

Pregnancy and Perinatal Outcomes of Women With Coronavirus Disease (COVID-19) Pneumonia: A Preliminary Analysis

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OBJECTIVE. The purpose of this study was to describe the clinical manifestations and CT features of coronavirus disease (COVID-19) pneumonia in 15 pregnant women and to provide some initial evidence that can be used for guiding treatment of pregnant women with COVID-19 pneumonia.

MATERIALS AND METHODS. We reviewed the clinical data and CT examinations of 15 consecutive pregnant women with COVID-19 pneumonia in our hospital from January 20, 2020, to February 10, 2020. A semiquantitative CT scoring system was used to estimate pulmonary involvement and the time course of changes on chest CT. Symptoms and laboratory results were analyzed, treatment experiences were summarized, and clinical outcomes were tracked.

RESULTS. Eleven patients had successful delivery (10 cesarean deliveries and one vaginal delivery) during the study period, and four patients were still pregnant (three in the second trimester and one in the third trimester) at the end of the study period. No cases of neonatal asphyxia, neonatal death, stillbirth, or abortion were reported. The most common early finding on chest CT was ground-glass opacity (GGO). With disease progression, crazy paving pattern and consolidations were seen on CT. The abnormalities showed absorptive changes at the end of the study period for all patients. The most common onset symptoms of COVID-19 pneumonia in pregnant women were fever (13/15 patients) and cough (9/15 patients). The most common abnormal laboratory finding was lymphocytopenia (12/15 patients). CT images obtained before and after delivery showed no signs of pneumonia aggravation after delivery. The four patients who were still pregnant at the end of the study period were not treated with antiviral drugs but had achieved good recovery.

CONCLUSION. Pregnancy and childbirth did not aggravate the course of symptoms or CT features of COVID-19 pneumonia. All the cases of COVID-19 pneumonia in the pregnant women in our study were the mild type. All the women in this study—some of whom did not receive antiviral drugs—achieved good recovery from COVID-19 pneumonia.

Since the outbreak of coronavirus disease (COVID-19) pneumonia in Wuhan, China, the World Health Organization (WHO) has declared COVID-19 a public health emergency of international concern [1]. It is reported that the homology between the genome of the virus that causes COVID-19 pneumonia, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and human severe acute respiratory syndrome coronavirus (SARS-CoV) is 82% [2]. Despite extensive studies on the CT and clinical manifestations of patients with COVID-19 pneumonia and treatment monitoring, studies of pregnant women with COVID-19 pneumonia remains relatively rare. It is not clear whether clinical characteristics of pregnant women with COVID-19 pneumo-

nia differ from those of nonpregnant women with COVID-19 pneumonia and pregnant women with SARS-CoV, whether pregnancy and childbirth aggravate COVID-19 pneumonia symptoms, and whether antiviral therapy is necessary for pregnant women with COVID-19 pneumonia. The purpose of this study was to describe the clinical manifestations and CT features of 15 pregnant women with COVID-19 pneumonia, monitor for changes before and after delivery, and provide some initial evidence for guiding the treatment of pregnant women with COVID-19 pneumonia.

Materials and Methods

Study Design and Patients

Our hospital is a designated hospital for pregnant women with COVID-19 pneumonia. We re-

viewed the clinical data and CT examinations of 15 consecutive pregnant women with COVID-19 pneumonia who were seen in our hospital from January 20, 2020, to February 10, 2020. The diagnosis and treatment of COVID-19 pneumonia were based on the diagnosis and treatment protocols for pneumonia caused by a novel coronavirus (later identified as SARS-CoV-2) published by the National Health Commission of the People's Republic of China (trial version 5) [3]. The clinical triage was carried out according to WHO guidelines [4]. After quantitative, counting, and semiquantitative analyses, the data were independently reviewed by two experienced radiologists with associate senior titles to verify the accuracy of the data.

This study was approved by the Ethics Committee of Union Hospital, Tongji Medical College, Huazhong University of Science and Technology. Informed consent for this retrospective study was waived.

CT Protocol and Chest CT Evaluation

Before undergoing chest CT examinations, pregnant women with COVID-19 pneumonia signed an informed consent, were instructed on breath-holding, and had their lower abdomen and pelvis covered with a lead blanket.

CT was performed on a commercial MDCT scanner (Ingenuity Core 128, Philips Healthcare) using the low-dose mode. For CT acquisition, the tube voltage was 120 kVp with automatic tube current modulation. From the raw data, CT images

were reconstructed with a matrix size of 512×512 as axial images (thickness of 1.5 mm and increment of 1.5 mm) using the hybrid iterative reconstruction algorithm (iDose5, Philips Healthcare). The mean volume CT dose index ($CTDI_{vol}$) was 4.1 ± 0.9 (SD) mGy (range, 2.3–5.8 mGy).

A semiquantitative CT scoring system was used to estimate pulmonary involvement of all abnormalities on the basis of the area involved. Each of the five lung lobes was visually scored from 0 to 5 as follows: 0, no involvement; 1, less than 5% involvement; 2, 25% involvement; 3, 26–49% involvement; 4, 50–75% involvement; or 5, more than 75% involvement. The total CT score was the sum of the five individual lobar scores and ranged from 0 (no involvement) to 25 (maximum involvement) [5]. Disease progression as revealed on the CT images was divided into four stages, as described by Pan et al. [6]: early stage (stage 1), progressive stage (stage 2), peak stage (stage 3), and absorption stage (stage 4).

Image analysis was performed using the institutional digital database system (Vue PACS, version 11.3.5.8902, Carestream Health) by three radiologists who had 26, 25, and 22 years of experience in thoracic radiology, respectively, at the time of the study. Final scores were determined by consensus.

Statistical Analysis

Statistical analysis was performed using SPSS software (version 20.0, IBM). Continuous vari-

ables are directly expressed as ranges, and categorical variables are expressed as numbers and percentages. Quantitative data are presented as mean \pm SD (minimum value–maximum value).

Results

All 15 pregnant women with COVID-19 pneumonia had a positive quantitative reverse transcription–polymerase chain reaction (RT-PCR) result for SARS-CoV-2 at the time of admission and a diagnosis of mild pneumonia. At the time of admission, the 15 women ranged in age from 23 to 40 years old, and gestational week ranged from 12 to 38 weeks (Table 1). One patient (patient 1 in Table 2) had thalassemia and gestational diabetes, patient 10 had mitral valve and tricuspid valve replacement 10 years earlier, and patient 11 had complete placenta previa. Among the 15 patients, 13 had fever with temperature of 37.6 – 39.0°C that started 2–10 days before admission. In addition, nine patients had cough; four patients, fatigue; three patients, muscle ache; one patient, dyspnea; one patient, sore throat; and one patient, diarrhea. Two patients had no clinical symptoms of COVID-19 pneumonia, so the onset time was not recognizable. One patient (patient 9 in Table 1) had postpartum fever, with highest temperature of 38.5°C , which improved 1 day after delivery. There were 12 patients with decreased

TABLE 1: Clinical and Laboratory Characteristics, Treatments, and Outcomes of 15 Pregnant Women With Coronavirus Disease (COVID-19)

Characteristic	All Patients (n = 15)	Patients Who Delivered Before End of Study Period (n = 11)	Patients Who Were Still Pregnant at End of Study Period (n = 4)
Clinical characteristics			
Age (y), range (mean \pm SD)	23–40 (32 \pm 5)	23–40 (32 \pm 5)	29–40 (34 \pm 5)
Gestational week at admission, range (mean \pm SD)	12–38 (32 \pm 8)	34–38 (37 \pm 1)	12–32 (21 \pm 8)
Time interval between symptom onset and admission (d), range	2–10	2–10	9–10
No. of patients with other conditions ^a	2	2	0
No. of patients with a history of surgery ^b	1	1	0
Symptoms of COVID-19, no. of patients			
Fever at admission (range of temperatures)	13 (37.6–39.0°C)	9 (37.6–39.0°C)	4 (37.8–38.8°C)
Fever postpartum (temperature)	1	1 (38.5°C)	NA
Cough	9	6	3
Sore throat	1	1	0
Dyspnea	1	0	1
Myalgia	3	3	0
Fatigue	4	3	1
Diarrhea	1	1	0

(Table 1 continues on next page)

Pregnancy and Perinatal Outcomes of Women With COVID-19

TABLE 1: Clinical and Laboratory Characteristics, Treatments, and Outcomes of 15 Pregnant Women With Coronavirus Disease (COVID-19) (continued)

Characteristic	All Patients (n = 15)	Patients Who Delivered Before End of Study Period (n = 11)	Patients Who Were Still Pregnant at End of Study Period (n = 4)
Laboratory characteristics			
Lymphopenia, no. of patients			
Before treatment	12	9	3
After treatment	0	0	0
Elevated C-reactive protein, no. of patients			
Before treatment	10	7	3
After treatment	0	0	0
Quantitative RT-PCR result, no. of patients			
Positive for SARS-CoV-2 before treatment	15	11	4
Negative for SARS-CoV-2 after treatment	14	11	4
Treatment for COVID-19, no. of patients			
Oxygen support (nasal cannula)	14	11	3
Antiviral therapy	11	11	0
Antibiotic therapy	15	11	4
Pregnancy outcome, no. of patients			
Cesarean delivery	10	10	NA
Natural labor and delivery	1	1	NA
Neonatal status			
Apgar scores at 1 min and 5 min		8 and 9	
Severe asphyxia		0	
Death		0	
No. of patients discharged from hospital by end of study period	2	2	0

Note—NA = not applicable, RT-PCR = reverse transcription–polymerase chain reaction, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

^aOne patient had Mediterranean anemia and gestational diabetes, and one patient had total placenta previa.

^bOne patient had undergone mitral valve and tricuspid valve replacement surgery 10 years earlier.

lymphocyte count and 10 patients with increased C-reactive protein value.

By the end of study, 11 patients had given birth and four patients were still pregnant. Among the 11 parturient women, 10 patients underwent cesarean section, and one delivered vaginally. No cases of neonatal death or neonatal asphyxia occurred. Apgar scores at the 1st minute and 5th minute were normal in all neonates.

All 11 parturient women were given oxygen support through a nasal cannula and empirical antibiotic treatment before delivery and antiviral treatment after delivery. The four women who were still pregnant at the end of the study period were treated with empirical antibiotics and did not receive antiviral therapy, and three were given oxygen support through nasal cannula from admission. Until the data were censored, 14 of the 15 patients' SARS-CoV-2 quantitative RT-PCR results had turned negative after treatment.

Lymphocytic counts had returned to normal in 14 patients, and C-reactive protein values and body temperatures had returned to normal in all 15 patients after treatment. Cough and other symptoms had disappeared in all 15 patients after treatment.

Radiation dose, dates of chest CT, semi-quantitative CT scores, and disease stages based on CT findings are shown in Tables 2 and 3. The early findings on chest CT were ground-glass opacities (GGOs). With disease progression, CT findings gradually evolved into crazy paving pattern and consolidations. Eventually, the lesions showed absorption (Fig. 1). In 25 chest CT examinations, the cumulative distribution of disease involvement by lung lobe was as follows: right upper lobe, 18 CT examinations; right middle lobe, 13 CT examinations; right lower lobe, 24 CT examinations; left upper lobe, 15 CT examinations; and left lower lobe, 24 CT examinations. Six patients underwent chest CT examinations be-

fore and after delivery: Four patients (patients 4, 6, 8, and 9 in Table 2) had a decrease in the total score after delivery, one patient (patient 7) had no change in total score after delivery, and one patient (patient 11) had an increase in the score from 5 to 9 after delivery. The 10 patients who underwent follow-up chest CT showed absorption stage manifestation.

Discussion

Pregnant women are particularly susceptible to respiratory pathogens and severe pneumonia, because they are at an immunosuppressive state, and physiologic adaptive changes during pregnancy (e.g., diaphragm elevation, increased oxygen consumption, and edema of respiratory tract mucosa) render them intolerant to hypoxia [7]. Pregnant women were more than four times more likely to be admitted to the hospital for 2009 swine-origin influenza A (H1N1) than the general population [8]. In addition, according

TABLE 2: CT Features of 15 Pregnant Women With Coronavirus Disease (COVID-19)

Patient No.	Date of Symptom Onset	Delivery Date	Date of Chest CT Examination	Time Interval Between Symptom Onset and CT Examination (d)	Disease Stage Based on CT Findings ^a	Semiquantitative CT Score ^b	CTDI _{vol} (mGy)
1	1/28	2/4	2/7, 2/11	10, 14	2, 4	5, 4	3.7, 3.7
2	—	2/6	2/10, 2/15	—	3, 4	9, 8	4.3, 3.7
3	1/29	2/7	2/11, 2/16	13, 18	3, 4	9, 7	3.4, 4.0
4 ^c	1/28	2/7	2/5, 2/13	8, 16	2, 4	6, 5	2.6, 3.7
5	1/27	2/9	2/11	15	4	5	4.4
6 ^c	1/29	2/10	2/5, 2/13	7, 15	2, 4	3, 2	2.3, 5.7
7 ^c	2/4	2/14	2/11, 2/16	7, 12	3, 4	5, 5	4.4, 5.8
8 ^c	1/29	2/15	2/11, 2/18	13, 20	4, 4	8, 5	4.1, 5.8
9 ^c	1/28	2/1	2/1, 2/7	4, 10	2, 4	3, 2	4.3, 2.8
10	—	2/13	2/9	—	2	1	4.7
11 ^c	1/24	1/29	1/28, 2/12	4, 19	1, 4	5, 9	4.3, 3.5
12	2/3	NA	2/13	10	3	10	4.6
13	1/30	NA	2/13	14	3	4	5.1
14	2/1	NA	2/14	13	4	4	4.8
15	1/26	NA	2/6, 2/12	11, 17	3, 4	8, 5	3.1, 4.2

Note—Dash (—) indicates patient did not have any symptoms of COVID-19 so data are unknown. CTDI_{vol} = volume CT dose index, NA = not applicable because patient was still pregnant at the end of the study period.

^aDisease progression as revealed on the CT images was divided into four stages, as described by Pan et al. [6]: early stage (stage 1), progressive stage (stage 2), peak stage (stage 3), and absorption stage (stage 4).

^bA semiquantitative scoring system was used to estimate the pulmonary involvement of all abnormalities on the basis of the area involved. Each of the five lung lobes was visually scored from 0 to 5 as follows: 0, no involvement; 1, less than 5% involvement; 2, 25% involvement; 3, 26–49% involvement; 4, 50–75% involvement; and 5, more than 75% involvement. The total CT score was the sum of the five individual lobar scores and ranged from 0 (no involvement) to 25 (maximum involvement).

^cPatient underwent CT before and after delivery.

TABLE 3: CT Score of Pulmonary Involvement and Time Interval Between Symptom Onset and CT Examination by Coronavirus Disease (COVID-19) Stage

COVID-19 Stage ^a (No. of CT Examinations ^b)	Total CT Score ^c	Time Interval Between Symptom Onset and CT Examination (d)
Stage 1 (<i>n</i> = 1)	4	5
Stage 2 (<i>n</i> = 4), mean ± SD	7 ± 3	4 ± 2
Stage 3 (<i>n</i> = 5), mean ± SD	11 ± 3	7 ± 3
Stage 4 (<i>n</i> = 12), mean ± SD	15 ± 3	5 ± 2

^aDisease progression as revealed on the CT images was divided into four stages, as described by Pan et al. [6]: early stage (stage 1), progressive stage (stage 2), peak stage (stage 3), and absorption stage (stage 4).

^bThree CT examinations of two patients who did not have any symptoms of COVID-19 pneumonia were excluded.

^cA semiquantitative scoring system was used to estimate the pulmonary involvement of all abnormalities on the basis of the area involved. Each of the five lung lobes was visually scored from 0 to 5 as follows: 0, no involvement; 1, less than 5% involvement; 2, 25% involvement; 3, 26–49% involvement; 4, 50–75% involvement; and 5, more than 75% involvement. The total CT score was the sum of the five individual lobar scores and ranged from 0 (no involvement) to 25 (maximum involvement).

to a previous report, approximately 50% of pregnant women with SARS were sent to the ICU, approximately 33% of pregnant women with SARS needed mechanical ventilation, and the death rate of pregnant women with SARS was as high as 25% [9].

Recent reports indicate that pregnant women with COVID-19 pneumonia showed

a pattern of clinical characteristics similar to that of nonpregnant adult patients with COVID-19 pneumonia [7, 10, 11]. In our study, the diagnosis for all pregnant women with COVID-19 pneumonia, including three patients with underlying diseases, was mild pneumonia without acute respiratory distress syndrome in the whole course. All parturient

patients were given oxygen support from admission and achieved good recovery without mechanical ventilation.

The most common onset symptoms for the pregnant women with COVID-19 pneumonia in our study were fever and cough. Lymphocyte count reduction was common at laboratory examinations. In our study group, two patients showed no clinical symptoms before hospitalization. SARS-CoV-2 infection was suspected in these two patients because of epidemiologic contact history. In these two patients, the laboratory test results were suspicious for COVID-19 pneumonia and lesions were detected on subsequent chest CT.

Among the 11 parturient women, one patient delivered vaginally and 10 patients delivered by cesarean section. Three patients delivered by cesarean section at 34–36 weeks because of the belief that antiviral treatment was needed as early as possible in the disease course. Apgar scores of all neonates were 8 or greater, and there were no cases of neonatal asphyxia or neonatal death. The fact that patient 9 was able to deliver naturally is evidence that there is a potential role for natural delivery in pregnant women with

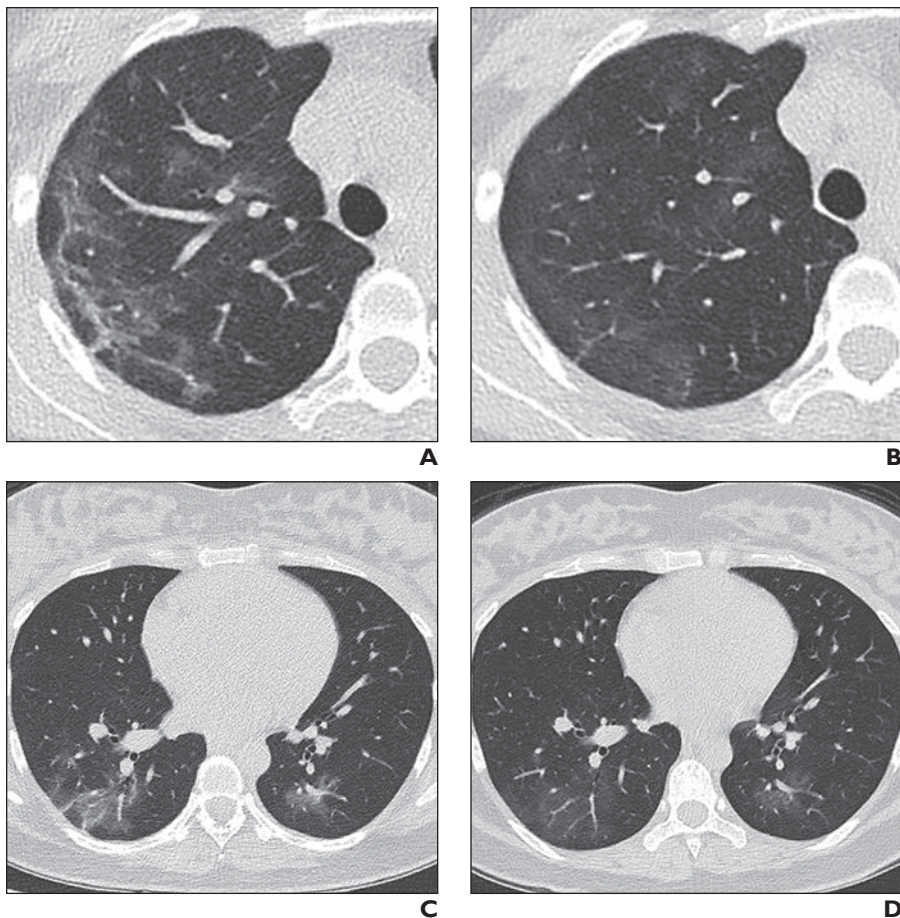


Fig. 1—30-year-old woman (patient 1 in Table 2) who presented with mild coronavirus disease (COVID-19) pneumonia when pregnant and underwent two CT examinations after delivery. **A and B**, Axial chest CT images obtained during progressive stage (stage 2) show multiple ground-glass opacities (GGOs) with partial consolidation in both lower lobes and right upper lobe. **C and D**, Follow-up axial chest CT images obtained 4 days after **A and B** during absorption stage (stage 4) show GGOs and consolidation have been partly absorbed.

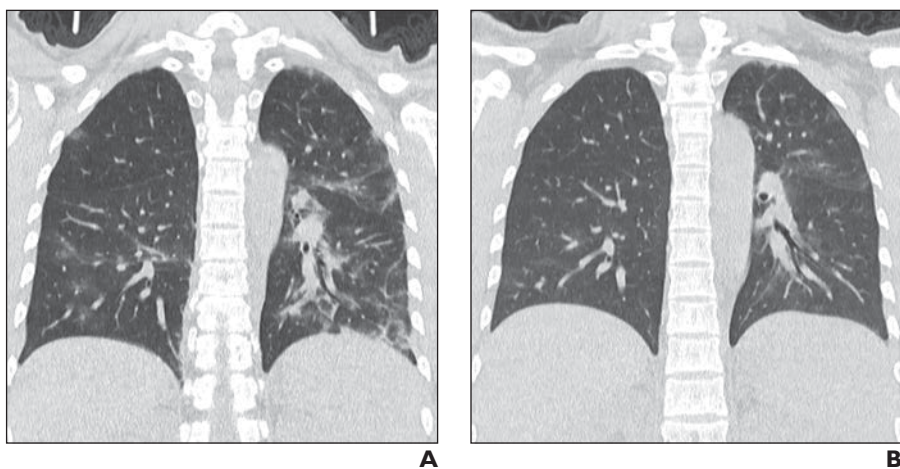


Fig. 2—29-year-old pregnant woman (patient 15 in Table 2) who presented with mild coronavirus disease (COVID-19) pneumonia when pregnant and underwent two CT examinations before delivery. **A**, Coronal chest CT image obtained during peak stage (stage 3) shows multiple ground-glass opacities (GGOs) with partial consolidation in both lungs. **B**, Follow-up coronal chest CT image obtained 6 days after **A** during absorption stage (stage 4) shows GGOs and consolidation have been partly absorbed.

mild COVID-19 pneumonia. Chen et al. [7] reported no evidence of vertical transmission of SARS-CoV-2 infection in late pregnancy.

During the treatment of all patients in this study, no relapse or sudden aggravation of pneumonia symptoms due to childbirth or pregnancy was found. After treatment, the quantitative RT-PCR result for SARS-CoV-2 was negative, clinical symptoms disappeared, and laboratory values returned to normal levels. Two patients were discharged from the hospital with a mean disease course of 16 days, which is similar to the course of 17 ± 4 days (mean \pm SD) reported by Pan et al. [6]. In addition, the four women who were still pregnant at the end of the study period had not received antiviral therapy; they received general support treatment and empirical antibiotics to prevent bacterial infection. However, at the end of the study period, the quantitative RT-PCR results for SARS-CoV-2 infection were also negative in these four patients, and the laboratory reexamination results showed lymphocyte counts had returned to normal values. Whether the mild type of COVID-19 pneumonia in pregnant women affects angiotensin-converting enzyme 2 (ACE2) expression and ACE2 distribution is not known and merits further investigations, because previous studies have suggested a strong association between COVID-19 and ACE2 expression [12].

Chest CT plays an important role in the diagnosis and treatment of COVID-19 pneumonia. Because pregnant patients could be particularly sensitive to exposure dose, some patients in our study underwent only one CT examination. Before CT examinations, the patient's lower abdomen and pelvis were covered with a lead blanket. The low-dose imaging mode was used for all 25 CT examinations, and the dose for a single examination was kept safe (mean \pm SD, 4.1 ± 0.9 mGy) [13].

With the progression of disease course, chest CT showed GGOs, crazy paving pattern, and consolidations, followed by gradual absorption. Most of the lesions were seen in the lower lobes of both lungs. The imaging manifestations, the timeline of progression, and the CT scores at each stage were similar to those reported by Pan et al. [6] and others [14, 15].

Patient 7 had no change in CT scores before and after delivery, but the CT scans showed stage 3 and stage 4 of the disease phases, respectively, and the lesions were partially absorbed during treatment. For patient 11 with an elevated CT score after delivery, the first

CT study showed findings that matched the characteristics of stage 1, whereas the second CT study showed findings that were rated as stage 4; these CT findings are consistent with the time course of the disease.

All 10 patients who underwent follow-up CT showed absorption stage changes, including one case of late pregnancy (Fig. 2). Johkoh et al. [16] studied the pathologic manifestations of crazy paving appearance. Other investigators reported that diffuse crazy paving changes, extensive consolidation, and pleural effusion may indicate poor prognosis in patients with acute Middle East respiratory syndrome coronavirus infection [17]. However, in our study of pregnant patients with SARS-CoV-2 infection, CT showed focal GGOs, small patches of crazy paving, and small areas of consolidation, and these CT findings may indicate a good prognosis.

The limitations of our study include the small number of patients and the lack of age-matched nonpregnant women as a control group in a retrospective study. Because most of the patients in this study were still in the hospital at the time of this writing, the final outcomes remain unclear.

Conclusion

All the pregnant women with COVID-19 pneumonia in our study presented with clinical manifestations and CT features of mild pneumonia. No SARS-CoV-2 infection was found in the neonates. Pregnancy and delivery did not aggravate the severity of COVID-19 pneumonia. In addition, our results raise the question of whether antiviral therapy is necessary for pregnant women with COVID-19 pneumonia and indicate that pregnant patients with COVID-19 pneumonia should be evalu-

ated for potential risks to the fetus considering both drug toxicity and the viral infection.

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