gave birth to five neonates with the weight ranging from 2.45 to 3.76 kg (Table 2). None of

neonates display respiratory infection-related symptoms, including fever, cough, polypnea, dyspnea, cyanosis of lips, and tri-retraction sign at birth. The Apgar scores ranged 7–8 for 1 min, 8–9 for 5 min, and 10 for 10 min (Table 2). Once they were born, the neonates were separated from their mothers without breast feeding. The neonate of Patient 1 but not the other neonates had scattered skin rashes in face and body, which was reduced in the next day and gradually disappeared within 7 days. The throat swab specimens from all five neonates were collected at 8, 1, 8, 1, 0 days after birth, respectively, and were all SARS-CoV-2 PCR tested negative (Table 2). According to our observation, as of Feb 24, none of these neonates developed any respiratory or systemic symptoms (10–33 days after birth), which were much longer than the currently reported SARS-CoV-2 incubation time (4.1–7.0 days, 95% confidence interval) [7].

SARS-CoV-2, a new member of the coronavirus family, is a newly identified single stranded RNA virus. Similar to SARS-CoV and MERS-CoV, it can cause severe respiratory illness in infected humans [8–10]. Early studies revealed that female patients accounted for 32%–44% of SARS-CoV-2-infected population [5,7]. Although our pregnant COVID-19 patients (average 29 years, Table 1) were younger than affected general adults (average 56 years) [4], they were vulnerable given their immune tolerant conditions during pregnancy [11–13]. Given that Wuhan has an estimated 120 thousands pregnant women annually [14], approximately 20,000 of them were currently under COVID-19 infection threat. Given the estimated size doubling-time 7.4 days [7] and the nationwide confirmed over 77,000 cases (as of Feb 24), more pregnant women are expected to be diagnosed. To provide more information on the management of pregnant COVID-19 patients and the vertical transmission of SARS-CoV-2, in this study, we retrospectively analyzed the clinical features of pregnant women with SARS-CoV-2-infected pneumonia and health conditions of their neonates.

Our data revealed some similarities and differences of these pregnant patients compared to general adults. The spectra of symptoms (100% fever vs. 82% fever), the rate of conventional oxygen support (100% vs. 89%), the rate of antiviral treatment (100% vs. 93%) and antibacterial therapy (100% vs. 76%), the percentage of patients with increased CRP (100% vs. 86%), and the CT imaging characteristics in these pregnant patients were largely comparable

Table 2
Clinical features and outcomes of the five neonates.

Neonates	Patient 1's	Patient 2's	Patient 3's	Patient 4's	Patient 5's
SARS-CoV-2 detection (throat swab specimen PCR)	Negative	Negative	Negative	Negative	Negative
Days from birth to SARS-CoV-2 detection	8	1	8	1	0
Sex	Male	Female	Male	Male	Male
Gestational age at admission	39 weeks	34 weeks + 4 days	37 weeks	36 weeks	37 weeks
Delivery	Cesarean	Cesarean	Cesarean	Cesarean	Eutocia
Reason for delivery	Abdominal pain	Viral pneumonia	Obstetric cause	Viral pneumonia	Obstetric cause, viral pneumonia
Amniotic fluid	Normal	Normal	Polyhydramnios	Normal	Normal
Umbilical cord	Normal	Normal	Normal	Normal	Normal
Placenta	Slight placental separation	Normal	Total placenta praevia	Normal	Normal
Neonatal death	No	No	No	No	No
Birth weight (kg)	3.05	2.58	3.76	2.45	3.12
Development	Rashes in face and body	Normal	Normal	Normal	Normal
Appearance (Score 2)	1-5-10 min: 1-2-2	1-5-10 min: 1-1-2	1-5-10 min:1-1-2	1-5-10 min:1-1-2	1-5-10 min:1-2-2
Grimace (Score 2)	1-5-10 min: 2-2-2	1-5-10 min: 2-2-2	1-5-10 min: 2-2-2	1-5-10 min: 2-2-2	1-5-10 min: 2-2-2
Respiration (Score 2)	1-5-10 min: 2-2-2	1-5-10 min: 2-2-2	1-5-10 min: 2-2-2	1-5-10 min: 2-2-2	1-5-10 min: 2-2-2
Pulse (Score 2)	1-5-10 min: 1-1-2	1-5-10 min: 2-2-2	1-5-10 min: 2-2-2	1-5-10 min: 2-2-2	1-5-10 min: 2-2-2
Activity (Score 2)	1-5-10 min: 2-2-2	1-5-10 min: 1-2-2	1-5-10 min: 1-1-2	1-5-10 min: 1-2-2	1-5-10 min: 1-1-2
Apgar score (Score 10)	1-5-10 min: 8-9-10	1-5-10 min: 8-9-10	1-5-10 min: 7-8-10	1-5-10 min: 8-9-10	1-5-10 min: 8-9-10

to general adults (Table 1) [5,6]. In contrast, these women had less underlying diseases than general adults, and exhibited differences in some biochemical markers. Increased D-dimer levels and lymphopenia were observed in all the patients (100%), higher than 36% and 35% in general adults, respectively (Table S1 online) [5]. These laboratory differences might be partly due to pregnancy-associated physiological alterations.

Eosinopenia was found to be tightly linked with lymphopenia, which was not reported in early COVID-19 literature [5–7], and in SARS-CoV and MERS-CoV infections [15,16]. In COVID-19 pneumonia, eosinopenia appeared early, at the onset of fever, with a significant reduction (Table S1 online). Although eosinopenia was reportedly observed in some pregnant women previously [17], such a drastic decrease in eosinophil counts (reduced to zero in four of five patients) was unusual. Given that lymphopenia was suggestive of diagnosis value for COVID-19 infection [5] and did not commonly appear in normal pregnant women [18], eosinopenia with early timing feature might be also useful for facilitating early diagnosis. Given that glucocorticosteroids were considered to be one of the major reasons accounting for reduction in the number of eosinophil [19,20], it is possible that COVID-19-infection influences the levels of endogenous glucocorticosteroids.

SARS-CoV and MERS-CoV were reported to result in severe complications during pregnancy [19,20]. In a 12-case study [21], the 2003 SARS-CoV reportedly caused the death of three women, miscarriage (57%, 4 of 7 first-trimester patients), fetal growth restriction (40%, 2 of 5 third trimester patients), and premature birth (80%, 4 of 5 patients). As for MERS-CoV, it caused even more detrimental outcomes with 91% women (10 of 11 patients) having poor outcomes and 82% neonates having critical conditions and even death [22]. In this study, all the COVID-19 infected patients gave safe birth. The neonates were immediately separated from their mothers once they were born. The skin rashes were observed in one (20%) of the five neonates (Patient 1) (Tables 1 and 2). From the birth of these neonates until now, none of these babies developed any respiratory systems or pneumonia-associated symptoms. They seemed not to be locally or systemically impacted by COVID-19 infection in their mothers. This was similarly observed for other coronaviruses, such as SARS-CoV and MERS-CoV-infected mothers and their infants [21,23,24]. All neonates' throat swabs were PCR tested negative (Table 2). Thus, collectively, our observations did not support vertical virus transmission between these five infected mothers and their babies, consistent with a recent study [1]. Meanwhile, to protect neonates from SARS-CoV-2 infections after birth, we recommend prevention measures as follows: the neonates should be immediately isolated for a 14-day medical observation; breast feeding should be avoided; a 14-day isolation is also required for their mothers after discharge.

This study is limited in several aspects. Due to shortage of diagnostics reagents in local hospitals at the early stage of this COVID-19 outbreak, the laboratory-confirmed patient number was not high. But all patients and neonates in the current study were tested with PCR. Although we did not observe vertical transmission in these patients and their neonates, more evidence and further study is still required for further validation. Due to the lack of SARS-CoV-2 antibody detection reagents during this study, the serum IgM of SARS-CoV-2 in neonates, which was a key indicator of new SARS-CoV-2 infection, was not detected. The nucleic acid of SARS-CoV-2 in peripheral blood of these patients was also not detected due to the lack and control of RT-PCR reagents at the early stage of COVID-19 epidemic in Wuhan. Although the COVID-19 putative receptor ACE2 is critical to virus infection [25], its expression and abundance in neonates' respiratory system remains unknown. All these questions still await future study. Additionally, the long-term follow-up is needed to evaluate physical and psychological development of these neonates.

In this study, we provided clinical features of SARS-CoV-2 infected women and reported health status of their fetuses. We observed no obvious vertical transmission between these mothers and their neonates, and suggested that immediate prevention measures should be taken for these patients and their neonates to avoid SARS-CoV-2 infections after birth. Lymphopenia and eosinopenia that were uncommon in normal pregnant women were observed at the onset of SARS-CoV-2 related symptoms, which might facilitate early recognition of COVID-19.

Conflict of interest

The authors declare that they have no conflict of interest.

Acknowledgments

Author contributions

Luming Xu, Qianqian Yang, Shijun Lei and Haojun Shi contributed equally to this work. Lin Wang, Geqing Xia, Zheng Wang and Zehua Wang designed and supervised the study. All the authors contributed to collection of epidemiological, clinical and laboratory data. Geqing Xia, Zheng Wang, Lin Wang, Luming Xu, and Qianqian Yang analyzed and interpreted the data. Luming Xu collected the clinical data and revised the manuscript. Qianqian Yang and Shijun Lei collected and analyzed the laboratory data and prepared the tables. Haojun Shi collected and analyzed the radiology data and revised the manuscript. Lin Wang and Geqing Xia provided the information of patients, participated in data analysis, drafted and revised the manuscript. Zheng Wang analyzed and interpreted the data, drafted and revised the manuscript. Zehua Wang also has equally contributions to the data analyses and manuscript preparing.

Appendix A. Supplementary materials

Supplementary materials to this article can be found online at https://doi.org/10.1016/j.scib.2020.04.040.

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