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# Clinical characteristics of pregnant women with COVID-19

Ying Yu; Yuping Guo; Di Lei; Huiyuan Pang; Tingting Liu; Cuifang Fan*

***Corresponding Author: Cuifang Fan**
Department of Obstetrics and Gynecology, Renmin Hospital of Wuhan University, Wuhan, Hubei, China
Email: 359568292@qq.com

## Abstract

**Aim:** To analyze the clinical characteristics and perinatal outcomes of pregnant women with COVID-19 to provide guidance for the diagnosis and treatment of this patient population.

**Methods:** 28 pregnant women with COVID-19 admitted to Renmin Hospital of Wuhan University were enrolled as the case group, and 42 concurrently hospitalized healthy pregnant women were recruited as controls to compare laboratory data and perinatal outcomes.

**Results:** There were no statistically significant differences between the two groups in maternal age or D-dimer levels (P>0.05). There was a trend toward lower birthweights in the case group that did not reach statistical significance. The gestational age at delivery in the case group (37.69 ± 2.23) was significantly lower than that of controls (38.84 ± 1.52) (P=0.017). C-reactive protein (CRP) levels (35.23 ± 37.67) in the case group were significantly higher than in controls (9.62 ± 20.50), (P=0.001), but all were within normal limits.

**Conclusion:** Pregnant women with COVID-19 often choose cesarean section for earlier delivery; birth weights are correspondingly lower. CRP was elevated in the case group, reflecting systemic inflammation. Clinically significant renal and hepatic complications were not observed in our study. Although D-dimer levels were similar in both groups, the role of intensified low-molecular-weight heparin prophylaxis in COVID-19 pneumonia warrants further study.

## Keywords

China; Coronavirus; COVID-19; SARS-CoV-2; Laboratory examination.

## Introduction

In December 2019, COVID-19 emerged and rapidly spread in a global pandemic. According to data released by the World Health Organization, as of June 10, 2020, the number of confirmed COVID-19 cases worldwide had exceeded 7 million, the number of deaths had exceeded 400,000, and the case fatality rate had reached 5.71% (https://www.who.int/). Typical symptoms of COVID-19 include fever, cough, fatigue, and dyspnea. Generally, there is a history of contact with confirmed cases, and lung computerized tomography (CT) images feature a typical ground-glass shadow [1]. In addition to nucleic acid testing, other laboratory assays have generated interest. For example, COVID-19 generally features a relative lymphopenia, similar to findings in other viral infections [2]. In addition, a retrospective analysis conducted at the Jinyintan Hospital showed that patients with coagulopathy are more likely to develop acute respiratory distress syndrome (ARDS) and less likely to survive [3]. Although much research has been conducted on non-pregnant COVID-19 patients, clinical studies of pregnant patients have been limited. This study compared clinical and laboratory findings of pregnant women with COVID-19 in Hubei Province to those of normal pregnant women who were concurrently hospitalized. In addition to imaging and nucleic acid testing, comprehensive clinical laboratory studies were performed. An understanding of the perinatal outcomes of pregnant women with COVID-19 is required to introduce appropriate interventions expeditiously.

## Materials and Methods

### Study participants

Twenty-eight pregnant women with COVID-19 admitted to Renmin Hospital of Wuhan University from January to March 2020 were enrolled as the case group. Inclusion criteria consisted of pregnancy and COVID-19 pneumonia diagnosed in accordance with the «New Coronavirus Infection Pneumonia Diagnosis and Treatment Plan (Trial Version 5)» of the National Health Commission of China [4]. Forty-two healthy pregnant women admitted during the same time period were recruited as the control group. This study was approved by the hospital's medical ethics committee, and all participants provided signed written informed consent (WDRY2020K015).

### Methods

Demographic and clinical data that were recorded were symptoms; age; gestational age; birth weight; and the results of chest CT and SARS-CoV-19 nucleic acid testing. Laboratory samples were collected by obtaining 5 mL of peripheral venous blood during a fasting state on the morning after admission. Samples were placed in vacuum anticoagulation tubes containing 0.2 mL of sodium citrate, manually agitated, and then centrifuged at 3000 r/min for 15 min (centrifugation radius 15 cm). After separation of the plasma and formed elements, supernatant was extracted and refrigerated at -70°C. An automatic blood cell morphology analyzer was used for routine clinical hematology analyses; an automated protein analyzer to was used to measure C-reactive protein (CRP) levels; enzyme-linked immunoassays were used for liver and kidney function testing; and coagulation assays were used to measure blood coagulation function.

### Statistical processing

SPSS20.0 statistical software was used for statistical processing. Data was expressed as mean values

and standard deviations, and the t-test was used for comparisons between the two groups. Statistical significance was defined by $P<0.05$.

## Results

### Demographic and clinical information

Gestational complications in the case group included gestational diabetes [4], severe preeclampsia [1], premature rupture of membranes [2], and premature delivery [4]. In the control group, complications were gestational diabetes [1], anemia [1], premature rupture of membranes [7], premature delivery [2], postpartum hemorrhage [1], and amniotic fluid contamination [1]. There was no significant difference between the two groups in maternal age. There was a trend toward lower birthweight in the case group that did not reach statistical significance ($P>0.05$). The gestational age at delivery in the case group was significantly lower than in controls ($P<0.05$) (Table 1).

**Table 1:** Demographic and clinical information

| | Case group | Control group | P value |
|---|---|---|---|
| Age (years) | 30 ± 4.2 | 29.98 ± 4.44 | 0.985 |
| Gestational age (weeks) | 37.69 ± 2.23 | 38.84 ± 1.52 | 0.017 |
| Birthweight (g) | 3060.8 ± 455.6 | 3295.95 ± 480.23 | 0.052 |

### Clinical hematology and biochemical indicators

There were no significant differences in leukocyte counts or percentages of neutrophils; eosinophils; basophils; lymphocytes; and monocytes between the two groups ($P>0.05$); whereas the mean CRP level of COVID-19 patients was significantly higher than that of the control group ($P<0.05$) (Table 2).

There were no statistically significant differences between the two groups in levels of alanine aminotransferase, blood urea nitrogen, creatine kinase, and lactate dehydrogenase ($P>0.05$). The aspartate aminotransferase, total bilirubin, and creatinine levels were higher in the case group compared to controls ($P<0.05$); however, all values were within the normal range (Table 2).

**Table 2:** Clinical hematology and CRP

| | Normal range | Case group | Control group | P value |
|---|---|---|---|---|
| Leukocytes (×109/L) | 3.5-9.5 | 9.336 ± 5.34 | 9.72 ± 3.22 | 0.71 |
| Neutrophils (%) | 40-75 | 75.94 ± 11.24 | 76.55 ± 7.23 | 0.784 |
| Eosinophils (%) | 0.4-8.0 | 0.98 ± 1.30 | 0.95 ± 1.30 | 0.926 |
| Basophils (%) | 0.0-1.0 | 0.22 ± 0.13 | 0.24 ± 0.20 | 0.641 |
| Lymphocyte (%) | 20-50 | 16.49 ± 8.71 | 16.19 ± 5.67 | 0.863 |
| Monocytes (%) | 3-10 | 5.76 ± 2.05 | 6.56 ± 1.46 | 0.062 |
| C-reactive protein | 0-10 | 35.23 ± 37.67 | 9.62 ± 20.50 | 0.001 |

### Coagulation function

There was no statistically significant difference in D-dimer values between the two groups (P>0.05), which were all within the third-trimester normal range. However, the prothrombin times and activated partial thromboplastin times in the case group were higher than those of controls (P<0.05). All results were within the normal range (Table 3).

**Table 3:** Liver and kidney function

| | Normal range | Case group | Control group | P value |
|---|---|---|---|---|
| Aspartate aminotransferase (U/L) | 13-35 | 22.24 ± 8.20 | 11.77 ± 5.56 | 0 |
| Alanine aminotransferase (U/L) | 7-40 | 20.24 ± 7.86 | 18.14 ± 3.45 | 0.132 |
| Total bilirubin (μmol/L) | 0-23 | 9.88 ± 3.20 | 6.56 ± 4.17 | 0.01 |
| Blood urea nitrogen (mmol/L) | 2.6-7.5 | 3.41 ± 0.84 | 3.09 ± 0.65 | 0.086 |
| Creatinine (μmol/L) | 41-73 | 45.88 ± 8.79 | 39.79 ± 9.08 | 0.009 |
| Creatine Kinase (U/L) | 40-200 | 40.06 ± 23.08 | 50 ± 21.04 | 0.074 |
| Lactate dehydrogenase (U/L) | 120-250 | 201.8 ± 52.84 | 176.59 ± 50.79 | 0.056 |

**Table 4:** Coagulation function

| | Normal range | Case group | Control group | P value |
|---|---|---|---|---|
| Prothrombin time (PT, sec) | 9-13 | 11.84 ± 3.65 | 10.70 ± 0.63 | 0.049 |
| Activated partial thromboplastin time (APTT, sec) | 25-31.3 | 27.33 ± 3.68 | 25.19 ± 3.65 | 0.017 |
| D-dimer (mg/L) | 0-0.55 | 2.65 ± 3.51 | 2.51 ± 1.95 | 0.827 |

## Discussion

The lower gestational age at delivery in the case group may be related to clinical intervention. In the early stage of the epidemic, COVID-19 was considered an indication for cesarean section to prevent vertical transmission [5]. We suggest that this practice may result in preterm deliveries and correspondingly lower birth weights [6]. However, subsequent reports have not associated vaginal delivery with intrapartum transmission. Current recommendations state that COVID-19 should not be the sole indication for delivery, and that cesarean section should be reserved for patients with critical illness or other obstetrical indications7.

The differential count of neutrophils was slightly above the normal range in both groups, reflecting a physiologic change of pregnancy [8]. CRP is an acute phase response protein that is upregulated during inflammation [9]. In non-pregnant patients with COVID-19 pneumonia, CRP is typically elevated and related to prognosis; high CRP levels are associated with ARDS and higher mortality rates [10].

Among non-pregnant COVID-19 patients, elevated liver function test values are associated with di-

sease severity [11]. Liver injury may be related to systemic inflammation and antiviral drug toxicity [12]. Whereas liver function test abnormalities are common in COVID-19, clinically significant hepatic injury is rare [13]. Although liver function test results of our two study groups were significantly different, they were all within normal ranges.

The incidence of acute kidney injury (AKI) in hospitalized COVID-19 patients is high. A retrospective cohort study found that AKI occurred in 9.4% of patients, and was associated with a 3.2-fold increased mortality rate [14]. The mean creatinine value of our case group COVID-19 was significantly higher in controls, albeit within the normal range. Although women in our case group were at risk of renal damage in the context of COVID-19 infection, we did not observe AKI in our study.

Prolonged PT and APTT and elevated D-dimers are common in COVID-19, suggesting disseminated intravascular coagulation. Elevated D-dimer level is an independent risk factor for poor prognosis in COVID-19; patients with high D-dimers are more likely to develop severe disease [15]. Systemic inflammation promotes coagulation [16]. Autopsies of COVID-19 patients have shown diffuse microvascular thrombi in the lungs and other organs. In addition, maternal blood is hypercoagulable; APTT and PT decrease, and D-dimer levels gradually increase during pregnancy [17]. In this study, there was no significant difference in the D-dimer levels between the two groups, and values were within an acceptable third-trimester range. APTT and PT were within the normal range, which may be due to the combined effects of pregnancy and COVID-19. However, the APTT and PT of the case group were longer than the control group, which may reflect the systemic inflammatory response of COVID-19. Low-dose use of low-molecular-weight heparin can improve the clinical outcomes of patients with COVID-19 and coagulopathy [18]. Low-molecular-weight heparin thromboprophylaxis is generally recommended for critically ill patients, including those with COVID-19 and elevated D-dimer levels. Clinical trials are needed to compare the efficacy of intensified vs. standard anticoagulant prophylaxis in critically ill COVID-19 patients19.

## Declarations

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**Authors Information:** MaYing Yu[#]; Yuping Guo[#]; Di Lei; Huiyuan Pang; Tingting Liu; Cuifang Fan*
Department of Obstetrics and Gynecology, Renmin Hospital of Wuhan University, Wuhan, Hubei, China.
[#]Equal contribution.

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