


One-year follow-up of 18 women who infected COVID-19 while pregnant

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Abstract

Data about the sequelae of women who infected COVID-19 while pregnant are scarce. We aimed to describe the prevalence of symptoms, pulmonary functions, and radiological changes at a follow-up of 12 months in 18 pregnant women who developed COVID-19 at different gestational ages. Our results showed that most women who infected COVID-19 while pregnant experienced a progressive improvement of their symptoms within 12 months, however, some still had little COVID-related symptoms but without a reduced quality of life. All their 18 newborns were growing up healthy.

KEYWORDS

coronavirus, psychology, SARS coronavirus, social science, virus classification

1 | INTRODUCTION

During the pandemic of COVID-19 in Wuhan, China, thousands of patients were infected by SARS-Cov-2 with different severity.¹ Of the infected cases, a small percentage were pregnant women of different gestational ages.² Studies have reported the maternal and perinatal features and adverse outcomes in pregnant women with symptomatic COVID-19 during the acute phase.²⁻⁵ However, no study has described the symptoms and sequelae during the recovery of women infected with SARS-CoV-2 while pregnant. In this prospective study, we aimed to describe the physiological and psychological outcomes at 12 months after recovery in a cohort of pregnant women with COVID-19.

2 | METHODS

During the whole pandemic of COVID-19 in Wuhan from January 7, 2020 to April 26, 2020, a total of 34 consecutive pregnant women with laboratory-confirmed symptomatic COVID-19 were hospitalized at Renmin Hospital of Wuhan University in China. Their diagnosis and disease severity conformed to the *Guidelines on the Diagnosis and Treatment of Novel Coronavirus Infected Pneumonia (Trial 7th edition)*.⁶ Of those, 6 were in the second trimester of pregnancy and the other 28 were in the third trimester. We followed up with them 12 months after recovery. The study flowchart is shown in Figure S1. Of them, four refused to answer the telephone call, two lost contact, eight declined to participate, and two did not arrange a time for follow-up.

Eventually, 18 females agreed to participate and completed the study. The study protocol was reviewed and approved by the Ethics Committee of the Renmin Hospital of Wuhan University (No. WDRY2020-K019) and all participants provided written informed consent.

At the first interview, each participant completed a comprehensive questionnaire including demographics, current comorbidities, respiratory and neurological symptoms, and psychological manifestations. Then they were scheduled for analysis of peripheral blood and antibodies for SARS-CoV-2, and for chest CT scans and lung function tests. We also retrospectively collected each pregnant woman's medical information during the hospitalization from the clinical electronic medical record system. Each patient's physical performance was assessed by the modified British Medical Research Council Dyspnoea Scale.⁷ The Insomnia Severity Index has evaluated the risk of insomnia and the Hospital Anxiety and Depression Scale⁸ has assessed the symptom severity of anxiety and depression.

All data were analyzed using SPSS version 25.0 statistical software (IBM Statistics). The medians and interquartile ranges (IQRs) were estimated for quantitative variables with nonnormal distributions, while absolute values and relative frequencies (%) were used for qualitative variables. Statistical comparisons were performed using the χ^2 test, Fisher's exact test, or one-way analysis of variance. A $p < 0.05$ was considered statistically significant.

3 | RESULTS

The main clinical characteristics associated with COVID-19 of the 18 study participants during the acute phase and at follow-up 12 months after COVID-19 are listed in Table 1. For severity during the acute infection, 18 patients with laboratory-confirmed COVID-19 were classified as mild ($n = 3$) or moderate ($n = 15$). Fever, cough, chest tightness, and dyspnea were the most commonly reported symptoms during the acute phase. Myalgia, arthralgia, ageusia, or anosmia were present in some patients. One year later, most of the respiratory symptoms had resolved, although chest tightness, myalgia, arthralgia, anosmia, and/or insomnia occurred in different individual patients (Table 1). For psychological symptoms, insomnia was reported in 27.8% of the cohort during the acute phase and in 11.1% during convalescence; 33.3% of this cohort reported an increased score on the Hospital Anxiety and Depression Scale during the acute phase, and 22.2% during convalescence.

During the follow-up at 12 months, this cohort showed normal spirometer tests. The diffusion lung carbon monoxide (DLCO; reflecting alveolar function) was less than 80% predicted in two cases (74% and 69%, respectively) but more severe impairment (<60%) was not observed (Table 1 and Table S1). Abnormal CT findings were found in 83.3% of cases during the acute phase and in 38.9% of cases at follow-up (Table 2). The predominant findings during the acute phase were ground-glass opacity,

consolidation, interlobular thickening, and reticular lesions. The main abnormalities at follow-up were mixed nodules with a diameter of 2–4 mm (27.8%), stripe fibrotic lesions (22.2%), and small ground-glass opacities (5.6%) (Figure S2). At follow-up, none had asymptomatic reinfection, and vaccination had not been recommended for them. All 18 mothers tested negative for nucleic acid at nasopharyngeal swabs, and they had high titers of specific serum IgG [37.25 (7.36–87.17) AU/ml, median (IQR)] but all were negative for serum IgM. All children at 1 year are growing up healthy.

4 | DISCUSSION

In this cohort study, we found that a proportion of pregnant women with COVID-19 experienced respiratory symptoms and some of them had psychological consequences 12 months after their hospital discharge. DLCO reduction has been reported as the most common functional alteration in patients with COVID-19 after hospital discharge,^{9,10} however, two individuals in this cohort had DLCO less than 80% of predicted at the follow-up of 12 months. COVID-19 has the possibility of sequelae of pulmonary fibrosis,¹⁰ but our 1-year follow-up in this group did not find that they had obvious pulmonary fibrosis on CT. Although abnormal findings were found in 38.9% of this cohort at follow-up, the predominant findings were mixed nodules with a diameter of 2–4 mm and stripe fibrotic lesions. These slight residual imaging findings did not cause the respiratory symptoms, nor did they weaken the lung physiology. No individual was observed to have impaired physical performances (the modified British Medical Research Council Dyspnoea Scale, 6-min walking test, and arterial blood gas). These findings suggest that COVID-19 patients during pregnancy do not have obvious physical sequelae on chest CT scans, which may be related to their milder illness in the acute phase. With regard to psychological health, it has been reported that approximately 20% of survivors of COVID-19 developed posttraumatic stress disorder.¹¹ In our study, clinically relevant symptoms of insomnia, depressive and anxious presentations were observed in 33.3% of the patients, which is consistent with other studies.¹¹

In short, most pregnant women hospitalized with COVID-19 had almost a complete recovery from their disease within 12 months, although a proportion of them still had some COVID-related symptoms but without a reduced quality of life, which suggests that most pregnant women who developed COVID-19 experienced a progressive improvement of their symptoms over time. However, there are some limitations in this cohort study: single-center, small sample size, no severe case, and without 24 h continuous blood pressure monitoring. Studies have reported that COVID-19 during pregnancy was strongly associated with high rates of maternal mortality, preeclampsia, and preterm birth,^{4,5} however, no similar findings were in this data. Therefore, our findings have to be confirmed in subsequent studies, with larger sample size and a longer follow-up.

TABLE 1 Demographics, DLCO, and clinical characteristics of pregnant women during the acute infection and 12 months after COVID-19 [median (IQR) or *n*]

Parameters (normal range)	Acute phase (<i>n</i> = 18)	At follow-up (<i>n</i> = 18)	<i>p</i> Value
Demographics			
Age (years)	31.5 (29.25–33.75)	32.5 (30.25–34.75)	0.439
Height (cm)	ND	161 (156.75–163)	NA
Weight (kg)	ND	56 (54.25–59.5)	NA
BMI (kg/m ²)	ND	22.47 (20.73–23.64)	NA
Symptom			
Fever ($T \geq 37.3^{\circ}\text{C}$, <i>n</i>)	16	0	0.000
T_{max} ($^{\circ}\text{C}$)	38.1 (37.6–39.1)	ND	NA
Cough (<i>n</i>)	13	0	0.000
Expectoration (<i>n</i>)	4	0	0.104
Chest tightness (<i>n</i>)	6	1	0.088
Dyspnea (<i>n</i>)	5	0	0.045
Myalgia (<i>n</i>)	4	1	0.338
Arthralgia (<i>n</i>)	1	1	1.000
Ageusia (<i>n</i>)	2	0	0.486
Anosmia (<i>n</i>)	3	1	0.603
Diarrhea (<i>n</i>)	2	0	0.486
Sore throat (<i>n</i>)	3	0	0.229
mMRC	ND	0.5 (0–1)	NA
Comorbidity			
Gestational hypertension, <i>n</i>	3	0	0.229
Diabetes, <i>n</i>	2	0	0.486
Thyroid disease, <i>n</i>	1	1	1.000
Chronic kidney disease, <i>n</i>	1	1	1.000
ISI score (range 0–28)	8.5 (4.75–16)	7.5 (4–10)	0.317
Insomnia (ISI score >15), <i>n</i>	5	2	0.402
HDAS, points	6.5 (4–8.25)	5 (3–7.25)	0.197
Anxiety/depression (HAS or HDS ≥ 8), <i>n</i>	6	4	0.457
Smoking status			
Never, <i>n</i>	18	18	1.000
Disease severity			
Mild, <i>n</i>	3	ND	NA
Moderate, <i>n</i>	15	ND	NA
Severe, <i>n</i>	0	ND	NA
Laboratory result			
WBC ($3.5\text{--}9.5 \times 10^9/\text{L}$)	4.82 (3.80–6.25)	5.26 (3.72–6.53)	0.136
N ($1.8\text{--}6.3 \times 10^9/\text{L}$)	2.78 (2.18–3.81)	2.57 (2.12–3.79)	0.723
L ($1.1\text{--}3.2 \times 10^9/\text{L}$)	1.12 (0.76–1.62)	1.51 (1.12–2.83)	0.081
Hemoglobin (130–175 g/L)	115 (103–129)	118.3 (104.6–125.8)	0.546
Platelet count ($125\text{--}350 \times 10^9/\text{L}$)	178 (164–223)	167.1 (126.5–227.6)	0.221

TABLE 1 (Continued)

Parameters (normal range)	Acute phase (n = 18)	At follow-up (n = 18)	p Value
CRP (0–10 mg/L)	21.6 (6.5–67.6)	2.8 (1.1–8.3)	0.002
Albumin (40–55 g/L)	36.4 (32.6–40.8)	41.0 (38.8–42.6)	0.021
ALT (9–50 U/L)	35 (18–67)	27 (20.0–33.5)	0.163
AST (15–40 U/L)	32 (22–43)	31 (27.5–38.0)	0.623
Alkaline phosphatase (45–125 U/L)	66 (52–96)	59.5 (51.00–70.75)	0.205
Urea (3.6–9.5 mmol/L)	4.9 (3.52–8.10)	4.17 (3.52–5.46)	0.332
Creatinine (57–111 μmol/L)	56 (43–78)	57.0 (48.0–75.0)	0.515
Creatine kinase (18–198 U/L)	59 (42.75–121)	ND	NA
LDH (120–250 U/L)	124 (91–203)	ND	NA
Ultra-TnI (0–0.04 ng/ml)	0.006 (0.006–0.01)	ND	NA
D-dimer (0–0.55 mg/L)	0.62 (0.42–2.12)	ND	NA
Fibrinogen (2–4 g/dl)	2.63 (2.24–3.72)	ND	NA
Prothrombin time (9–13 s)	11.6 (11.3–12.4)	ND	NA
APTT (25–31.3 s)	28.2 (25.7–30.3)	ND	NA
IL-2 (≤11.4 pg/ml)	3.62 (3.41–4.12)	ND	NA
IL-4 (≤12.9 pg/ml)	3.45 (2.76–4.15)	ND	NA
IL-6 (≤20.0 pg/ml)	6.17 (4.92–15.32)	ND	NA
IL-10 (≤5.9 pg/ml)	5.87 (4.54–7.32)	ND	NA
TNF (≤5.5 pg/ml)	3.64 (2.89–5.23)	ND	NA
Interferon-γ (≤18 pg/ml)	3.52 (3.02–4.26)	ND	NA
Duration of viral shedding, day	27 (21.75–33)	ND	NA
Length of hospital stay, day	10 (7–14.75)	ND	NA
Days in ICU, day	0	ND	NA
Virology			
Positive for SARS-COV-2 nucleic acid, n	18	0	1.000
IgM for SARS-CoV-2 (<10 AU/ml)	25.6 (16.3–79.7)	1.65 (0.36–3.52)	0.001
IgG for SARS-CoV-2 (<10 AU/ml)	136.8 (66.4–182.2)	37.25 (7.36–87.17)	0.003
DLCO			
DLCO, (%) predicted	ND	92 (85.75–99.75)	NA
DLCO < 80%, (n)	ND	2	NA
Alveolar ventilation (VA), L	ND	4.45 (4.24–4.83)	NA
DLCO/VA, (%) predicted	ND	97 (90.25–111.75)	NA
Newborns			
Height (cm)	ND	76.25 (72.75–80)	NA
Weight (kg)	3.47 (3.26–3.76)	10.1 (9.80–10.625)	0.003
Positive SARS-COV-2 nucleic acid, n	0	ND	NA
IgM for SARS-CoV-2 (<10 AU/ml)	Negative	ND	NA
IgG for SARS-CoV-2 (<10 AU/ml)	Negative	ND	NA

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; CRP, C-reactive protein; DLCO, diffusing capacity of the lung for carbon monoxide; HAS, Hospital Anxiety Scale; HDS, Hospital Depression Scale; IL, interleukin; IQR, interquartile range; ISI, Insomnia Severity Index; HADS, Hospital Anxiety and Depression Scale; L, lymphocyte count; LDH, lactate dehydrogenase; mMRC, the modified British Medical Research Council Dyspnoea Scale; N, neutrophil count; NA, not available; ND, no data; Tmax, maximum body temperature; TNF, tumor necrosis factor; Ultra-TnI, ultra troponin I; WBC, white blood cell count;

TABLE 2 CT imaging findings of pregnant women during the acute infection and 12 months after COVID-19 [median (IQR) or n (%)]

Parameters	Acute phase (n = 18)	At follow-up (n = 18)	p Value
Abnormal CT, n (%)	15 (83.3)	7 (38.9)	0.006
Ground-glass opacity, n (%)	12 (66.7)	1 (5.6)	0.000
Stripe fibrotic lesion, n (%)	0 (0)	4 (22.2)	0.104
Consolidation, n (%)	10 (55.6)	0 (0)	0.000
Interlobular thickening, n (%)	5 (27.8)	0 (0)	0.045
Mixed nodule, n (%)	0 (0)	5 (27.8)	0.045
Reticular lesion, n (%)	3 (16.7)	0 (0)	0.229

Abbreviations: IQR, interquartile range.

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CONFLICT OF INTERESTS

The authors declare no conflict of interest.

AUTHOR CONTRIBUTIONS

Yunyan Xianyu, Mengmei Wang, Fang Yue, Xiaoyu Xu, and Haizhen Yang were responsible for enrollment and follow-up, collection of clinical data. Dong Zhao was responsible for statistical data. Yunyan Xianyu and Mengmei Wang drafted the manuscript. Ke Hu was responsible for study conception, funding, revising, and submitting manuscript.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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