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Clinical characteristics and laboratory results of pregnant women with COVID-19 in Wuhan, China

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Abstract

Objective: To evaluate the clinical characteristics and laboratory test results in pregnant women with coronavirus disease 2019 (COVID-19).

Methods: A retrospective study to review and compare clinical data including electronic medical records and laboratory tests from pregnant and nonpregnant patients admitted the Central Hospital of Wuhan, China from December 8, 2019 to April 1, 2020.

Results: A total of 72 women (30 pregnant and 42 nonpregnant) with COVID-19 were included. No patients developed severe pneumonia during the study. Compared with the nonpregnant group, pregnant patients were admitted to hospital earlier (0.25 vs 11.00 days; $P<0.001$), presented milder symptoms, had a higher rate of asymptomatic infection (26.7% vs 0%), and shorter length of hospital stay (14.5 vs 17.0 days; $P<0.01$). Laboratory test results showed that levels of inflammation markers such as white blood cell count, neutrophil count and percentage, C-reactive protein, procalcitonin, and D-dimer were significantly higher in pregnant women, whereas mean lymphocyte percentage was significantly lower compared with nonpregnant women.

Conclusion: In some respects, the clinical characteristics and laboratory test results of COVID-19 in pregnant patients seems to be distinctive from their nonpregnant counterparts. Appropriate advice and positive treatment might be critical to the prognosis when dealing with these pregnant patients. Pregnant patients with COVID-19 had their own positive clinical characteristics and special laboratory test results. Responsive medical advice and active treatment for those patients are critical to recovery.

KEYWORDS

China; Clinical characteristics; Coronavirus; COVID-19; Laboratory tests; Pregnancy; SARS-Cov-2

1 | INTRODUCTION

The outbreak of coronavirus disease 2019 (COVID-19), a respiratory infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), began in December 2019 in Wuhan, Hubei province, spreading across China and then globally. As the disease continued to rapidly spread it was declared a global pandemic, greatly challenging health systems.[1]

The underlying mechanisms and adverse effects of COVID-19 have generated much attention; however, limited data are available on its management in pregnancy. Previous studies reported that the clinical characteristics of COVID-19 in pregnant and nonpregnant patients

were similar.[2] However, the potential of the virus to cause severe complications for both mothers and newborns requires rigorous screening in pregnancy and long-term follow-up.[3] Although available studies provide vital knowledge,[2,4] research in this field is limited and the results vary. Therefore, the aim of the present study was to investigate and report the clinical characteristics and laboratory test results of pregnant women with COVID-19 to strengthen the knowledge base.

2 | MATERIALS AND METHODS

We conducted a retrospective study at the Central Hospital of Wuhan. The study received approval from the Medical Ethical Committee of the Central Hospital of Wuhan. Informed written consent was waived owing to the retrospective nature of the study. All patients with suspected COVID-19 admitted to our hospital between December 8, 2019 and April 1, 2020 were screened for the disease. Two authors back to back assessed the all possibly eligible cases for compliance with the inclusion criteria for the study.

Clinical data of epidemiological history, clinical presentation, laboratory test results, and disease outcomes were collected from each patient's electronic medical record and reviewed by designated researchers (ZQW, ZGW). Exclusion criteria were negative results obtained by nasopharyngeal swabs and real-time PCR, and were repeated twice every two days in two different laboratories, male patients, and female patients younger than 20 years or older than 40 years. In addition, patients with a referral history from the local department to another department or from our hospital to other hospitals were excluded owing to the difficulty in obtaining their medical data. The records of two nonpregnant women who died during the study period were also excluded because they had severe underlying health conditions.

Patients were discharged from hospital once they had met the following criteria: (1) body temperature returned to normal and remained consistent for more than 3 days; (2) respiratory symptoms improved; (3) computed tomography (CT) of the chest showed decreased exudative lesions; and (4) for pregnant patients, there were no puerperal complications and they had fully recovered from any perineum or abdominal incision. Considering the limited performance of the nucleic acid test for the detection of COVID-19,[5] patients with typical manifestations of COVID-19 on chest CT were also included as diagnosed patients. Typical CT manifestations of COVID-19 such as bilateral ground-glass opacities, consolidation, an occasionally rounded morphology, and peripheral lung distribution were consistent with the guidelines of the Fleischner Society.[6] The treatment strategy in the present study followed the protocols published by the National Health Commission of the People's Republic of China.[7]

The clinical characteristics of pregnant patients extracted from medical records were gestational age; time interval between symptom onset and admission; time interval between hospitalization and delivery; delivery mode; length of hospital stay; initial symptoms (fever, cough, abdominal pain, blood-tinged mucus, ruptured membranes at term, chest tightness, asthma, fatigue, poor appetite, headache, nausea, and vomiting); and maternal comorbidities (gestational diabetes, gestational hypertension, intrahepatic cholestasis of pregnancy, premature rupture of membranes, and obesity). Reviewed laboratory tests included white blood cell (WBC) count, neutrophil count and percentage, lymphocyte count and percentage, platelet count, coagulation indicators (D-dimer), and liver and kidney function markers (e.g. aminotransferase and creatinine).

Statistical analyses were performed using SPSS version 21.0 (IBM, Armonk, NY, USA). Continuous variables are presented as median and interquartile range (IQR), while categorical variables are expressed as number (percentage). Comparisons between pregnant and nonpregnant groups were made using the χ^2 or Fisher exact test for categorical variables, whereas the *t* test or Mann-Whitney *U* test was used for continuous variables. $P<0.05$ was considered statistically significant.

3 | RESULTS

A total of 240 nonpregnant patients with suspected COVID-19 were initially enrolled and 42 were eligible after exclusions. A total of 30 pregnant patients with suspected COVID-19 were included, for a total study population of 72 participants (Fig. 1). Of the pregnant patients, 13 (43.3%) tested positive by SARS-Cov-2 nucleic acid test and 17 (56.7%) had typical chest CT manifestations of COVID-19. All 42 nonpregnant patients tested positive and showed typical manifestations of COVID-19 on chest CT scan.

The demographic and clinical characteristics of the two groups are shown in Table 1. Median age of pregnant patients was 29.9 years compared with 30.0 years for nonpregnant patients. For pregnant women, median gestational age at admission was 37.8 weeks (range, 30.0–40.9 weeks). A total of 23 (76.7%) pregnant women delivered by cesarean, whereas 7 (23.3%) delivered vaginally. Interval between symptom onset and hospital admission was significantly shorter

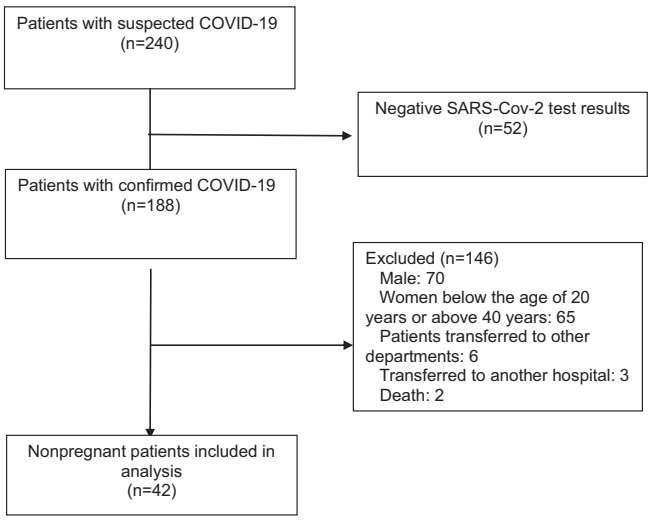

FIGURE 1 Sample flow and comparison groups for eligible women were identified through a query of the hospital electronic medical records.

TABLE 1 Clinical characteristics of the study population (n=72).[a]

Clinical characteristics	Pregnant women (n=30)	Nonpregnant women (n=42)	*P* value
Positive for SARS-CoV-2	13 (43.3)	42 (100.0)	—
Manifestations on chest CT	17 (56.7)	42 (100.0)	—
Age, y	29.9 (26.8–33.3)	30.0 (27.0–34.0)	0.50
Onset of symptoms to admission, d	0.25 (0–1.0)	11.0 (5.0–15.0)	<0.001
Hospitalization, d	14.5 (12.8–17.5)	17.0 (14.0–24.0)	0.01
Gestational age, wk	37.8 (30–40.9)	—	—
Delivery mode			—
Cesarean	23 (76.7)	—	—
Vaginal	7 (23.3)	—	—
Hospitalization to delivery, d	1.1 (0–1.0)	—	—
Initial symptoms			—
No clinical symptoms	8 (26.7)	0	—
Fever	11 (36.7)	28 (66.7)	—
Cough	5 (16.7)	21 (50.0)	—
Abdominal pain	4 (13.3)	—	—
Blood-tinged mucus	4 (13.3)	—	—
Ruptured membranes at term	5 (16.7)	—	—
Chest tightness	1 (3.3)	4 (9.5)	—
Asthma	0	5 (11.9)	—
Fatigue	3 (10.0)	3 (7.1)	—
Poor appetite	6 (20.0)	3 (7.1)	—
Headache	0	1 (2.4)	—
Nausea or vomiting	0	1 (2.4)	—
Complications			—
Pneumonia	30 (100.0)	42 (100.0)	—
Hypertension	5 (16.7)	1 (4.8)	—
Diabetes	2 (6.6)	1 (2.4)	—
Twin pregnancy	1 (3.3)		—
Hypothyroidism	1 (3.3)		—
Intrahepatic cholestasis of pregnancy	1 (3.3)		—
Premature rupture of membranes	6 (20.0)		—
Obesity	1 (3.3)		—

[a]Values are given as number (percentage) or median (interquartile range) unless otherwise indicated.

in pregnant women compared with nonpregnant women (0.25 vs 11.0 days, respectively; *P*<0.001. Median duration of hospitalization was longer in nonpregnant women compared with pregnant women (17.0 vs 14.5 days, respectively; *P*=0.01) (Table 1).

The most common symptoms of COVID-19 such as fever (defined as an axillary temperature above 37.3°C in this study), cough, asthma, and poor appetite were observed in both groups. Eight pregnant patients (26.7%) were asymptomatic. Among pregnant patients, 4 (13.3%) had blood-tinged mucus and 5 (16.7%) had full-term rupture of membranes. Six patients had premature rupture of membranes, among whom two had gestational diabetes (6.6%), five had gestational hypertension (16.7%), one had intrahepatic cholestasis of pregnancy (3.3%), and there was one case of twin pregnancy (3.3%).

Peripheral blood of all patients was collected 4 hours after admission. Laboratory analysis of blood, coagulation tests, and liver and kidney function tests were performed using an XN-9000 hematology analyzer (Sysmex Corp, Kobe, Japan), STAR coagulation analyzer (Stago, Asnières sur Seine, France), and ADVIA chemistry analyzer (Siemens, Munich, Germany), respectively.

Table 2 summarizes the laboratory test results of the two groups. Median WBC count, neutrophil count, and neutrophil percentage were significantly higher in pregnant patients compared with nonpregnant patients (7.5×10^9/L vs 5.6×10^9/L, *P*=0.01; 5.9×10^9/L vs 3.1×10^9/L, *P*<0.001; 77.5% vs 58.9%, *P*<0.001, respectively). While median lymphocyte percentage was significantly lower in pregnant women compared with nonpregnant women (16.1% vs 31.5%;

TABLE 2 Laboratory test results of patients with COVID-19 (n=72).

Test	Median (IQR)			*P* value
	Normal range	Pregnant women (n=30)	Nonpregnant women (n=42)	
White blood cell count, $\times10^9$/L	3.5–9.5	7.5 (6.4–10.3)	5.6 (4.1–7.3)	0.01
Neutrophil %	40–75	77.5 (67.5–82.6)	58.9 (50.6–68.0)	<0.001
Lymphocyte %	20–50	16.1 (11.5–23.6)	31.5 (21.5–37.5)	<0.001
Neutrophil count, $\times10^9$/L	1.8–6.3	5.9 (4.5–9.2)	3.1 (2.2–4.7)	<0.001
Lymphocyte count, $\times10^9$/L	1.1–3.2	1.4 (1.1–2.0)	1.6 (1.3–2.0)	0.130
Hemoglobin, g/L	130–175	117 (108–129)	132.0 (121.8–141.3)	0.002
Platelet count, $\times10^9$/L	125–350	189 (159–262)	214.0 (170.8–255.5)	0.238
Total bile acid, μmol/L	2–20.4	8.7 (7.2–10.3)	11.4 (7.8–15.9)	0.10
Alanine transaminase, U/L	7–40	9.4 (7.1–14.0)	21.5 (12.5–43.0)	<0.001
Aspartate aminotransferase, U/L	13–35	15.6 (12.6–21.4)	16.8 (14.6–23.0)	0.717
Albumin, g/L	40–55	35.9 (34.0–39.8)	42.7 (40.4–45.6)	<0.001
Globulin, g/L	20–40	28.0 (24.9–30.7)	28.6 (22.5–33.8)	0.393
Blood urea nitrogen, mmol/L	2.9–8.2	2.7 (2.2–3.0)	3.9 (3.2–5.0)	<0.001
Creatinine, μmol/L	41–73	43.4 (35.9–55.9)	58.8 (48.7–69.1)	<0.001
D-dimer, μg/mL	0–1	2.5 (1.4–4.6)	0.3 (0.1–0.85)	<0.001
C-reactive protein, mg/dL	0–0.6	1.0 (0.28–2.84)	0.1 (0.04–0.91)	0.022
Procalcitonin, ng/mL	<0.046	0.06 (0.04–0.16)	0.04 (0.03–0.06)	0.025
Lactate dehydrogenase, U/L	80–285	148.0 (127.0–182.0)	162.0 (129.5–190.0)	0.801
Interleukin-6, pg/mL	<7	5.9 (2.9–8.7)	1.5 (1.5–2.4)	0.115

P<0.01), there was no significant difference in median lymphocyte count between the two groups (1.4 × 10^9/L vs 1.6 × 10^9/L, *P*=0.130).

Although significant differences (all *P*<0.001) between the groups were found in the levels of some liver and kidney function tests (e.g. alanine transaminase, albumin, blood urea nitrogen, and creatinine), the levels of these indicators fell within the medical reference range. D-dimer was a routine coagulation test and the median level of this marker was significantly higher in the pregnant group compared with the nonpregnant group (2.5 μg/mL vs 0.3 μg/mL, *P*<0.001). No difference was observed in median platelet count between the two groups (189.0 × 10^9/L vs 214.0 × 10^9/L, *P*=0.238), which is also an indicator of coagulation. Hypersensitive C-reactive protein, procalcitonin, and interleukin-6 are three markers widely used to detect the acute phase of systemic inflammation, while procalcitonin is particular for the differentiation of bacterial and virus infections; hence, this test was recommended as a screening tool to detect COVID-19. Pregnant patients had higher median levels of C-reactive protein (1.0 mg/dL vs 0.1 mg/dL, *P*=0.022) and procalcitonin (0.06 ng/mL vs 0.04 ng/mL, *P*=0.025) compared with nonpregnant patients, but there was no difference in interleukin-6 (5.9 pg/mL vs 1.5 pg/mL; *P*=0.115).

4 | DISCUSSION

The virus causing COVID-19 is believed to have originated from a local seafood market in Wuhan, which is surrounded by many residential buildings.[8,9] This may be one reason that the pandemic spread so quickly at the beginning. The Central Hospital of Wuhan, a designated hospital for the diagnosis and treatment of COVID-19 patients, is 2 kilometers away from this market. Most of the enrolled patients were residents of the area.

Several findings from the present study are consistent with previous reports. The most common symptoms reported in pregnant patients with COVID-19 were fever, cough, fatigue, and poor appetite; however, a considerable proportion of asymptomatic infections may also be observed in practice,[4,10] with 8 (26.7%) pregnant patients in the present study admitted without symptoms. Other symptoms also included blood-tinged mucus, a sudden gush of fluid, and constant leakages of vaginal fluid from the cervical ostium in late pregnancy. Notably, length of hospital stay was much shorter in pregnant patients, which may be because pregnant women were more willing to seek treatment earlier and their health conditions were not severe. A total of 29 (96.7%) pregnant patients underwent successful delivery on the day of admission, except one patient with hypertension who was delivered by cesarean at 35.6 weeks of pregnancy after 11 days of hospitalization.

The present study also found that the typical symptoms of COVID-19 may have been milder in pregnant patients than in nonpregnant patients, which was also reported in an earlier study.[11] Carriers of SARS-CoV-2 often presented with milder or no symptoms in the incubation period, the duration of which could be as long as 14 days, which increased the risk of infecting others before diagnosis and implied that positive treatment monitoring might be delayed.[12] Medical personnel should be alert that they run a high risk of becoming infected when performing a physical examination on these patients.

Among the 30 pregnant patients, 25 delivered at full term, three were delivered by cesarean because of premature rupture of membranes, one had hypothyroidism, and one had intrahepatic cholestasis of pregnancy. Pregnant patients seemed more likely to undergo cesarean delivery during the emergence of COVID-19. In the present study, rate of cesarean delivery was higher than that of vaginal delivery (76.7% vs 23.3%, respectively), given that the main concern might be neonatal infection.[13] Presumably, delivering the neonate benefited the recovery of these patients from COVID-19, since some antiviral remedies such as ribavirin are teratogenic during pregnancy and, to date, no definitely effective drugs for this disease have been determined. All newborns, regardless of gestational age, underwent nucleic acid test after birth and all results were negative, suggesting that the risk of viral transmission from mother to baby may not be high.[14] It is currently unclear whether vaginal delivery or cesarean delivery is of greater benefit for these patients. Nonetheless, it is recommended that operations should be performed in isolation wards or negative pressure rooms as these measures reduce the length of labor and the frequency of breath-holding during deliveries.[15] Reduced labor duration and frequency of breath-holding during vaginal delivery on a pregnant woman's cardiorespiratory load should be beneficial.

Lymphocytes act as the primary immune barrier to viral infection and their dysregulation can be observed when the body is invaded. Consistent with an earlier report,[16] the present study showed that peripheral lymphocyte count and lymphocyte percentage were normal or decreased in pregnant patients in the early stages of COVID-19. Although lymphocyte count varied in pregnancy, it often returned to levels in the postpartum period that were equal to those in nonpregnant patients.[13] This may indicate a poor prognosis as lymphocyte percentage was correlated with the severity of COVID-19.[17] Except for the deaths of two nonpregnant women who had severe underlying conditions, all enrolled patients had recovered by the end of the study.

Patients with mild symptoms could have increased levels of C-reactive protein but normal procalcitonin.[17] Procalcitonin is a biomarker with higher diagnostic accuracy than C-reactive protein for bacterial infection.[18] However, procalcitonin levels were slightly higher in pregnant patients in the present study and, further considering the higher neutrophil count in this group, clinicians should be well-informed of the risk of puerperal infection in these patients. D-dimer is an indicator of fibrinolysis and is widely used as a criterion for thromboembolism. The correlation of high levels of this indicator with the occurrence of severe COVID-19 in adult patients has been reported previously.[19] The present study showed that pregnant patients with COVID-19 had higher levels of D-dimer; however, its application in these patients may be restricted because it would increase physiologically over the course of delivery. The levels of some indicators of liver and kidney function, such as alanine transaminase, albumin, blood urea nitrogen, and creatinine in pregnant patients also differed significantly from those in nonpregnant patients; however, their values all fell within the medical reference range. The significance of these markers in patients with COVID-19 needs further research.

This study has several limitations. The first is that we included 13 pregnant women whose SARS-CoV-2 nucleic acid test results were positive, but who had typical manifestations of COVID-19 on chest CT based on the evidence that CT could be an auxiliary diagnostic tool for the disease.[20] The second is that we did not make a comparison between pregnant women with and without COVID-19, therefore some of the conclusions drawn from current data might be limited. The third weakness is the relatively small sample size. Results and conclusions from the present study need to be validated by multiple center trials in the future.

In conclusion, this study included 72 patients with COVID-19, focusing on the clinical characteristics and laboratory test results of this disease in pregnancy. The characteristics and laboratory test results in pregnant patients seemed to be distinctive from nonpregnant patients in some respects. Pregnant patients with COVID-19 had their own positive clinical characteristics and special laboratory test results. Responsive medical advice and active treatment for those patients are critical to the recovery.

AUTHOR CONTRIBUTIONS

All authors contributed to writing the manuscript and approval of the final version. GPX designed the study, ZQW and GPX collected the data, ZQW and ZGW analyzed and interpreted the results.

CONFLICTS OF INTEREST

The authors have no conflicts of interest.

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