

# Clinical Manifestation and Neonatal Outcomes of Pregnant Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China

Shuang Xu,<sup>1</sup> Fei Shao,<sup>2,3</sup> Banghe Bao,<sup>4</sup> Xuedi Ma,<sup>5</sup> Zhouming Xu,<sup>5,6</sup> Jiwen You,<sup>5</sup> Peng Zhao,<sup>5</sup> Yuwei Liu,<sup>5</sup> Michael Ng,<sup>6</sup> Hao Cui,<sup>3</sup> Changxiao Yu,<sup>3</sup> Qing Zhang,<sup>7</sup> Dandan Li,<sup>8</sup> Ziren Tang,<sup>2,3,a</sup> and Peng Sun<sup>1,a</sup>

<sup>1</sup>Department of Emergency Medicine, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, <sup>2</sup>Beijing Key Laboratory of Cardiopulmonary Cerebral Resuscitation, Beijing Chaoyang Hospital, Beijing, China, <sup>3</sup>Department of Emergency Medicine, Beijing Chaoyang Hospital, Capital Medical University, Beijing, China, <sup>4</sup>Department of Hepatobiliary Surgery, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, <sup>5</sup>AI Research Division, A.I. Phoenix Technology Co., Ltd, Hong Kong, China, <sup>6</sup>Research Division for Mathematical and Statistical Science, University of Hong Kong, Hong Kong, China, <sup>7</sup>Department of Anesthesiology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China, <sup>8</sup>Sanquan College Of Xinxiang Medical University, Xinxiang, China

**Background.** Clinical manifestation and neonatal outcomes of pregnant women with coronavirus disease 2019 (COVID-19) were unclear in Wuhan, China.

**Methods.** We retrospectively analyzed clinical characteristics of pregnant and nonpregnant women with COVID-19 aged from 20 to 40, admitted between January 15 and March 15, 2020 at Union Hospital, Wuhan, and symptoms of pregnant women with COVID-19 and compared the clinical characteristics and symptoms to historic data previously reported for H1N1.

**Results.** Among 64 patients, 34 (53.13%) were pregnant, with higher proportion of exposure history (29.41% vs 6.67%) and more pulmonary infiltration on computed tomography test (50% vs 10%) compared to nonpregnant women. Of pregnant patients, 27 (79.41%) completed pregnancy, 5 (14.71%) had natural delivery, 18 (52.94%) had cesarean section, and 4 (11.76%) had abortion; 5 (14.71%) patients were asymptomatic. All 23 newborns had negative reverse-transcription polymerase chain results, and an average 1-minute Apgar score was 8–9 points. Pregnant and nonpregnant patients show differences in symptoms such as fever, expectoration, and fatigue and on laboratory tests such as neutrophils, fibrinogen, D-dimer, and erythrocyte sedimentation rate. Pregnant patients with COVID-19 tend to have more milder symptoms than those with H1N1.

**Conclusions.** Clinical characteristics of pregnant patients with COVID-19 are less serious than nonpregnant. No evidence indicated that pregnant women may have fetal infection through vertical transmission of COVID-19. Pregnant patients with H1N1 had more serious condition than those with COVID-19.

**Keywords.** COVID-19; H1N1; neonatal; pregnancy; vertical transmission.

Coronavirus disease 2019 (COVID-19), caused by infection of the novel coronavirus severe acute respiratory syndrome (SARS-CoV-2), is a new type of respiratory disease that may lead to multiple organ failure and death [1]. Similar to other coronavirus-associated diseases such as SARS and Middle East respiratory syndrome (MERS), COVID-19 is highly infectious and spreads rapidly across the world, posing a severe threaten to global public health [2]. As of June 9, 2020, a total of 7.03

million cases of COVID-19 pneumonia have been diagnosed with over 404 396 deaths worldwide [3].

Results from several influenza studies have shown that the risk of maternal morbidity is significantly increased compared with nonpregnant women [4, 5]. Although COVID-19-associated SAR-CoV-2 could infect pregnant women [6], it has not been found to spread vertically and perinatal transmission is suspected instead. To our knowledge, limited studies have been done on the epidemiology and clinical characteristics of pregnant women with COVID-19 pneumonia, and the transmission route from pregnant women with COVID-19 pneumonia to fetuses remained largely unknown [7–10].

## METHODS

### Study Design

This was a single-centered, retrospective, and observational study in women with COVID-19 pneumonia aged 20–40 years in the west campus of Union Hospital in Wuhan between January 15 and March 15, 2020. All patients were tested for

Received 20 May 2020; editorial decision 28 June 2020; accepted 1 July 2020.

<sup>a</sup>Z. T. and P. S. contributed equally to this work.

Correspondence: Peng Sun, MD, PhD, Department of Emergency Medicine, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology, No. 1277 Jiefang DaDao, Wuhan 430022, Hubei Province, China (simple1111@hust.edu.cn).

### Open Forum Infectious Diseases®

© The Author(s) 2020. Published by Oxford University Press on behalf of Infectious Diseases Society of America. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs licence (<http://creativecommons.org/licenses/by-nc-nd/4.0/>), which permits non-commercial reproduction and distribution of the work, in any medium, provided the original work is not altered or transformed in any way, and that the work is properly cited. For commercial re-use, please contact [journals.permissions@oup.com](mailto:journals.permissions@oup.com)  
DOI: 10.1093/ofid/ofaa283

SARS-CoV-2 nucleic acid and confirmed with COVID-19 pneumonia and discharged based on the “New Coronavirus Pneumonia Prevention and Control Plan” (7th edition) issued by the National Health Commission of China [11]. The discharge criteria are as follows: (1) body temperature returned to normal for more than 3 days; (2) respiratory symptoms were clearly improved; (3) lung images showed a significant improvement in acute exudative lesions; (4) positive nucleic acid tests of respiratory specimens, such as sputum and nasopharyngeal swab test results, in 2 consecutive negative results (sampling interval  $\geq 24$  hours) [11]. We compared the symptoms of the pregnant patients with COVID-19 pneumonia with those of pregnant patients with H1N1 in previous reports. The study was approved by the Ethics Committee Boards of Union Hospital, Tongji Medical College, Huazhong University of Science and Technology and Beijing Chaoyang Hospital, Capital Medical University, and the requirement for informed consent was waived.

### Setting

The west campus of Union hospital, which is a teaching tertiary hospital in Wuhan, was one of the designated hospitals for severe COVID-19 pneumonia. Since January 2020, a total of 800 beds have been converted into isolation wards and opened to severe patients with COVID-19 pneumonia for treatment. All pregnant women are treated in obstetrics and gynecology after admission, the treatments included antibiotic therapy, antiviral therapy, corticosteroids, Chinese medicine treatment, and oxygen support.

### Data Collection

We collected the demographic and clinical characteristics, laboratory tests, chest computed tomography (CT) results, treatment pregnancy outcome, and neonatal outcomes of these patients with COVID-19 pneumonia from an electronic medical record. Routine blood examinations comprised complete blood count, coagulation profile, and serum biochemical tests (including renal and liver function, creatine kinase, and lactate dehydrogenase). Data from H1N1 patients are from a previous study [12].

### Statistical Methods

Continuous variables are expressed by mean  $\pm$  standard deviation or median interquartile range, and categorical variables are expressed by the number and percentage of patients in each category. We stratified patients according to whether they are pregnant. Nonparametric tests are used for continuous variables, and  $\chi^2$  tests are used for categorical variables.  $P < .05$  was considered statistically significant. The odds ratio and 95% confidence interval were accordingly calculated. All analyses were conducted using Python, version 3.6 (Python Software Foundation).

## RESULTS

### Demographic of Pregnant Patients With Coronavirus Disease 2019 Pneumonia

Data were collected from 64 patients, including 34 (53.13%) pregnant women and 30 (46.88%) nonpregnant women of childbearing age. None of the patients had history of exposure to the South China Seafood Wholesale Market or were medical staff. The 34 pregnant patients were mostly aged 30–34 years (47.06%), with  $2.29 \pm 1.56$  mean gestation times and  $0.43 \pm 0.50$  mean parity times. Ten (29.4%) of these patients had a history of contact with family members diagnosed with COVID-19 pneumonia and 5 (14.71%) had asymptomatic infections. Other complications of the pregnant patients include scarred uterus ( $n = 9$ , 26.47%), gestational diabetes ( $n = 2$ , 5.88%), hypothyroidism during pregnancy ( $n = 1$ , 2.94%), and severe pre-eclampsia ( $n = 1$ , 2.94%).

Eight patients (23.53%) were in the first and second trimesters, and 26 patients (76.47%) were in the third trimester. Among them, 5 patients (14.71%) had normal delivery, 18 patients (52.94%) had cesarean section, and 4 patients (11.76%) chose abortion to terminate pregnancy. The mean amount of bleeding during delivery was approximately  $326.47 \pm 50.37$  mL, and the mean amount of amniotic fluid was approximately  $200 \pm 270$  mL. Seven (20.59%) pregnant women chose to use oxytocin, and 3 (8.82%) developed postpartum fever. (Table 1)

### Neonatal Outcomes and Vertical Transmission Potential

All of the 23 newborns of the participants were live births, and no stillbirths, neonatal deaths, nor neonatal asphyxia were observed. All 23 newborns were tested with neonatal pharyngeal swabs and all were negative for COVID-19. Five (21.74%) neonates had premature delivery, 4 (17.39%) had premature rupture of membranes, 1 (4.35%) had fetal distress, and 3 (13.04%) had meconium-stained amniotic fluid. All newborns had an Apgar score of 8–9 in 1 minute (Table 1).

### Clinical Characteristics of Pregnant Women With Coronavirus Disease 2019 (COVID-19) Pneumonia and Nonpregnant Women With COVID-19 Pneumonia

At admission, most patients presented with fever (75.00%) or cough (70.31%). Other symptoms included fatigue (34.38%,  $n = 22$ ), sputum (28.13%,  $n = 18$ ), dyspnea (25.56%,  $n = 17$ ), chest tightness (14.06%,  $n = 9$ ), muscle soreness (10.94%,  $n = 7$ ), nausea or vomiting (10.94%,  $n = 7$ ), abdominal pain (7.81%,  $n = 5$ ), diarrhea (7.81%,  $n = 5$ ), and rash (4.08%,  $n = 2$ ). Fever ( $P = .043$ ), sputum ( $P = .011$ ), and fatigue ( $P = .003$ ) are significantly less common in pregnant patients (64.71%, 64.71%, and 17.65%, respectively) than in nonpregnant patients (86.67%, 76.67%, and 53.33%, respectively).

Regarding the general characteristics, the average age of women is significantly different ( $P < .001$ ) between the pregnant women ( $30 \pm 4.26$  years) and nonpregnant women ( $34.77 \pm 3.71$  years).

**Table 1. Basic Information and Clinical Characteristics of Pregnant Women<sup>a</sup>**

Characteristics	Pregnant Women (n = 34) N (%)
<b>Age (Years)</b>	
<25	3 (8.82)
25–29	11 (3.24)
30–34	16 (47.06)
35–39	3 (8.82)
≥40	1 (2.94)
<b>Gestational weeks of Infection (Weeks)</b>	
>28 weeks	26 (76.47)
≤28 weeks	8 (23.53)
Exposure history	10 (29.40)
<b>Pregnancy Outcome</b>	
Natural delivery	5 (14.71)
Cesarean section	18 (52.94)
Abortion <sup>b</sup>	4 (11.76)
Use of oxytocin	7 (20.59)
Postpartum fever	3 (8.82)
<b>Pregnancy Complications</b>	
Gestational diabetes	2 (5.88)
Pregnancy induced hypertension or pre-eclampsia	1 (2.94)
Hypothyroidism	1 (2.94)
Uterine scarring	9 (26.47)
Preterm birth	5 (14.71)
Premature rupture of membranes	4 (11.76)
Fetal distress	1 (2.94)
Meconium-stained amniotic fluid	3 (8.82)
Neonatal death	0 (0.00)
Severe neonatal asphyxia	0 (0.00)
Newborn COVID-19 nucleic acid test positive	0 (0.00)
Apgar score (1 minutes)	8–9
Pregnancy times	2.29 ± 1.56
Parity times	0.43 ± 0.50
Intraoperative blood loss (mL)	326.47 ± 50.37
Amniotic fluid volume at delivery (mL)	200 ± 270

Abbreviations: COVID-19, coronavirus disease 2019.

<sup>a</sup>Data are mean ± standard, n (%).

<sup>b</sup>These abortions were induced because of the patient's concern about COVID-19.

The time from illness onset to hospital admission of pregnant women ( $9.38 \pm 11.36$  days) was significantly shorter ( $P = .008$ ) than that of nonpregnant patients ( $12.17 \pm 7.35$  days). The number of pregnant women (29.41%) who were infected due to contact with a confirmed family member is significantly higher ( $P = .020$ ) than that of nonpregnant women (6.67%). Of the 64 patients, 4 (12.9%) had influenza B virus, 5 (16.13%) had parainfluenza virus infection, 5 (16.13%) had mycoplasma infection, and 5 (16.13%) had chlamydia infection. All of these were not significantly different between pregnant women and nonpregnant women ( $P > .05$ ) (Table 2).

#### Laboratory Examination

Laboratory test results showed that the mean neutrophil count of pregnant women ( $7.74 \pm 10.79$  g/L) was significantly higher

( $P = .006$ ) than that of nonpregnant women ( $3.85 \pm 3.41$  g/L). In the coagulation system, the mean fibrinogen of pregnant women ( $4.41 \pm 0.67$  g/L) and D-dimer ( $1.37 \pm 1.11$  μg/mL) were also higher ( $P = .001$  and  $P = .003$ ) than that of nonpregnant women ( $3.46 \pm 0.73$  g/L and  $1.79 \pm 2.91$  μg/mL, respectively). Additional laboratory test results with statistically significant difference between pregnant and nonpregnant women include mean erythrocyte sedimentation rate ( $61.41 \pm 18.35$  mm/hour vs  $52.11 \pm 36.08$  mm/hour,  $P = .022$ ), blood urea nitrogen ( $3.27 \pm 1.83$  mmol/L vs  $6.44 \pm 10.99$  mmol/L,  $P = .002$ ), and creatinine ( $47.01 \pm 7.26$  μmol/L vs  $106.15 \pm 204.02$  μmol/L,  $P = .001$ ). (Table 2)

#### Chest Computerized Tomography Image

Based on chest x-ray and CT examinations, the most common imaging feature among all patients is ground-glass shadow. A total of 42 (65.63%) patients developed ground-glass shadow in the lungs. Although there was no significant difference between pregnant and nonpregnant women (55.88% vs 76.67%,  $P = .081$ ), pulmonary infiltration in pregnant women (50%) was significantly more common ( $P = .001$ ) than in nonpregnant women (10%). A total of 15 (23.44%) cases had lung consolidation, with no significant difference ( $P = .079$ ) between pregnant (14.71%) and nonpregnant women (33.33%) (Table 2).

#### Treatment

All patients were treated in quarantine. Thirty (88.24%) pregnant women were treated with antibiotics, similar to the nonpregnant women (80%) ( $P = .365$ ). Nineteen (55.88%) pregnant women were treated with corticosteroids, whereas only 9 (30%) nonpregnant women ( $P = .037$ ) were treated with corticosteroids. A similar percentage of pregnant (44.12%,  $n = 15$ ) and nonpregnant women (50.00%,  $n = 15$ ) had treatment with traditional Chinese medicine ( $P = .638$ ). The ratio of patients who received antiviral therapy was not different between the 2 patient populations ( $P = .104$ ) (Table 2).

#### DISCUSSION

Many emerging viral infections often lead to adverse obstetric outcomes, including maternal morbidity and mortality, mother-to-child transmission of the virus, and perinatal infection and death [2, 13]. In previous studies, researchers showed that coronaviruses associated with SARS and MERS can cause severe adverse pregnancy outcomes, such as miscarriage, premature delivery, intrauterine growth restriction, and maternal death [14]. However, SARS-CoV was not detected in all infants. The clinical outcome of pregnant women with SARS is worse than that of infected women who are not pregnant [7, 14, 15]. In addition, viral infections can lead to premature pregnancy and preterm birth infections with other superimposed microorganisms [16].

**Table 2. Comparison of General Information Between Pregnant Women and Nonpregnant Women**

Variables	Total (n = 64)	Pregnant Women (n = 34)	Nonpregnant Women of Reproductive Age (n = 30)	P Value	OR (95% CI) <sup>a</sup>
<b>Demographics and Clinical Characteristics</b>					
Age, years	32.23 ± 4.65	30 ± 4.26	34.77 ± 3.71	<.001	
Length of hospitalization, days	12.80 ± 8.36	10.62 ± 4.77	15.27 ± 10.68	.025	
Time from illness onset to hospital admission, days	10.69 ± 9.72	9.38 ± 11.36	12.17 ± 7.35	.256	
ICU (%)	1 (1.56)	1 (2.94)	0 (0.00)	.344	Inf (Nah, inf)
Asymptomatic number (%)	5 (7.81)	5 (14.71)	0 (0.00)	.085	Inf (Nah, inf)
Exposure history	12 (18.75)	10 (29.41)	2 (6.67)	.020	5.83 (1.16–29.27)
<b>Comorbidities</b>					
Hypertension	0 (0.00)	0 (0.00)	0 (0.00)		Inf (Nah, inf)
Diabetes	2 (3.13)	2 (5.88)	0 (0.00)	.177	Inf (Nah, inf)
Cardiovascular disease	1 (1.56)	1 (2.94)	0 (0.00)	.344	Inf (Nah, inf)
<b>Signs and Symptoms</b>					
Fever (temperature ≥37.3°C)	48 (75.00)	22 (64.71)	26 (86.67)	.043	0.28 (0.08–1.00)
Cough	45 (70.31)	22 (64.71)	23 (76.67)	.296	0.56 (0.19–1.68)
Fatigue	22 (34.38)	6 (17.65)	16 (53.33)	.003	0.19 (0.06–0.58)
Sputum	18 (28.13)	5 (14.71)	13 (43.33)	.011	0.23 (0.07–0.74)
Dyspnoea	17 (25.56)	7 (20.59)	10 (33.33)	.249	0.52 (0.17–1.60)
Chest tightness	9 (14.06)	3 (8.82)	6 (20.00)	.199	0.39 (0.09–1.71)
Headache	12 (18.75)	5 (14.71)	7 (23.33)	.378	0.57 (0.16–2.02)
Myalgia	7 (10.94)	3 (8.82)	4 (13.33)	.564	0.63 (0.13–3.07)
Nausea or vomiting	7 (10.94)	2 (5.88)	5 (16.67)	.168	0.31 (0.06–1.75)
Abdominal pain	5 (7.81)	3 (8.82)	2 (6.67)	.748	1.35 (0.21–8.71)
Diarrhoea	5 (7.81)	2 (5.88)	3 (10.00)	.540	0.56 (0.09–3.62)
Rash	2 (4.08)	2 (5.88)	0 (0.00)	.177	Inf (Nah, inf)
<b>Laboratory Findings</b>					
Platelet (g/L)	209.27 ± 65.48	199.05 ± 55.87	222.69 ± 76.09	.283	
<100	0 (0.00)	0 (0.00)	0 (0.00)		Inf (Nah, inf)
Monocyte count (g/L)	0.39 ± 0.19	0.40 ± 0.21	0.38 ± 0.21	.987	
Lymphocyte count (g/L)	1.25 ± 0.55	1.24 ± 0.63	1.27 ± 0.47	.604	
<0.8	10 (27.03)	6 (30.00)	4 (23.53)	.659	1.39 (0.35–5.50)
Neutrophil count (g/L)	5.95 ± 8.39	7.74 ± 10.79	3.85 ± 3.41	.006	
White blood cell count (g/L)	6.45 ± 3.42	7.17 ± 3.15	5.57 ± 3.62	.965	
<4	10 (26.32)	2 (9.52)	8 (47.06)		1.00
4–10	22 (57.89)	14 (66.67)	8 (47.06)	.022	0.14 (0.02–0.84)
>10	6 (15.79)	5 (23.81)	1 (5.88)		0.35 (0.03–3.55)
CRP (mg/L)	26.77 ± 32.58	25.07 ± 30.67	28.47 ± 35.09	.871	
FIB (g/L)	4.04 ± 0.83	4.41 ± 0.67	3.46 ± 0.73	.001	
D-dimer (µg/mL)	1.54 ± 2.02	1.37 ± 1.11	1.79 ± 2.91	.033	
≤0.5	10 (29.41)	1 (5.00)	9 (64.29)		1.00
>0.5 to ≤1	10 (29.41)	9 (45.00)	1 (7.14)	<.001	0.01 (0.00–0.23)
>1	14 (41.18)	10 (50.00)	4 (28.57)		3.60 (0.34–38.48)
ESR (mm/h)	58.71 ± 24.52	61.41 ± 18.35	52.11 ± 36.08	.022	
ALT (U/L)	27.43 ± 23.32	23.67 ± 16.81	31.58 ± 28.80	.155	
>40	7 (17.50)	3 (14.29)	4 (21.05)	.574	0.63 (0.13–3.07)
AST (U/L)	31.03 ± 20.35	28.76 ± 12.84	33.53 ± 26.48	.787	
TB (µmol/L)	10.23 ± 3.18	11.14 ± 2.91	9.22 ± 3.22	.560	
BUN (mmol/L)	4.81 ± 7.85	3.27 ± 1.83	6.44 ± 10.99	.002	
Cr (µmol/L)	75.86 ± 143.85	47.01 ± 7.26	106.15 ± 204.02	.001	
>133	1 (2.44)	0 (0.00)	1 (5.00)	.819	0.00 (0.00–NaN)
CK (U/L)	105.19 ± 72.94	94 ± 62.82	118.25 ± 84.17	.382	
>185	4 (15.38)	3 (21.43)	1 (8.33)	.356	2.81 (0.28–28.53)
CK-MB (U/L)	14.5 ± 9.81	12.29 ± 4.81	17.08 ± 13.33	.411	
LDH (U/L)	225.68 ± 111.77	196.76 ± 52.55	257.63 ± 148.14	.194	
>245	10 (25.00)	4 (19.05)	6 (31.58)	.361	0.53 (0.13–2.11)
BNP (pg/mL)	97.21 ± 105.16	119.56 ± 98.91	83.24 ± 113.09	.057	

**Table 2. Continued**

Variables	Total (n = 64)	Pregnant Women (n = 34)	Nonpregnant Women of Reproductive Age (n = 30)	P Value	OR (95% CI) <sup>a</sup>
Influenza B	4 (12.90)	2 (13.33)	2 (12.50)	.945	0.88 (0.12–6.63)
Parainfluenza virus	5 (16.13)	1 (6.67)	4 (25.00)	.166	0.20 (0.02–1.87)
Mycoplasma	5 (16.13)	2 (14.29)	3 (33.33)	.280	0.56 (0.09–3.62)
Chlamydia	5 (16.13)	3 (21.43)	2 (50.00)	.261	1.35 (0.21–8.71)
Imaging Features					
Pulmonary infiltration	20 (31.25)	17 (50.00)	3 (10.00)	.001	9.00 (2.29–35.39)
Ground glass shadow	42 (65.63)	19 (55.88)	23 (76.67)	.081	0.39 (0.13–1.14)
Consolidation	15 (23.44)	5 (14.71)	10 (33.33)	.079	0.34 (0.1–1.16)
Treatments					
Antibiotic therapy <sup>b</sup>	54 (84.38)	30 (88.24)	24 (80.00)	.365	1.88 (0.47–7.41)
Antiviral therapy	38 (59.38)	17 (50.00)	21 (70.00)	.104	0.43 (0.15–1.2)
Corticosteroids	28 (43.75)	19 (55.88)	9 (30.00)	.037	2.96 (1.05–8.31)
Chinese medicine treatment	30 (46.88)	15 (44.12)	15 (50.00)	.638	0.79 (0.29–2.11)
Oxygen support	27 (42.19)	15 (44.12)	12 (40.00)	.739	1.18 (0.44–3.21)

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; BNP, brain natriuretic peptide; CI, confidence interval; CK, creatine kinase; Cr, creatinine; CRP, C-reactive protein concentration; ESR, erythrocyte sedimentation rate; FIB, fibrinogen; ICU, Intensive Care Unit; LDH, lactate dehydrogenase; MB, myocardial band; OR, odds ratio; TB, total bilirubin.

<sup>a</sup>Pregnant women compared to nonpregnant women of reproductive age, and data were adjusted for multiple comparisons.

<sup>b</sup>The antiviral therapies included ribavirin, abidor, oseltamivir. Data are mean ± standard, n (%). P values were calculated by Mann-Whitney U test, or  $\chi^2$  test, as appropriate.

NOTE: The signs and symptoms listed include those reported to occur before admission and during hospitalization. Data were extracted from the medical record and may not reflect complete accounting of symptoms.

This study summarized the relevant data of 64 women of childbearing age with laboratory-confirmed COVID-19 pneumonia. The clinical manifestations of the pregnant women are similar to the nonpregnant adult patients [17]. Moreover, the clinical characteristics of pregnant women with COVID-19 pneumonia are also similar to nonpregnant women. In our study, none of the 34 pregnant women progressed to severe pneumonia or death, indicating that COVID-19 did not cause a significant threat to the mother's life, despite comorbidities observed in some women, some of which were obstetrical in etiology. Note that these comorbidities, including preeclampsia, pregnancy with hypothyroidism, gestational diabetes, and scarred uterus, did not appear to be a risk factor for COVID-19 intrauterine transmission to the fetus [18].

A couple of discrepancies in clinical characteristics were observed between the pregnant and nonpregnant women in our study. On average, pregnant patients were younger than nonpregnant patients. Our data show that the mean age of pregnant versus nonpregnant was 30 versus 35 years old. Because most of the pregnant women had contact with a diagnosed family member, clinicians may be more inclined to test pregnant women. As a result, pregnant women may be more likely to be hospitalized or coexist with mild disease. The length of hospitalization was significantly shorter for the pregnant women. Potential explanations may be as follows: (1) there are pregnant women with asymptomatic infections in the data; (2) the conditions of pregnant women were lighter; and (3) pregnant women recovered faster. The pulmonary infiltration of pregnant women was significantly higher than those of nonpregnant women, probably because of the anatomical and physiological

changes during pregnancy that reduce the body's ability to clear respiratory secretions [18]. The neutrophils of pregnant women were significantly higher than those of nonpregnant women. To avoid the rejection of the fetus, the mother is in a state of immune nonresponse and immune tolerance and is therefore more susceptible to infection by other pathogens [17]. The increase of D-dimer is more common in pregnant women. During pregnancy, the body's fibrinolytic system often changes and is in a physiological hypercoagulable state, but excessive hypercoagulability is prone to thrombosis [19]. Studies have shown that after the development of acute respiratory distress syndrome in patients with COVID-19 pneumonia, the D-dimer of dead patients is significantly higher than that of survivors [20].

We found that patients with COVID-19 pneumonia in the third trimester had negative nucleic acid tests for neonates after natural delivery and cesarean section. Judging from the current domestic and international reports, no cases of vertical transmission from mother to child have been found [9, 21]. A small number of sample reports indicate that newborns may obtain immunoglobulin G antibodies through the placenta and have immunity as soon as they are born [22]. Studies have shown that although the placenta can be infected by viruses, it has a unique ability to prevent the spread of the virus to the fetus [23–25]. An interesting finding is that in those cases in which the placenta was detected as COVID-19, the result was negative [9]. This lack of COVID-19 mother-to-child transmission is consistent with other coronavirus infections (SARS and MERS) that have occurred in pregnant women in the past.

It has been reported that the newborn was diagnosed with COVID-19 pneumonia 30 hours after delivery, indicating that



the virus may be transmitted vertically through intrauterine contact with maternal secretions [26]. There are some reports of neonatal infections because the family members or adults caring for the newborns are infected and have close contact with the newborns. However, there is insufficient evidence to support the presence of COVID-19 in breast milk, but based on SARS experience, breastfeeding is not recommended.

Five early pregnant women in our study chose abortion to terminate pregnancy. Although no infection has been reported in infants born to women with COVID-19 pneumonia, these infants may have a subtle effect due to the presence of COVID-19 pneumonia in their mothers. It is unclear how COVID-19 pneumonia affects the fetus. For example, COVID-19 pneumonia is often associated with fever, which leads to an increased risk of neural tube defects in the first 3 months of pregnancy, and with other adverse neonatal or developmental outcomes in late pregnancy [27, 28]. All patients undergoing cesarean section were suitable for indications of cesarean section [29].

Five of 34 pregnant women (14.71%) had asymptomatic infections in our dataset. In a recent study, a COVID-19 pneumonia census study of pregnant women in 2 hospitals in New York City found that 15.4% of pregnant women were positive for COVID-19. Among them, asymptomatic infections were 7.25 times more than that of patients with COVID-19 pneumonia [22]. Special pathological or physiological changes during the perinatal period and the impact of specialty conditions, especially in the third trimester of pregnancy, often have different degrees of dyspnea. More people are attributed to physiological changes during pregnancy, so pneumonia is easily overlooked, which increases the difficulty of diagnosing COVID-19 pneumonia in pregnancy. This may also be the reason for the higher incidence of asymptomatic infections among pregnant women. At the same time, changes in blood stasis and water and sodium retention in body organs may partially limit the spread of infection, resulting in atypical symptoms after infection, resulting in a continuous latent state of infection and hidden infection [30]. Therefore, during a pandemic, we need to focus on the risk of COVID-19 pneumonia in asymptomatic pregnant women.

In this study, we also compared the clinical characteristics between pregnant women with COVID-19 pneumonia and H1N1. Acute respiratory infection is always the first manifestation of these 2 respiratory infections [31]. Among the large number of pregnant women and postpartum patients who were hospitalized or died due to H1N1 flu in 2009, almost one fifth required intensive care [32], and the flu has postpartum symptom onset, including serious complications and death. This fact highlights the continued high risk after pregnancy [33]. Because of the different therapies, prognoses, and protective measures, it is necessary to distinguish these 2 diseases through early clinical manifestations. Our research shows that fever, fatigue, and dry cough are the most common symptoms of pregnant women with COVID-19 pneumonia. However, in addition to fever and

cough, H1N1 patients also often have runny noses (Supplement 1). Therefore, we speculate that the condition of pregnant women with H1N1 infection seems to be more severe than that of pregnant women with COVID-19 pneumonia.

However, there is currently no clear treatment for COVID-19 infection during pregnancy [34]. Our data show that only 50% of patients used antiviral therapy during hospitalization, including ribavirin, abidor, oseltamivir, etc. In some cases, pregnant women may ask to avoid antiviral therapy during pregnancy [35], and thus the initiation of antiviral therapy seems to be delayed. As with most medicines, there is little information on the safety and effectiveness of these antiviral drugs during pregnancy [36–39]. Communication information for pregnant women and their healthcare providers should include information about the benefits and risks of flu medicines as well as information about the increased risk of influenza complications among pregnant women.

Therefore, it is important to construct a management plan for pregnancy combined with COVID-19 pneumonia to ensure the health and safety of pregnant women. In addition, it must be remembered that as the development of the COVID-19 vaccine progresses, consideration should be given to the inclusion of pregnant women in clinical trials, as well as the eventual vaccine distribution, unless the risks outweigh the potential benefits [40].

This study had some limitations. First, patient number is relatively small, which limits the possible conclusions. Second, the incidence, infection rate, and virulence of COVID-19 may be different at different locations and stages of the pandemic. Third, this is a single-center study and the results may not be applicable to other settings and healthcare systems.

## CONCLUSIONS

The clinical characteristics of pregnant women with COVID-19 pneumonia are less serious than those of nonpregnant women with COVID-19 pneumonia. According to our research, there is no evidence to indicate that pregnant women can cause fetal infection through vertical transmission, currently. The condition of pregnant women infected with H1N1 seems to be more serious than that of pregnant women infected with COVID-19 pneumonia.

## Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

## Acknowledgments

We thank the following colleagues who collected and calculated medical information of the patients in this study: Hui Qiu, Xinyu Wan, Hongmei Gao, and Shan Huang. We thank the patients and their families for making this study possible. We are very grateful to other colleagues at A.I. Phoenix

Technology Co., Ltd (Jiayou Lyu, Shihao Wang, and Yunfei Tang) who have made great contributions in the process of data cleaning and analytics.

**Disclaimer.** The funding source was not involved in the study design, collection, analysis, and data interpretation, or manuscript submission for publication.

**Financial support.** This study was funded by the National Nature Science Foundation of China (No. 81571866).

**Potential conflicts of interest.** All authors: no reported conflicts of interest. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest.

## References

- World Health Organization. Naming the coronavirus disease (COVID-19) and the virus that causes it. Available at: [https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-\(covid-2019\)-and-the-virus-that-causes-it](https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it). Accessed 11 February 2020.
- Schwartz DA. An analysis of 38 pregnant women with COVID-19, their newborn infants, and maternal-fetal transmission of SARS-CoV-2: maternal Coronavirus infections and pregnancy outcomes. *Arch Pathol Lab Med* 2020. doi:10.5858/arpa.2020-0901-SA.
- World Health Organization. Novel coronavirus (2019-nCoV) situation reports. Available at: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports/>. Accessed 15 April 2020.
- Silasi M, Cardenas I, Kwon JY, et al. Viral infections during pregnancy. *Am J Reprod Immunol* 2015; 73:199–213.
- Rasmussen SA, Jamieson DJ, Uyeki TM. Effects of influenza on pregnant women and infants. *Am J Obstet Gynecol* 2012; 207:S3–8.
- Fan C, Lei D, Fang C, et al. Perinatal transmission of COVID-19 associated SARS-CoV-2: should we worry? *Clin Infect Dis* 2020. doi:10.1093/cid/ciaa226.
- Schwartz DA, Graham AL. Potential maternal and infant outcomes from (Wuhan) coronavirus 2019-nCoV infecting pregnant women: lessons from SARS, MERS, and other human coronavirus infections. *Viruses* 2020; 12:194.
- Qiao J. What are the risks of COVID-19 infection in pregnant women? *Lancet* 2020; 395:760–2.
- Chen H, Guo J, Wang C, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet* 2020; 395:809–15.
- Schwartz DA. COVID-19, SARS-CoV-2 and pregnancy: does the past predict the present? Available at: <https://www.contagionlive.com/news/covid19-sarscov2-and-pregnancy-does-the-past-predict-the-present>. Accessed 28 February 2020.
- China NHCPsRo. New diagnosis and treatment scheme for novel coronavirus infected pneumonia (Trial edition 7). Available at: <http://www.nhc.gov.cn/yzygj/s7653p/202003/46c9294a7dfe4cef80dc7f5912eb1989/files/ce3e6945832a438eae415350a8ce964.pdf>. Accessed 4 March 2020.
- Jamieson DJ, Honein MA, Rasmussen SA, et al.; Novel Influenza A (H1N1) Pregnancy Working Group. H1N1 2009 influenza virus infection during pregnancy in the USA. *Lancet* 2009; 374:451–8.
- Song Z, Xu Y, Bao L, et al. From SARS to MERS, thrusting coronaviruses into the spotlight. *Viruses* 2019; 11:59.
- Wong SF, Chow KM, Leung TN, et al. Pregnancy and perinatal outcomes of women with severe acute respiratory syndrome. *Am J Obstet Gynecol* 2004; 191:292–7.
- Maxwell C, McGeer A, Tai KFY, Sermer M. No. 225-management guidelines for obstetric patients and neonates born to mothers with suspected or probable Severe Acute Respiratory Syndrome (SARS). *J Obstet Gynaecol Can* 2017; 39:e130–7.
- Kwon JY, Romero R, Mor G. New insights into the relationship between viral infection and pregnancy complications. *Am J Reprod Immunol* 2014; 71:387–90.
- Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020. doi:10.1001/jama.2020.1585.
- Xinghua H. [Pregnancy with pneumonia]. *Zhonghua Fu Chan Ke Za Zhi* 1997; 32:61–3.
- Réger B, Péterfalvi A, Litter I, et al. Challenges in the evaluation of D-dimer and fibrinogen levels in pregnant women. *Thromb Res* 2013; 131:e183–7.
- Arachchillage DRJ, Laffan M. Abnormal coagulation parameters are associated with poor prognosis in patients with novel coronavirus pneumonia. *J Thromb Haemost* 2020; 18:1233–4.
- Chen S, Liao E, Cao D, Gao Y, Sun G, Shao Y. Clinical analysis of pregnant women with 2019 novel coronavirus pneumonia. *J Med Virol* 2020. doi:10.1002/jmv.25789.
- Sutton D, Fuchs K, D'Alton M, Goffman D. Universal screening for SARS-CoV-2 in women admitted for delivery. *N Engl J Med* 2020; 382:2163–4.
- Bayer A, Delorme-Axford E, Sleigher C, et al. Human trophoblasts confer resistance to viruses implicated in perinatal infection. *Am J Obstet Gynecol* 2015; 212:71.e1–8.
- Romero R, Espinoza J, Gonçalves LF, et al. The role of inflammation and infection in preterm birth. *Semin Reprod Med* 2007; 25:21–39.
- Cardenas I, Mor G, Aldo P, et al. Placental viral infection sensitizes to endotoxin-induced pre-term labor: a double hit hypothesis. *Am J Reprod Immunol* 2011; 65:110–7.
- Yu N, Li W, Kang Q, et al. Clinical features and obstetric and neonatal outcomes of pregnant patients with COVID-19 in Wuhan, China: a retrospective, single-centre, descriptive study. *Lancet Infect Dis* 2020; 20:559–64.
- Jordan DN, Jordan JL. Association of maternal fever during labor with neonatal and infant morbidity and mortality. *Obstet Gynecol* 2001; 98:1152–4.
- Grether JK, Nelson KB. [Maternal infection and cerebral palsy in infants of normal birth weight. *JAMA* 1997; 278:207–11.
- Weiyuan Zhang, YY. Expert consensus on cesarean section (in Chinese). *Chin J Obstet Gynecol* 2014; 49:721–4.
- Zhang L, Jiang Y, Wei M, et al. [Analysis of the pregnancy outcomes in pregnant women with COVID-19 in Hubei Province]. *Zhonghua Fu Chan Ke Za Zhi* 2020; 55:166–71.
- Tang X, Du R, Wang R, et al. Comparison of hospitalized patients with ARDS caused by COVID-19 and H1N1. *Chest* 2020; 158:195–205.
- Louie JK, Acosta M, Jamieson DJ, Honein MA; California Pandemic (H1N1) Working Group. Severe 2009 H1N1 influenza in pregnant and postpartum women in California. *N Engl J Med* 2010; 362:27–35.
- ANZIC Influenza Investigators and Australasian Maternity Outcomes Surveillance System. Critical illness due to 2009 A/H1N1 influenza in pregnant and postpartum women: population based cohort study. *BMJ* 2010; 340:c1279.
- Favre G, Pomar L, Qi X, et al. Guidelines for pregnant women with suspected SARS-CoV-2 infection. *Lancet Infect Dis* 2020; 20:652–3.
- Rasmussen SA, Jamieson DJ, Macfarlane K, et al.; Pandemic Influenza and Pregnancy Working Group. Pandemic influenza and pregnant women: summary of a meeting of experts. *Am J Public Health* 2009; 99:S248–54.
- Cono J, Cragan JD, Jamieson DJ, Rasmussen SA. Prophylaxis and treatment of pregnant women for emerging infections and bioterrorism emergencies. *Emerg Infect Dis* 2006; 12:1631–7.
- Tanaka T, Nakajima K, Murashima A, et al. Safety of neuraminidase inhibitors against novel influenza A (H1N1) in pregnant and breastfeeding women. *CMAJ* 2009; 181:55–8.
- Freund B, Gravenstein S, Elliott M, Miller I. Zanamivir: a review of clinical safety. *Drug Saf* 1999; 21:267–81.
- Ward P, Small I, Smith J, et al. Oseltamivir (Tamiflu) and its potential for use in the event of an influenza pandemic. *J Antimicrob Chemother* 2005; 55:5–21.
- Krubiner CFR, Karron RA. In the race for Coronavirus vaccines, don't leave pregnant women behind. Available at: <https://www.statnews.com/2020/02/25/coronavirus-vaccine-covid-19-pregnant-women/>. Accessed 25 February 2020.