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Clinical analysis of pregnant women with 2019 novel coronavirus pneumonia

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Abstract

Objective: To evaluate the pregnant women infected with coronavirus disease 2019 (COVID-19) and provide help for clinical prevention and treatment.

Methods: All 5 cases of pregnant women confirmed COVID-19 were collected among patients who admitted in Maternal and Child Hospital of Hubei Province between January 20 and February 10, 2020.

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Results: All patients, aging from 25 to 31 years old, had the gestational week from 38th weeks to 41st weeks. All pregnant women did not have an antepartum fever but developed a low-grade fever (37.5-38.5℃) within 24 hours after delivery. All patients had normal liver and renal function, two patients had elevated plasma levels of the myocardial enzyme. Unusual chest imaging manifestations, featured with ground-grass opacity, were frequently observed in bilateral (3 cases) or unilateral lobe (2 cases) by computed tomography (CT) scan. All labors smoothly processed, the Apgar scores were 10 one and five minutes after delivery, no complications were observed in the newborn.

Interpretation: Pregnancy and perinatal outcomes of patients with COVID-19 should receive more attention. It is probable that pregnant women diagnosed with COVID-19 have no fever before delivery. Their primary initial manifestations were merely low-grade postpartum fever or mild respiratory symptoms. Therefore, the protective measures are necessary on admission; the instant CT scan and real-time reverse-transcriptase polymerase-chain-reaction (RT-PCR) assay should be helpful in early diagnosis and avoid cross-infection on the occasion that patients have fever and other respiratory signs.

Keywords: pregnancy, COVID-19, labor, clinical manifestations

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Introduction

In December 2019, a novel coronavirus (SARS-CoV-2) induced pneumonia, started in Wuhan and rapidly spread in China and other countries, is causing a global health problem[1,2]. As February 8, 2020, the National Health Commission announced 37,198 confirmed cases and 28,942 suspected cases in China. Pregnant women were also reported being infected with COVID-19, which possesses a similarity with sever acute respiratory syndrome (SARS). As reported by the previous SARS-related studies, pregnant women were more susceptible to coronavirus infection and at a high risk of poor perinatal outcomes[3,4]. Nevertheless, studies on COVID-19 are still quite limited, leading to a great challenge for pregnant women care. Our study aimed to describe the clinical characteristics of pregnant women infected with COVID-19, and we

hope this study could provide a guidance for clinical prevention and treatment of COVID-19 in pregnant women.

Material and Methods

Data sources

Our study collected a total of 5 pregnant women with COVID-19, who were hospitalized for regular delivery in Maternal and Child Hospital of Hubei Province between January 20 and February 10, 2020 (Table 1). All patients were regularly given a prenatal routine examination that started from the first trimester. Ultrasound examination and fetal heart monitoring were offered regularly before delivery, no symptoms of viral pneumonia was observed. On latest admission, all patients received routine fetal heart monitoring and laboratory examinations including complete blood count, blood chemistry, coagulation test, liver and renal function, electrolytes, C-reactive protein, procalcitonin, lactate dehydrogenase and creatine kinase. The delivery strategy is determined according to the pregnant women's general situation. Apgar scoring and nursing was routinely given for the newborn after delivery. Once patient had suspected symptoms, chest CT scan and other blood analysis were instantly performed, antibiotics were empirically given in time to prevent bacterium-related infection, patients were quarantined for an intensive

treatment, and newborns were closely monitored with breastfeeding restriction. This study was approved by the ethical committee of Maternal and Child Hospital of Hubei Province, the work undertaken in this study conforms to the provisions of the Declaration of Helsinki (as revised in Tokyo 2004). Informed consent was obtained from all pregnant women.

Diagnostic criteria

Cases were suspected based on the WHO interim guidance and the definition of COVID-19 issued by the National Health Commission of China[5]. (1) Severe acute respiratory infection that required hospitalized treatment, (2) with no other etiology that thoroughly explains the clinical presentation, (3) and a history of travel to or residence in the city of Wuhan, or contact with the environment of COVID-19 as a healthcare worker. Abnormal results included the aforementioned imaging characteristics of pneumonia, decreased white blood cell (WBC) or lymphocyte counts in the early stage of disease.

The diagnostic criteria for COVID-19 are based on the criteria for the suspected cases. Positive results from real-time RT-PCR assay with samples like as sputum, throat swabs, lower respiratory tract secretions or other specimens, or sequencing-confirmed SARS-CoV-2 infection. All patients in

this study were reported positive for SARS-CoV-2 infection through quantitative RT-PCR tests.

Results

Demographic characteristics

According to the demographic data of 5 patients (Table 1), they were between the ages of 25 and 31 years old. None was a healthcare worker. All of them were physically fit and conceived naturally. The gestational weeks on admission were the third trimester (38th-41st weeks). Patient 1 and 5 had gestational diabetes and patient 2 had preeclampsia before delivery. All patients lived in Wuhan, Hubei province.

On admission, all patients had no fever or cough before delivery. However, all patients' low-grade fever (37.5℃-38.5℃), the most common onset symptom of COVID-19, occurred after delivery within 24 hours, and the highest body temperature of patient 1 was 38.5℃. Patient 3 had a cough one day before giving birth, and patient 5 had the symptoms of coughing and nasal runny ten days before delivery. All patients had no symptoms such as hemoptysis, dyspnea, shortness of breath, nausea and vomiting. All oxygen saturation tests were normal.

Laboratory findings

Laboratory findings showed (Table 2) that in the early stage of disease, the counts of white blood cells in all patients was normal, and two patients developed an increased WBC counts 24 hours after the symptom onset. The WBC counts of patient 5 were always abnormally high during hospital admission. CRP levels increased in all patients but except patient 4, particularly in patient 5 who had a substantial increase (40.98 mg/L-125.90mg/L). There was no obvious abnormality of the PCT levels observed in all patients. The levels of albumin were decreased in all patients, whereas the levels of ALT, AST and TBIL were normal. All patients except patient 1 presented with the elevated levels of ALP. CK was reduced in patient 1 (21 U/L) while increased in patient 3 (227 U/L), respectively.

All the serum samples of patients were tested for seven common respiratory pathogens (Chlamydia pneumoniae, mycoplasma pneumoniae, adenovirus, parainfluenza virus, respiratory syncytial virus, influenza a virus, and influenza b virus) and N7 subtype avian influenza virus antigen. All the tests were negative except for the positive results of mycoplasma pneumoniae in patients 3 and patient 5. Unusual chest imaging manifestations, featured with ground-grass opacity, were frequently observed in bilateral (3 cases) or unilateral lobe (2 cases) by computed tomography (CT) scan (Figure 1). All COVID-19 were laboratory-confirmed by the RT-PCR method.

Perinatal outcomes

The perinatal outcomes and newborns were described in Table 3. Patient 2 underwent an emergent caesarean section due to the fetal tachycardia during pregnancy, patient 5 underwent elective caesarean section due to gestational diabetes. Patient 1,3 and 4 had a natural delivery. All patients had a smooth labor process, and no partial complications occurred. The weights of newborns ranged from 3, 235g and 4, 050 g. Apgar scores were 10 points one and five minutes after delivery. No newborns showed the signs of perinatal COVID-19 infection, umbilical cord blood and amniotic fluid were not applied for virus detection due to the lack of reagent. No complications of placenta infarction and chorionic amniotic inflammation were reported. All patients were advised to stop breastfeeding and empirically given oseltamivir and azithromycin for treatment.

Discussion

A study that analyzed 12 cases of pregnant women with SARS in 2004, Hong Kong, found that pregnant women with SARS were associated with high morbidity and mortality[6]. Alfaraj and colleagues reported that the neonatal mortality rate was up to 27% for pregnant women with Middle East Respiratory Syndrome (MERS)[7]. Pregnant women infected with influenza showed a higher

risk in hospitalizing than healthy pregnant women.[8] Therefore, during the outbreak of COVID-19, a disease that still lack of specific and effective treatment, the prevention and management of pregnant women and newborns should be emphasized during the peripartal period.

The data in our study showed that all pregnant women had no fever before delivery, but after delivery two patients developed coughing and low-grade fever. Their CT scan results demonstrated the typical images of viral pneumonia. All five patients were confirmed with COVID-19 by the test of nucleic acid examination. The fetal tachycardia was observed in one pregnant woman who subsequently received emergent cesarean section. Chen et al.[9] reported that pregnancy with pneumonia would have a higher risk of cesarean section, premature delivery, decreased Apgar score of the newborn, and low birth weight of the newborn, etc. Even patients with COVID-19 may only have the mild respiratory symptoms during pregnancy, they are still at a high risk of severe pneumonia and adverse pregnancy outcomes, especially for patients who have preeclampsia or other complications, as pneumonia may aggravate pulmonary edema and oxygen saturation reduction.

Our study showed that the strategy of delivery was not affected by the co-existence of COVID-19, the choice of cesarean section was mainly determined by obstetric factors. According to the previous researches on

SARS, the peritoneal fluid[10] and faeces[11] could be positive for virus detection, and the virus might be transmitted during vaginal and cesarean delivery. As reported by a recent newspaper, a newborn was diagnosed as COVID-19 30 hours after delivery, which suggested that there may be a risk of virus intrauterine vertical transmission or infection through contacting with the maternal secretion. However, another research including nine pregnant women showed no direct evidence of intrauterine infection[12], which was consistent with the research on pregnant women with SARS[13], therefore, we need to be alert to take preventive and treatment measures for newborns in such period. According to China experts' consensus, it is recommended to quarantine the infants whose mother is suspected or diagnosed with COVID-19 for fourteen 14 days. Currently, there is not enough evidence supporting the presence of SARS-CoV-2 in breast milk, however, breastfeeding is not recommended according to the experience from SARS[4].

Owing to the absence of symptoms before delivery, all patients neglected CT scan and nucleic acid screening on admission, like most Chinese pregnant women usually do. It is probable to miss the diagnosis of COVID-19, which could delay the diagnosis and treatment of patients, and increase the risk of transmission for surrounding people, containing healthcare workers. The pregnant women's exposure to CT radiation barely reaches the dose that

causes harm to the fetus[14], so it is plausible to perform a COVID-19 screening during early pregnancy. In terms of treatment, pregnant women with MERS were not recommended to use ribavirin because of its risk to lead to fetal deformities[15]. New drugs for the treatment of COVID-19 are still being tested in clinical trials[16], and the effects for pregnant women are still not definitive and require further study[12].

Conclusion

Pregnant women infected with COVID-19 need to receive more intensive attention. COVID-19 could asymptotically occur during gestation but get diagnosed after delivery. The manifestations include postpartum fever, mild respiratory symptoms, and typical CT images. Therefore, the protective measures for COVID-19 are necessary on admission; The CT scan and real-time RT-PCR assay could be helpful for the prevention of cross-transmission and early treatment of pregnant women with COVID-19.

Conflicts of interest

None.

Authors' contributions

The corresponding author Dr. Yong Shao developed the study concept and design, critically reviewed the data and decided the content of the manuscript.

All other authors acquired and/or analyzed data, performed statistical analysis and/or provided technical or material support and/or wrote and/or critically reviewed the manuscript. These authors Dr. Siyu Chen and Dr. E Liao contributed equally to this work. All authors finally decided the content of the manuscript.

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Figures

Chest CT image of the pregnant women with COVID-19. Chest CT images of patient1 showed ground glass opacity in left lung on day 1 after symptom onset. Chest CT images of patient2 showed ground glass opacity in both lungs on day 1 after symptom onset. Chest CT images of patient3 showed ground glass opacity in right lung on day 1 after symptom onset. Chest CT images of patient4 showed ground glass opacity in right lung on day 1 after symptom onset. Chest CT images of patient5 showed ground glass opacity in both lungs on day 1 after symptom onset.

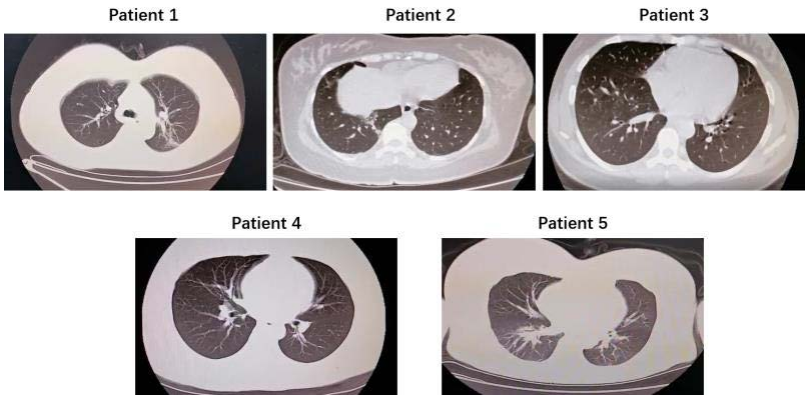

Table 1. Maternal characteristics and symptoms of pregnant women with COVID-19

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age(years)	29	30	25	31	29
Date of Admission	23/01/2020	26/01/2020	25/01/2020	27/01/2020	26/01/2020
Date of Delivery	24/01/2020 17:51	26/01/2020 22:55	25/01/2020 09:17	27/01/2020 21:30	27/01/2020 09:00
Date of Diagnosis	27/01/2020 14:30	27/01/2020 09:50	25/01/2020 23:43	28/01/2020 02:36	28/01/2020 08:31
Place of Residence	Wuhan, Hubei	Wuhan, Hubei	Wuhan, Hubei	Wuhan, Hubei	Wuhan, Hubei

Obstetrical Complications	Gestational Diabetes	Preeclampsia	None	None	Gestational Diabetes
Post-partum fever (℃)	38.5	37.5	37.4	37.4	37.8
Cough	—	—	+	—	—
Sputum	—	—	—	—	+
Coryza	—	—	—	—	+
Myalgia	—	—	—	—	—
Malaise	—	—	—	—	—
Dyspnea	—	—	—	—	—
Other symptoms	—	—	—	—	—
Systolic Blood Pressure（mmHg）	125	153	104	95	119

Table 2. Laboratory characteristics of pregnant women with COVID-19

Laboratory characteristics	Normal range	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
White blood cell count (WBC), $*10^9$/L	3.5-9.5	6.77	10.78 ↑	9.31	16.27 ↑	12.97 ↑
Lymphocyte count (LYMPH), $*10^9$/L	1.1-3.2	1.05 ↓	0.77 ↓	0.91 ↓	0.97 ↓	2.48
Neutrophil Cell Count (NEUT), $*10^9$/L	1.8-6.3	5.28	9.44 ↑	7.91 ↑	15.52 ↑	9.54 ↑
Platelet count (PLT), $*10^9$/L	125-350	240	167	105	194	326
C-reactive protein (CRP), mg/L	<4	18.46 ↑	19.56 ↑	NA	8.96 ↑	82.14 ↑
Procalcitonin (PCT), ng/mL	<0.05	0.053	0.212	0.070	0.048	0.122
Hemoglobin (HGB), g/L	115-150	125	119	113	103 ↓	105 ↓
Prothrombin Time (PT), s	9.4-12.5	10.3	9.9	11.1	11.4	12.1
Activated Partial Thromboplastin Time (APTT), s	25.1-36.5	25.7	29.5	28.0	29.1	30.1
D-dimer (D-DI), μg/mL	<0.5	0.54 ↑	NA	NA	1.90 ↑	1.64 ↑
Albumin (ALB), g/L	40-55	35.5 ↓	31.3 ↓	31.8 ↓	29.4 ↓	28.3 ↓
Total bilirubin (TBIL),	5-21	5.5	4.0	6.2	7.3	8.1

μg/mL						
Alanine aminotransferase (ALT), U/L	0-35	14.7	15.5	7.6	5.9	7.6
Aspartate aminotransferase (AST), U/L	0-35	13.8	30.3	26.1	14.5	16.4
Alkaline phosphatase (ALP), U/L	35-100	100.0	145.0 ↑	234.0 ↑	266 ↑	146.0 ↑
Creatinine (CREA), μmol/L	41-73	62.0	58.0	38.4 ↓	56.0	51.0
Sodium (Na), mmol/L	137-147	143	138.0	133.0 ↓	140.0	143.0
Potassium (K), mmol/L	3.5-5.3	4.36	4.78	4.40	4.59	3.50
Calcium (Ca), mmol/L	2.11-2.52	2. 13	1.91 ↓	1.97 ↓	2.25	2.13
Chloride (CL), mmol/L	99-110	105.0	100.0	104.0	104.0	104.0
Lactose dehydrogenase (LDH), U/L	120-250	245.0	412.0 ↑	247.0	221.0	194.0
Creatinine kinase (CK), U/L	40-200	21.0 ↓	105.0	227.0 ↑	69.0	199.0
SARS-CoV-2 quantitative RT-PCR	—	+	+	+	+	+
Seven common	—	—	—	—	—	—

respiratory pathogens	

Positive:－; Negative:＋; NA: Not available.

Table 3. Perinatal outcomes of pregnant women with COVID-19

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Gestational age on delivery (weeks)	40^{+4}	39^{+1}	38^{+6}	39^{+6}	39
Gravidity (n) Parity (n)	G1P0	G1P0	G3P1	G3P0	G1P0
Fetal heart rate trace	Normal	Fetal tachycardia	Normal	Normal	Normal
Mode of delivery	natural birth	C-section	natural birth	natural birth	C-section
Complications after delivery	no	no	no	no	no
Weighs of newborns (g)	3235	3800	3670	3700	4050
Apgar scores (5min/10min)	10/10	10/10	10/10	10/10	10/10
Neonatal	no	no	no	no	no

symptoms infected with COVID-19						
Neonatal SARS-CoV-2 quantitative RT-PCR	Negative	Negative	Negative	Negative	Negative	