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Clinical Features and Outcomes of Pregnant Women Suspected of Coronavirus Disease 2019

Hui yang , Guoqiang Sun , Fei Tang , Min Peng , Ying Gao , Jing Peng , Hui Xie , Yun Zhao , Zhichun Jin

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Highlights

- The newly identified 2019 novel coronavirus disease (COVID-19) is spreading nationwide. Previous studies mainly focus on non-pregnant population with COVID-19. The purpose of this study is to investigate and analysis the clinical features, imaging findings, related laboratory indicators and outcomes of maternal-fetal for cases of of 55 pregnant women who had been initials dignosed with suspected infection COVID-19 at Maternal and Child Health Hospital of Hubei Province, Tongji Medical College, Huazhong University of Science and Technology, a tertiary care teaching hospital in Hubei province, Wuhan, China from January 23 to March 5, 2020 . Among the 55 cases, 13 patients were assigned into the confirmed COVID-19 group and the other 42 patients were assigned into the control group for being ruled out COVID-19 pneumonia. All the 13 confirmed pregnant women were diagnosed with asymptomatic and mild COVID-19, and no one of the patients developed severe COVID-19 or died. For the parturient women with asymptomatic and mild COVID-19, the clinical symptoms and laboratory indicators are not obvious. Pulmonary CT image of those manifestations is not the specific clinical features of COVID-19 pneumonia. The count of Lymphocyte was lower in the confirmed COVID-19 cases, but there was no change in the normal cases. In Wuhan where the incidence of COVID-19 is high, pulmonary CT screening on admission may be necessary to reduce the

transmission of COVID-19 during the outbreak period. Pulmonary CT scan plus blood routine examination of WBC, Neutrophil and Lymphocyte are more suitable for finding pregnancy women with asymptomatic or mild COVID-19 infection once pregnant women are in labor and have no time to confirm COVID-19, and thus protecting normal pregnancy women and medical staffs.

Clinical Features and Outcomes of Pregnant Women Suspected of Coronavirus Disease 2019

Hui YANG[1]*, Guoqiang Sun[1]*, Fei TANG[1], Min PENG[1], Ying GAO[1], Jing PENG[1], Hui XIE[2], Yun ZHAO[#1], Zhichun JIN[#3]

*These authors contributed equally to this work.

#Corresponding authors: Prof Yun ZHAO (Email: zhao020060@163.com) and Prof Zhichun JIN (Email: jzc88@163.com)

1. *Department of Obstetrics*, Maternal and Child Health Hospital of Hubei Province, Tongji Medical College, Huazhong University of Science and Technology, No. 745, Wuluo Road, Hongshan District, Wuhan 430070, China.
2. *Department of Radiology*, Maternal and Child Health Hospital of Hubei Province, Tongji Medical College, Huazhong University of Science and Technology, No. 745, Wuluo Road, Hongshan District, Wuhan 430070, China.
3. *Department of prenatal diagnosis*, Maternal and Child Health Hospital of Hubei Province, Tongji Medical College, Huazhong University of Science and Technology, No. 745, Wuluo Road, Hongshan District, Wuhan 430070, China.

Hui YANG, Email: keaiyh@163.com

Guoqiang SUN, Email: sunguoqiang@hbfy.com

Fei TANG, Email: tangfei87169226@163.com

Min PENG, Email: pm19751023@163.com

Ying GAO, Email: gaoying123114@163.com

Jing PENG, 15670513217@163.com

Hui XIE. Email: 1165557196@qq.com

Yun ZHAO, Email: zhao020060@163.com

Zhichun JIN, Email: jzc88@163.com

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Abstract

Background: 2019 novel coronavirus disease (COVID-19) has become a worldwide pandemic. Under such circumstance pregnant women are also affected significantly.

Objective: This study aims to observe the clinical features and outcomes of pregnant women who have been confirmed with COVID-19.

Methods: The research objects were 55 cases of suspected COVID-19 pregnant women who gave a birth from Jan 20th 2020 to Mar 5th 2020 in our hospital-a big birth center delivering about 30,000 babies in the last 3 years. These cases were subjected to pulmonary CT scan and routine blood test, manifested symptoms of fever, cough, chest tightness or gastrointestinal symptoms. They were admitted to an isolated suite, with clinical features and newborn babies being carefully observed. Among the 55 cases, 13 patients were assigned into the confirmed COVID-19 group for being tested positive sever acute respiratory syndrome coronavirus 2(SARS-CoV-2) via maternal throat swab test, and the other 42 patients were assigned into the control group for being ruled out COVID-19 pneumonia based on new coronavirus pneumonia prevention and control program(the 7th edition).

Results: There were 2 fever patients during the prenatal period and 8 fever patients during the postpartum period in the confirmed COVID-19 group. In contrast, there were 11 prenatal fever patients and 20 postpartum fever patients in the control group ($p > 0.05$). Among 55 cases, only 2 case had cough in the confirmed group. The imaging of pulmonary CT scan showed ground- glass opacity (46.2%, 6/13), patch-like shadows(38.5%, 5/13), fiber shadow(23.1%, 3/13), pleural effusion (38.5%, 5/13)and pleural thickening(7.7%, 1/13), and there was no statistical difference between the confirmed COVID-19 group and the control group ($p > 0.05$). During the prenatal and postpartum period, there

was no difference in the count of WBC, Neutrophils and Lymphocyte, the radio of Neutrophils and Lymphocyte and the level of CRP between the confirmed COVID-19 group and the control group($p<0.05$). 20 babies (from confirmed mother and from normal mother) were subjected to SARS-CoV-2 examination by throat swab samples in 24 hours after birth and no case was tested positive.

Conclusion: The clinical symptoms and laboratory indicators are not obvious for asymptomatic and mild COVID-19 pregnant women. Pulmonary CT scan plus blood routine examination are more suitable for finding pregnancy women with asymptomatic or mild COVID-19 infection, and can be used screening COVID-19 pregnant women in the outbreak area of COVID-19 infection.

Key Words: COVID-19, Novel Cornonavirus, outcomes, pregnant women, pulmonary CT scan

Introduction

The Novel Coronavirus (COVID-19) causing an outbreak of pneumonia in Wuhan- China was recently discovered in December 2019. By the date of Mar 5th 2020, a total of 49797 confirmed cases of the COVID-19 had been reported, and 2328 people had died of such infection in Wuhan[1]. COVID-19 has spread around world rapidly, with the number of reported confirmed cases reaching a total of 14053[2], imposing a threat to the global public health. Based on the understanding of the pathogen, epidemiology, clinical characteristics, the National Health Committee decided to include COVID-19 pneumonia as category B infectious diseases according to in the Law of the People's Republic of China on the Prevention and Treatment of Infectious Diseases, and to control it by taking prevention and control measures of Category A infectious diseases[3]. People know little about COVID-19 although a series of related studies have been reported. Moreover, there were fewer reports on COVID-19pregnant women and their outcomes. The pathophysiological changes of SARS and MERS during pregnancy are more likely to lead to severe adverse pregnancy outcomes[4,5]. Currently, there are insufficient data to investigate the effect of COVID-19 on pregnant women and their outcomes[6,7]. During the outbreak period, prevention and control of COVID-19 infection in pregnant women and new- babies are becoming more important, especially when they undergo delivery during hospitalization. In order to control

COVID-19 infection, the isolation suites in our hospital were set up, including outpatient suite, operation room, labor and delivery room, maternal suite, new-baby suite and suite for treating suspected pregnant patients. In order to address the clinical features and outcomes of pregnant women with confirmed COVID-19, we retrospectively reviewed clinical records, laboratory findings and chest CT scan results of 55 suspected pregnant patients who were admitted to Maternal and Child Health Hospital of Hubei Province, Tongji Medical College, Huazhong University of Science and Technology, from January 20th to Marth 23th, 2020.

Materials and Methods

Ethical approval

The study was reviewed and approved by the Ethics Committee of Maternal and Child Health Hospital of Hubei Province, Tongji Medical College, Huazhong University of Science and Technology (Record number 2020001). Written informed consent was obtained from enrolled patients. All pregnant women requiring the pulmonary CT scan had signed informed consent.

Isolation unite for COVID-19 infection

During the out-break of COVID-19 infection, the hospitals in Wuhan were divided into designated hospitals and non-designated hospitals [8]. Our hospital belongs to non-designated hospitals including department for high fever to accept normal pregnant women and suspected pregnant patients. From January 20th 2020, the

isolation suites in our hospital were set up including outpatient suite, operation room, labor and delivery room, maternal suite and new-baby suite. If the confirmed cases and suspected cases were in labor, they could deliver their babies in isolation suites. During hospitalization, if the suspected patients were laboratory-confirmed COVID-19 infection via throat swab test for severe acute respiratory syndrome coronavirus 2(SARS-CoV-2) by using of quantitative RT-PCR(qPT-PCR)[9], they would be transferred to designated hospital for further treatment. If they were tested negative for more than twice, they could continue to stay in our isolation maternal suite, then go home for isolated observation for two weeks. Additionally, if the cases were not timely diagnosed for suspected COVID-19 on admission, they could be transferred to isolation suite anytime for observation based on symptoms such as fever and/or cough, chest CT scan, and laboratory finding.

Study design and patients

The suspected cases of COVID-19 infection were screened based on pulmonary CT scan and routine blood test in combination with symptoms such as fever, cough, chest tightness or gastrointestinal symptoms, and admitted to an isolated suite in our hospital (at Maternal and Child Health Hospital of Hubei Province, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China). We retrospectively reviewed the clinical features and outcomes of pregnant women with suspected COVID-19 infection from January 20 to March 5, 2020. All selected women were Chinese pregnant women. Those with non- Chinese nationality

and non-pregnant women were excluded. A total of 75 cases were selected in this study, excluding 20 cases of non-pregnant women, then the remaining 55 cases were divided into 2 groups, including the confirmed COVID-19 group containing 13 cases and the control group containing 42 cases.

Data collection

All data were inputted into SPSS software (v.19.0, SPSS Inc, ChicagBasic information (age, BMI on admission, pregnant week at delivery, delivery modes, volume of postpartum hemorrhage, newborn gender, weight) was collected for each patient. Clinical manifestations were recorded, such as fever, coughing, expectoration, myalgia, fatigue, hemoptysis, headache, heart palpitations, diarrhea or dyspnea.

Medical imaging of pulmonary CT scan was collected. The topical involvement in lung computed tomography scan was multiple patch-like shadows (early stage), ground-glass opacity (middle stage), and consolidation shadow (late stage)[10].

Laboratory test results were compiled, including standard blood counts (absolute white blood cells, neutrophils and lymphocytes), cell ratio of neutrophils and lymphocytes, and C-reactive protein.

Other data collected included maternal and infant treatment progress, recovery and discharge information, treatment mode information, and death information.

Data analysis

o, IL, USA) for statistical analysis. The values and variables were reported in the form of mean±standard deviation. Student's test was performed to compare the variables in Gaussian distribution. Chi-square test and Fisher's exact test were used to evaluate the categorical variables. Wilcoxon test was used to evaluate the difference of the level of CRP in the prenatal and postpartum period. All statistical tests were performed with 2-sided *P* values. If p value<0.05, the difference was considered statistically significant.

Results

Among the 55 suspected cases of COVID-19 infection, there was only one case having the history of close contacting with a confirmed case of COVID-19 infection in the confirmed group. Of 13 cases of prenatal fever, there was only 1 case of high fever with the temperature reaching38.5℃ in the prenatal period and negative result of SARS-CoV-2 test, while the the rest fever cases was ranged from 37.3^0C to 38.0^0C body temperature and lasted for 2-3 days without special treatment. There were 28 cases of postpartum fever with temperature ranging from 37.3℃ to 39.2℃, including 13 cases with temperature above 38℃.Only 2 cases had dry cough in the postpartum period, which had been confirmed by the test of SARS-CoV-2. No one had expectoration, myalgia or fatigue, hemoptysis, headache, heart palpitations, diarrhea or dyspnea. Basic information and

clinical manifestations of 55 cases are shown in **Table 1**. There was no statistical difference between the confirmed group and the control group in terms of maternal age, BMI of pregnant women on admission, delivery mode, volume of postpartum hemorrhage, newborn gender and birth weight and gestational week of newborn($p < 0.05$).

During hospitalization, all patients underwent pulmonary CT scan at least twice and at most 5 times, with interval period ranging from 2 days to 5 days. A total of 127 pulmonary CT scans were carried out, and the results are listed **in Table 2**. According to the standard of Treat Plan for Novel Coronavirus Pneumonia (Trial Version 7) [11] that pleural effusion is rare. It can be seen from table 2 that the proportion of pregnant women with pleural effusion in the imaging manifestations was 29.1 (16/55), which was significantly higher than that of non-pregnant patients. The pleural effusion reviewed for the first time after delivery has an increasing trend, which may be related to the increase of reactive inflammatory exudation, and the latter stage is characterized by gradual absorption. Certain trend changes presented in the pulmonary lesions. When lung imaging findings reflected as grinding glass sample lesions and patch-like shadows, the frequency of occurrence is gradually decreased with the extension of time. Some cases of pulmonary lesions disappeared, and fiber cable and pleural thickening frequency increased with the extension of time. Pulmonary CT scan on admission was carried out for all 55 cases, among them 3 patients were normal, 52 cases were found abnormal in different degrees including

ground-glass opacity, patch-like shadows, fiber shadow, pleural effusion and pleural thickening, and there was no different between the two groups ($p<0.05$) as shown **in table 3**.

Blood indexes including the white blood cell count (WBC), Neutrophil ratio, Neutrophil count, Lymphocyte count and Lymphocyte ratio were analyzed on admission and at the third day after delivery. There was no difference between the two groups no matter on admission or after delivery. The WBC count, Neutrophil radio and count, CRP were higher and Lymphocyte radio was lower after delivery for two groups($p<0.05$). Lymphocyte count was lower only in the confirmed COVID-19 group after delivery($p<0.05$), but Lymphocyte count had no change in the control group($p>0.05$). Details are shown **in Table 4**.

57 newborn babies, including 2 cases of twins, were transferred to the isolation suite of neonatal intensive care unit (NICU) after birth. Twenty of them were tested for SARS CoV-2, and the results were all negative.

57 newborns were followed up by telephone, and only 1 who was delivered by a pregnant woman confirmed with COVID-19 had a fever up to 37.7℃ lasted for 1 day after birth. There were 3 cases of neonatal respiratory distress syndrome after birth, among which 2 were premature babies with gestational age <35 weeks (confirmed mother), and 1 was a full-term baby (normal mother). It was found that the newborn had chromosomal disease after perfect examination due to special facial features.

Discussion

The COVID-19 epidemic broke out quickly around the world [12]. The COVID-19 virus is mainly transmitted by respiratory system and likely to infect people in all ages. Clinically, COVID-19 pneumonia is divided into mild, normal and serious degrees [11], at the same time, asymptomatic infection of COVID-19 also existed during the outbreak period. Novel Coronavirus Pneumonia Emergency Response Epidemiology team [13] found that there were 1.2% asymptomatic cases from China's Infectious Disease Information System. Hu Z et al. [14] found that from close contacts confirmed with COVID-19 in Nanjing, China, there were 24 cases of asymptomatic infection. At present, there are limited data on COVID-19 pregnant women. Chen H et al. [6] reported COVID-19 infection in nine pregnant women who presented typical symptoms in a designated hospital of Wuhan, and found seven patients presented with fever and other symptoms including cough(in four), myalgia(in three), core throat(in two), and malaise(in two). In our study conducted in a non-designated hospital of Wuhan, 13 pregnant women confirmed with COVID-19 were all in mild or asymptomatic degree, including only 15.4%(2/13) prenatal fever and 61.6%(8/13) postpartum fever, and 15.4%(2/13) coughing cases, and no one had expectoration, myalgia or fatigue, hemoptysis, headache, heart palpitations, diarrhea or dyspnea. This is probably because our study was limited to a non-designated hospital of COVID-19 infection and we have paid more attention to distinguish the normal and suspected COVID-19 infection to prevent cross-contamination.

Pulmonary CT scan plays an important role in diagnosis of COVID-19 infection and observation of therapeutic effect, and the imaging abnormalities presented even in asymptomatic patients [14,15]. Zhao W [15] studied 101 cases of COVID-19 pneumonia and found that most patients with COVID-19 pneumonia had topical imaging features, such as ground-glass opacities(86.1%) or mixed ground-glass opacities and consolidation(64.4%), vascular enlargement in the lesion(71.3%), and traction bronchiectasis(52.5%), and lesions present on CT images were more likely to have a peripheral distribution(87.1%) and bilateral involvement(82.2%) and be lower lung predominant(54.5%) and multifocal(54.5%). Patients with confirmed COVID-19 pneumonia had typical imaging features, which can be helpful in early screening of highly suspected cases and in evaluation of the severity and extent of the disease. Moreover, CT involvement score is of reference value in evaluation of the severity and extent of the disease.

Hu Z et al. [14] investigated 24 cases with asymptomatic infection and found that during hospitalization, twelve (50.0%) cases showed typical CT images of ground-glass chest, 5 (20.8%) presented stripe shadowing in the lungs, the remaining 7 (29.2%) cases showed normal CT image with no symptoms during hospitalization. None of the 24 cases developed severe COVID-19 pneumonia or died. With the rapid development from focal unilateral ground-glass opacity to diffused bilateral ground-glass opacity, early diagnosis of COVID-19 may be facilitated based on clinical and laboratory findings [16]. In our observation, among 13 cases of COVID-19

infection, there were 6/13 presenting ground-glass opocity, 5/13 patch-like shadows, 3/13 fiber shadow, 5/13 pleural effusion, 1/13 pleural thickening and 3/13 normal. Pulmonary CT image of those manifestations is not the specific clinical features of COVID-19 pneumonia. Compared with the common pneumonia in the control group, the imaging showed no difference.

Termination of pregnancy can a stress for the cases with confirmed COVID-19 pneumonias whatever undergoing cesarean or vaginal delivery. In our study,

there was no difference in white blood cell count, Neutrophil granulocyte count & proportion, lymphocyte count & proportion, and CRP between COVID-19 confirmed group and control group before and after delivery. However, for each group, the white blood cell count, Neutrophil granulocyte count & proportion and CRP was higher after delivery than those before delivery. It reflected that normal immunologic function was activated to help recovery. The count of Lymphocyte was lower in the confirmed COVID-19 cases, but there was no change in the normal cases, which indicates that Lymphocyte was a susceptible index for progress of COVID-19 infection.

There are several limitations in our study. First, the sample size was smal and all of the pregnant women confirmed with COVID-19 were in mild or asymptomatic degree and no serious degree with typical symptoms. Second, we did not take throat swab

samples of all the newborns to check for COVID-19 infection. Third, the samples such as placenta, amniotic fluid and cord blood were not collected for COVID-19 test.

Conclusion

It took time to confirm COVID-19 in the laboratory at a particular time, but pregnant women were in labor and had no time to confirm COVID-19. Pulmonary CT scan plus blood routine examination of WBC, Neutrophil and Lymphocyte are more suitable for finding pregnancy women with asymptomatic or mild COVID-19 infection, and thus protecting normal pregnancy women and medical staffs.

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Contributors

Hui Yang: Conceptualization, Investigation, Data curation, Writing-original draft. **Guoqiang Sun:** Conceptualization, Investigation, Visualization, Writing-original draft. **Yun Zhao:** Conceptualization, Data curation, Visualization, Writing-review

and editing. **Zhichun Jin:** Conceptualization, Supervision, Writing-review and editing. **Fei Tang:** Investigation. **Min Peng:** Investigation. **Ying Gao:** Investigation. **Jing Peng:** Investigation. **Hui Xie:** Investigation.

Declaration of Competing Interest

We declare no competing interests

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Table 1. Basic Information and Clinical Manifestation for 55 Cases Student's test, Chi- square test were used

Groups	**Confirmed group (n=13)**	**Control group (n=42)**	***t/x2***	***P***
Age（y， $\bar{X} \pm s$）	30.2±2.3	29.8±3.4	0.410	0.681
Body mass index（kg/m2， $\bar{X} \pm s$）	20.39±2.33	21.38±2.76	-0.980	0.331
Prenatal fever (n，%)	2, 15.4	11, 26.2	0.642	0.725

Postpartum fever (n，%)	8, 61.5	20, 47.6	0.770	0.681
Delivery mode(n，%)				
Vaginal delivery	4, 30.8	12, 28.6	0.023	0.988
Cesarean delivery	9, 69.2	30, 71.4		
Newborn gender (n，%)				
Male	8, 57.1	28, 65.1	0.289	0.866
Female	6, 42.9	15, 34.9		
Newborn weight (g, $\bar{X} \pm s$)	3063.2±536.4	3317.1±522.5	-1.570	0.122
gestational week of newborn (w, $\bar{X} \pm s$)	38.2±2.3	38.8±1.8	-1.286	0.210
Volume of postpartum hemorrhage(mL, $X \pm s$)	356.1±45.4	336.9±93.6	0.713	0.479

Table 2

Pulmonary CT scan of 55 Pregnant Women with suspected COVID-19 at Different Time

Time	n	Normal	Ground-glass opacity(n, %)	Patch-like shadow (n, %)	Fiber shadow (n, %)	Pleural effusion (n, %)	Pleural thickening (n, %)
Admission	55	3	32, 58.2	20, 36.4	6, 10.9	16, 29.1	4. 7.3
2~＜5d	52	0	29, 55.8	13, 25.1	8, 15.4	18, 34.6	7, 13.5
5~＜9d	13	3	7, 53.8	1, 7.7	3, 23.1	4, 30.8	-
9~＜13d	4	0	4*	-	1	-	-
≥13d	1	0	1*	-	-	-	-

Time: from the examination day to the admission

*Lesions to narrow

Table 3

Imaging of pulmonary CT scan between in the confirmed and in the control groups for the first time

groups	n	Normal	Ground-glass opacity (n, %)	Patch-like shadows (n, %)	Fiber shadow (n, %)	Pleural effusion (n, %)	Pleural thickening (n, %)
Confirmed group	13	1,7.7	6,46.2	5,38.5	3,23.1	5,38.5	1,7.7
Control group	42	2,4.8	26,61.9	15,35.7	3,7.1	11,26.2	3,7.1
X^2			1.012	0.032	-	0.725	-
p		0.488	0.314	0.857	0.136	0.395	1.000

Chi- square test and Fisher's exact test were used

Table 4

Blood routine and CRP between in the confirmed and in the control groups

	Confirmed group		Control group		① - ③		② - ④		①-②		③-④	
	Prenatal ①	Postpartum ②	Prenatal ③	Postpartum ④	*t*/*Z*	*p*	*t*/*Z*	*p*	*t*/*Z*	*p*	*t*/*Z*	*p*
WBC (*10^9, $\bar{X}$ ± s)	8.9±1.5	12.6±3.6	10.0±2.9	13.3±4.2	-1.294	0.201	-0.606	0.547	-4.595	0.001	-5.252	0.000
Neutrophil % (%, $\bar{X}$ ± s)	77.1±5.8	85.1±7.2	77.5±8.1	84.4±5.5	-0.128	0.898	0.368	0.715	-3.678	0.003	-4.444	0.001
Neutrophil (*10^9, $\bar{X}$ ± s)	6.9±1.4	10.9±3.9	7.8±3.0	11.4±4.1	-1.071	0.289	-0.380	0.705	-4.405	0.001	-5.313	0.000

Lymphocyte ($*10^9$, $\bar{X} \pm s$)	1.4±0.4	1.1±0.4	1.6±0.5	1.3±0.5	-0.711	0.480	-1.388	0.171	2.364	0.036	1.690	0.117
Lymphocyte% (%, $\bar{X} \pm s$)	16.4±5.1.	9.8±5.6	16.9±7.4	10.7±4.5	-0.216	0.830	-0.545	0.588	3.395	0.005	4.372	0.001
CRP [mg/L, (median,95%CI)]	3.7,1.9-7.8	19.6,8.3-49.1	2.9,1.4-3.8	52.7,21.5-108.7	-0.357	0.721	-1.109	0.267	-2.830	0.005	-5.620	0.000

Student’s test and Kolmogorov-Smirnov Z were used