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Coronavirus disease 2019 in pregnancy

Xu Qiancheng[a,1], Shen Jian[b,1], Pan Lingling[c,1], Huang Lei[b], Jiang Xiaogan[a], Lu Weihua[a], Yang Gang[d], Li Shirong[d], Wang Zhen[a], Xiong GuoPing[b,*], Zha Lei[e,f,**], the sixth batch of Anhui medical team aiding Wuhan for COVID-19

[a] Department of Critical Care Medicine, The First Affiliated Hospital of Wannan Medical College (Yijishan Hospital of Wannan Medical College), No. 2, West Road of Zheshan, Jinghu District, Wuhu, Anhui, 241000 China
[b] Department of Obstetrics and Gynecology, The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology, 26 Shengli Street, Jiang,an District, Wuhan, Hubei, 430014 China
[c] Department of Cardiology, The First Affiliated Hospital of Wannan Medical College (Yijishan Hospital of Wannan Medical College), No. 2, West Road of Zheshan, Jinghu District, Wuhu, Anhui, 241000 China
[d] Department of Respiratory and Critical Care Medicine, The Second People's Hospital of Wuhu, No. 265, Jiuhua Road, Jinghu District, Wuhu, Anhui, 241000 China
[e] Department of Biological Sciences, Xi'an Jiaotong-Liverpool University, No. 111, Ren'ai Road, Dushu Lake Higher Education Town, Suzhou Industrial Park, Suzhou, 215123 China
[f] Emergency and Critical Care Unit, Conch Hospital, Wuhu, Anhui, 241000 China

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ABSTRACT

Objectives: This study aimed to compare clinical courses and outcomes between pregnant and reproductive-aged non-pregnant women with COVID-19, and to assess the vertical transmission potential of COVID-19 in pregnancy.
Methods: Medical records of pregnant and reproductive-aged non-pregnant women hospitalized with COVID-19 from January 15 to March 15, 2020 were retrospectively reviewed. The severity of disease, virus clearance time, and length of hospital stay were measured as the primary objective, while the vertical transmission potential of COVID-19 was also assessed.
Results: Eighty-two patients (28 pregnant women, 54 reproductive-aged non-pregnant women) with laboratory-confirmed COVID-19 were enrolled in this study. Univariate regression indicated no association between pregnancy and severity of disease (OR 0.73, 95% CI 0.08–5.15; $p = 0.76$), virus clearance time (HR 1.16, 95% CI 0.65–2.01; $p = 0.62$), and length of hospital stay (HR 1.10, 95% CI 0.66–1.84; $p = 0.71$). Of the pregnant women, 22 delivered 23 live births, either by cesarean section (17, 60.7%) or vaginal delivery (5, 17.9%), and no neonate was infected with SARS-CoV-2.
Conclusions: Pregnant women have comparable clinical courses and outcomes with reproductive-aged non-pregnant women when infected with SARS-CoV-2. No evidence supported vertical transmission of COVID-19 in the late stage of pregnancy, including vaginal delivery.

1. Introduction

On March 11, 2020, coronavirus disease 2019 (COVID-19), caused by the emerging severe acute respiratory distress syndrome coronavirus 2 (SARS-CoV-2) (Zhu et al., 2020), was announced as a pandemic by the World Health Organization (Cucinotta and Vanelli, 2020). At at the writing, there were 191 127 confirmed cases reported globally, with a mortality rate of 4.08% (WHO, 2020). Epidemiological studies indicated that people of any age were at risk of infection, and the severity was associated with age and comorbidities (Wu and McGoogan, 2020). For example, cancer patients infected with SARS-CoV-2 have shown a higher risk of severe events and mortality rate compared with those without

* Corresponding author. Department of Obstetrics and Gynecology, The Central Hospital of Wuhan, Tongji Medical College, Huazhong University of Science and Technology, 26 Shengli Street, Jiang,an District, Wuhan, Hubei, 430014, China. Tel.: +86 027-65692987 / +86 15207195765.
** Corresponding author. Department of Biological Sciences, Xi'an Jiaotong-Liverpool University, No. 111, Ren'ai Road, Dushu Lake Higher Education Town, Suzhou Industrial Park, Suzhou, 215123, China. Tel: +86 18155396100.
E-mail addresses: Hyh0120@163.com (X. GuoPing), Lei.zha@liverpool.ac.uk (Z. Lei).
[1] These authors contributed equally to this work.

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cancer (Liang et al., 2020), and COVID-19 patients with pre-existing digestive diseases were associated with more complications (Mao et al., 2020). The higher vulnerability of these patients is likely to be caused by a suppressed immune system due to the underlying diseases or the side-effects from treatments, including surgery, chemotherapy, and immunosuppressive agents.

Pregnant women develop a special immunological adaptation, which is necessary for maintaining tolerance of the fetal semi-allograft (Weetman, 2010). This state of transient suppressed immunity is modulated by suppressing T cell activity, and hence predisposes pregnant women to viral infections (Longman and Johnson, 2007; Pazos et al., 2012). In addition, the physiological changes occurring in the respiratory and circulatory systems might worsen clinical outcomes when infected with a virus during pregnancy (Rasmussen et al., 2020).

During the 2009 H1N1 influenza pandemic, pregnancy caused a higher risk of severe pneumonia, ARDS, mechanical ventilation, and death when compared with reproductive-aged non-pregnant women (Jamieson et al., 2009). Similar results were also reported for the severe acute respiratory distress syndrome (SARS) and Middle East respiratory distress syndrome (MERS) epidemics, where pregnant patients were more likely to develop organ dysfunction and die (Rasmussen and Jamieson, 2020; Schwartz and Graham, 2020; Wang et al., 2020a,b). However, in the current COVID-19 outbreak, pregnant women seemingly have had fewer maternal and neonatal adverse events than were reported for SARS and MERS (Qiao, 2020), but whether pregnant women have a comparable clinical course and outcome with non-pregnant women is still unclear.

To facilitate the understanding of pregnancy in COVID-19, we carried out a retrospective observational study to compare the clinical courses and outcomes of pregnant and non-pregnant women, and also summarized the neonatal outcomes, including the vertical transmission potential of COVID-19.

2. Methods

2.1. Study design and participants

This was a single-center, retrospective study performed in The Central Hospital of Wuhan, one of five designated hospitals for pregnant women with COVID-19 in the epicenter of the SARS-CoV-2 outbreak in China. We included pregnant women hospitalized with COVID-19 and reproductive-aged (defined as 18–41 years old; modified from a previous study (Creanga et al., 2010)) non-pregnant women infected with SARS-CoV-2 as the comparison, from January 15 to March 15, 2020. COVID-19 was diagnosed according to Chinese Clinical Guidance for COVID-19 Pneumonia Diagnosis and Treatment, published and updated by the National Health Commission of China (NHFPC, 2020). All the COVID-19 patients had either positive reverse transcription polymerase chain reaction (RT-PCR) results from respiratory samples (Chen et al., 2020a) or positive serological tests for the specific IgM antibody to SARS-CoV-2. The sensitivity and specificity of the serological test for SARS-CoV-2 were 82.7% and 98.6%, respectively (Zhao et al., 2020a).

The study was approved by the ethics committee of The Central Hospital of Wuhan (2020-34).

2.2. Patient identification and data collection

All patients consecutively admitted to The Central Hospital of Wuhan with the diagnosis of COVID-19, between January 15 and March 15, 2020 were selected from the electronic medical records. Males were excluded. The included females were then classified by age, with only those between 18 and 41 years being subjected to further analysis. The medical records of the included patients of reproductive age were reviewed independently by two physicians (QC. X and SR. L) to confirm whether the diagnosis of COVID-19 met the criteria according to the guidance published by the National Health Commission of China. All the confirmed cases were then allocated to the pregnant women group or the reproductive-aged non-pregnant women group for further analysis.

Data extracted from the patient records included age, time from onset of symptoms to hospital admission, the severity of COVID-19, comorbidities, symptoms at onset, vital signs on admission, laboratory tests, computed tomography (CT) findings, treatments (antivirus regimens, antibiotics, corticosteroids, gamma globulin), virus clearance time, and length of hospital stay (LOS). For the pregnant women, gestational age on admission, the outcome of pregnancy, and information on neonates (including birthweight, Apgar score, and perinatal complications) were also recorded.

2.3. Outcomes and definitions

The outcomes of interest included: severity of COVID-19, LOS, and virus clearance time. The neonates were tested for infection with SARS-CoV-2. Viral clearance was confirmed by serial RT-PCR, using samples from throat swab, with at least two consecutive negative results taken 24 hours apart considered cleared. Virus clearance time, in days, was defined as starting at the onset of symptoms and ending on the date of the first negative RT-PCR test. The diagnostic criteria for COVID-19 in neonates were the same as for adults, with at least two negative RT-PCR tests from throat swabs after birth and no evidence of pneumonia being considered as free from SARS-CoV-2 infection. The severity of disease was classified as mild (mild symptoms and without pneumonia on chest imaging), moderate (fever and respiratory symptoms, radiological findings of pneumonia), severe (shortness of breath, with respiratory rate $\geq$ 30 breaths/minute, or oxygen saturation $\leq$ 93% at rest, or alveolar oxygen partial pressure/faction of inspiration O_2 (PaO_2/FiO_2) $\leq$ 300 mmHg), and critical (respiratory failure requiring mechanical ventilation, or shock, or other organ failures that needed intensive care unit admission), according to the Chinese Clinical Guidance for COVID-19 Pneumonia Diagnosis and Treatment (NHFPC, 2020).

2.4. Statistical analysis

Continuous variables were summarized as either means and standard deviations or medians and interquartile ranges (IQR), as appropriate. Categorical variables were described as frequencies and percentages. The differences between pregnant and reproductive-aged non-pregnant were analyzed using Fisher's exact test or the Wilcoxon signed-rank test for categorical variables, and the Mann-Whitney U-test for continuous variables. LOS and virus clearance time were estimated using the Kaplan-Meier method and the log rank test. Univariate Cox proportional hazard regression and ordinal logistic regression were performed to estimate associations between pregnancy and clinical outcomes and severity of disease. Hazard ratios (HR), odds ratios (OR), and 95% confidence intervals (CI) were reported. $p < 0.05$ was considered statistically significant. All analyses were performed using R software, version 3.6.2 (R Foundation for Statistical Computing).

3. Results

3.1. Data declaration

At the time of submission of the manuscript (March 30, 2020), no studies were identified as including data from this study. During the revision period (April 17–21, 2020), an online correspondence

was published on April 18 in the New England Journal of Medicine (Chen et al., 2020b), which reported 118 pregnant women with COVID-19 in Wuhan, among which 11 cases were from the same hospital as our study.

3.2. Patient characteristics

719 patients were admitted to the hospital during the study period, of which 339 were male and 380 were female. 298 females were excluded on the basis of age – they were older than 41 years. Eventually, 82 patients were enrolled in the study, of which 28 were pregnant and 54 were reproductive-aged non-pregnant women (Fig. 1). The median age of pregnant women was 30 years (IQR 26.75–32), which was similar to that of non-pregnant women – 31 years (IQR 28–35). Comorbidities were not frequently reported in both groups: of the pregnant women, one (3.6%) had probable gestational hypertension, two (7.1%) had probable gestational diabetes, two (7.1%) had chronic hepatitis B, and one (3.6%) had hypothyroidism; of the non-pregnant women, four (7.4%) had diabetes, two (3.7%) had chronic hepatitis B, and one (1.9%) had hypothyroidism. No cases of cancer, chronic respiratory disease, or heart disease were reported.

Pregnant women had a shorter median time from illness onset to admission compared with non-pregnant women (1 day, IQR 1–6.5 vs 7 days, IQR 5–10; $p < 0.001$). This result might be explained by the waiting time for SARS-CoV-2 tests being shorter for priority patients, such as pregnant women, children, and patients in critical situations) than for other patients. The severity of disease was comparable in the two groups. Aside from two (7.1%) patients in the pregnant group presenting as mild type, most patients were categorized as having moderate pneumonia (24, 85.7% vs. 53, 98.1%), with only two (7.1%) patients in the pregnant group and one (1.9%) in the non-pregnant group being classified as having severe pneumonia. The main complaints on admission were slightly different, with fever and cough being more frequent in the non-pregnant group, while abdominal pain was only reported among pregnant women (Table 1).

3.3. Laboratory and radiological presentations

More leukocytosis ($> 9.5 \times 10^9$/L) (10, 35.7% vs. 2, 3.7%; $p < 0.001$) and elevated C-reactive protein levels (> 0.6 mg/dL) (17, 68% vs. 14, 25.9%; $p = 0.001$) were detected in pregnant women than in the non-pregnant group, while there was no statistical difference in procalcitonin. Baseline hemoglobin level (117.5 g/L, IQR 106.75–129.00, vs. 126.00 g/L, IQR 121.25–135.50; $p = 0.018$) and albumin level (35.50 g/L, IQR 34.00–38.65 vs. 43.00 g/L, IQR 41.00–43.85; $p < 0.001$) were lower in pregnant patients compared with reproductive-aged non-pregnant women. Elevated alanine aminotransferase was observed in two (3.7%) non-pregnant women, with no reports in pregnant women ($p = 0.80$). A small number of patients in both groups had elevated creatine ($\geq$ 75 μmol/L) (one, 3.8% vs. five, 9.3%; $p = 0.683$), lactate dehydrogenase ($\geq$ 220 U/L) (four, 16% vs. one, 2.4%; $p = 0.116$), and creatine kinase ($\geq$ 140 U/L) (three, 12.5% vs. two, 4.8%; $p = 0.51$), but without statistical significance. Aside from two pregnant patients, all others showed typical changes on chest CT, with multiple patchy ground-glass shadows (Table 2).

3.4. Treatments and outcomes

21 (75%) patients in the pregnant group received antivirus therapy; of these, all except one (20, 71.4%) received ribavirin alone. In contrast, all non-pregnant women received antivirals, of which 19 (35.2%) received ribavirin, 11 (20.4%) received umifenovir, 17 (31.5%) received a ribavirin and umifenovir combination, and seven (13.0%) received a triple combination, adding interferon-alpha inhalation to ribavirin and umifenovir.

Similar percentages of patients (24, 85.7% vs. 47, 87%) in both groups received prophylactic antibiotic therapy. Non-pregnant patients used more combination antibiotics, including cephalosporin and quinolone, than the pregnant women (32, 59.3%), while single cephalosporin therapy was the major antibiotic regimen among pregnant women (20, 71.4%). In addition, reproductive-aged non-pregnant women also received more corticosteroid (21, 38.9% vs. four, 14.3%; $p = 0.041$) and immunoglobulin (19, 35.2% vs. three, 10.7%; $p = 0.035$) therapy compared with pregnant patients (Table 2).

In terms of clinical outcomes, no fatal cases were reported in both groups and there were no significant associations between pregnancy and virus clearance time (HR 1.16, 95% CI 0.65–2.01; $p = 0.62$), LOS (HR 1.10, 95% CI 0.66–1.84; $p = 0.71$), and severity of disease (OR 0.73, 95% CI 0.08–5.15; $p = 0.76$) (Fig. 2).

3.5. Maternal and neonatal outcomes

The median gestational age on admission was 38 weeks (IQR, 36.5–39), with three (10.7%) in the first trimester, one (3.6%) in the second trimester and 24 (85.7%) in the third trimester. All pregnant women in the first and second trimester terminated pregnancy due to concerns of side-effects from drugs, radiological examination and COVID-19, and the decisions were made by themselves after

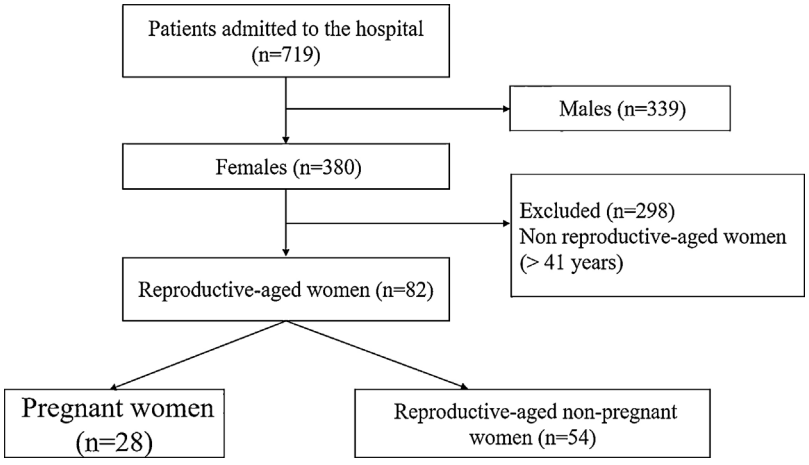

Fig. 1. Flow chart of the study inclusion process.

Table 1
Baseline characteristics of pregnant and non-pregnant reproductive-aged women with coronavirus disease 2019 (COVID-19)

Characteristics	Pregnant women ($n=28$)	Non-pregnant women ($n=54$)	p-value
Baseline			
Age (years)	30 (26.75–32)	31.00 (28.00–35.00)	0.097
Time from illness onset to hospital admission (days)	1.00 (1.00–6.50)	7.00 (5.00–10.00)	< 0.001
Severity of disease			
Mild	2 (7.1)	0 (0.0)	0.062
Normal pneumonia	24 (85.7)	53 (98.1)	–
Severe	2 (7.1)	1 (1.9)	–
Comorbidities			
Hypertension	1 (3.6)	0 (0.0)	0.599
Diabetes	2 (7.1)	4 (7.4)	–
Chronic hepatitis B virus infection	2 (7.1)	2 (3.7)	–
Hypothyroidism	1 (3.6)	1 (1.9)	–
Symptoms			
Fever	5 (17.9)	29 (53.7)	0.004
Malaise	1 (3.6)	3 (5.6)	1
Cough	7 (25.0)	32 (59.3)	0.007
Dyspnea	2 (7.1)	6 (11.1)	0.856
Abdominal pain	5 (17.9)	0 (0.0)	0.007
Signs			
Respiratory rate	20 (18–22)	20 (18–20)	0.239
Heart rate	84 (80–91)	82 (77.25–99.5)	0.537
Systolic pressure (mmHg)	113 (109–128)	120.00 (112.5–125)	0.534
Diastolic pressure (mmHg)	70.5 (64.75–77.25)	74.5 (69.25–79.75)	0.067
Peripheral oxygen saturation (%)	98 (97–98)	98 (97–99)	0.868
Laboratory tests			
White blood cell count ($\times 10^9$/L)	7.54 (6.58–10.26)	4.69 (3.87–5.77)	< 0.001
< 3.5	0 (0.0)	8 (14.8)	< 0.001
3.5–9.5	18 (64.3)	44 (81.5)	–
> 9.5	10 (35.7)	2 (3.7)	–
Neutrophil count ($\times 10^9$/L)	5.87 (4.62–8.62)	2.88 (1.99–3.57)	< 0.001
Lymphocyte count ($\times 10^9$/L)	1.29 (0.91–1.71)	1.54 (1.09–2.03)	0.148
< 1.0	8 (28.6)	14 (25.9)	0.906
≥ 1.0	20 (71.4)	40 (74.1)	–
Hemoglobin (g/L)	117.5 (106.75–129)	126 (121.25–135.5)	0.018
Platelet count ($\times 10^9$/L)	175.00 (154–233)	210 (164.75–249)	0.235
< 100	2 (7.1)	0 (0.0)	0.22
≥ 100	26 (92.9)	54 (100)	–
D-dimer (mg/L)	2.80 (1.36–4.29)	0.26 (0.13–0.42)	< 0.001
< 0.5	2 (7.7)	40 (75.5)	< 0.001
≥ 0.5	24 (92.3)	13 (24.5)	–
Fibrinogen	2.88 (2.64–3)	2.18 (2.03–2.5)	< 0.001
Alanine aminotransferase (U/L)	9.8 (7.05–12.15)	13.00 (10.0–18.3)	0.006
< 40	27 (100)	52 (96.3)	0.80
≥ 40	0 (0.0)	2 (3.7)	–
Albumin (g/L)	35.5 (34–38.65)	43.00 (41–43.85)	< 0.001
Creatine (μmol/L)	43.25 (35.6–52.72)	53.25 (48.4–62.85)	0.001
< 75	25 (96.2)	49 (90.7)	0.683
≥ 75	1 (3.8)	5 (9.3)	–
Lactate dehydrogenase (U/L)	146 (127–182)	140 (118.25–163.75)	0.233
< 220	21 (84.0)	41 (97.6)	0.116
≥ 220	4 (16.0)	1 (2.4)	–
Creatine kinase (U/L)	46 (35.75–74.5)	65 (45–75)	0.34
< 140	21 (87.5)	40 (95.2)	0.51
≥ 140	3 (12.5)	2 (4.8)	–
Procalcitonin (ng/ml)	0.06 (0.04–0.13)	0.04 (0.03–0.05)	< 0.001
0.1-0.5	22 (95.7)	53 (100)	0.665
> 0.5	1 (4.3)	0 (0)	–
C reactive protein (mg/dl)	1.81 (0.44–4.84)	0.12 (0.03–0.61)	< 0.001
> 0.6	17 (68)	14 (25.9)	0.001
Radiological findings			
Pneumonia	26 (92.9)	54 (100)	0.74

discussion with their families. Two pregnant women in early third trimester continued pregnancy (30, and 33 gestational weeks, respectively) at the time of writing, while the others (22, 78.6%) delivered 23 live births (included two twins) either by cesarean section (17, 60.7%) or vaginal delivery (five, 17.9%).

One patient had preterm labor at 35 gestational weeks, but had a healthy neonate with a birthweight of 2940 g. Only one of the twins born had a birthweight less than 2500 g (2350 g), and the median birthweight of neonates was 3130 g (IQR, 2915–3390). No fetal death, neonatal death, or neonatal asphyxia was observed. All

Table 2
Treatments and clinical outcomes in pregnant and non-pregnant reproductive-aged women with coronavirus disease 2019 (COVID-19)

Treatments and outcomes	Pregnant women (n = 28)	Non-pregnant women (n = 54)	p-value
Treatments			
Antivirals			
Ribavirin	20 (71.4)	19 (35.2)	< 0.001
Umifenovir	1 (3.6)	11 (20.4)	–
Ribavirin + umifenovir	0 (0.0)	17 (31.5)	–
Interferon alpha inhalation	0 (0.0)	7 (13.0)	–
Antibiotics	24 (85.7%)	47 (87%)	
Cephalosporin	20 (71.4)	9 (16.7)	< 0.001
Quinolone	4 (14.3)	6 (11.1)	–
Cephalosporins + quinolone	0 (0)	32 (59.3)	–
Corticosteroids	4 (14.3)	21 (38.9)	0.041
Gamma globulin	3 (10.7)	19 (35.2)	0.035
Outcomes			
Hospitalization	7 (25)	0 (0)	< 0.001
Discharge	21 (75)	54 (100)	–
Death	0 (0)	0 (0)	–
Virus clearance time (days)	12 (8–26.5)	18 (12–25)	0.613
Length of hospital stay (days)	14 (12–22.25)	18 (10.25–22)	0.635

the neonates received at least two subsequent SARS-CoV-2 infection RT-PCR tests, 24–48 hours apart, with none producing a positive result. Furthermore, there was no evidence to support pneumonia diagnosis (Table 3).

4. Discussion

One of the major concerns for obstetricians during the COVID-19 outbreak was whether pregnant women would have worse outcomes compared with non-pregnant women of similar ages when infected with SARS-CoV-2. Studies had reported that pregnant women were at a higher risk of infection with H1N1 influenza and SARS-CoV, and were also associated with poorer clinical outcomes, including the need for mechanical ventilation, organ dysfunction, ICU admission, and death, in comparison with reproductive-aged non-pregnant women (Creanga et al., 2010; Jamieson et al., 2009; Lam et al., 2004). However, in our study, we found no association between pregnancy and outcomes (including severity of disease, virus clearance time, and LOS). Similar results were also reported in a recently published case series (Chen et al., 2020a).

Pregnant women infected with other respiratory viruses, such as H1N1 influenza and SARS-CoV, were reported to experience more adverse fetal events, for example miscarriage in the early trimester, fetal distress, and intrauterine growth restriction (Rasmussen and Jamieson, 2020). In our study, four patients had their pregnancy terminated in the first or second trimester, which prevented analysis of the effect of SARS-CoV-2 infection in earlier stages of pregnancy. Aside from two patients with ongoing pregnancy, all the other pregnant women in the third trimester in our study delivered a total of 23 live births without documented perinatal complications, except for one preterm birth.

Recently, a high rate of pregnancy complications was reported in a case series with 10 SARS-CoV-2 infected pregnant women, with five of them undergoing emergency caesarean section because of fetal distress (three, 30%), premature rupture of the membrane (one, 10%), and stillbirth (one, 10%), even though the severity of COVID-19 in most of these patients was classified as mild to moderate, with only one developing severe pneumonia (Liu et al., 2020). By contrast, another study enrolled 16 pregnant women with COVID-19 and 45 pregnant women without infection in their third trimester. The results did not indicate any increased risk of perinatal complications in the SARS-CoV-2 infected women, including the occurrence of severe preeclampsia, premature rupture of the membrane, fetal distress, meconium-stained amniotic fluid, premature delivery, neonatal asphyxia, and postpartum hemorrhage (Zhang et al., 2020). These contradictory results might be caused by selection bias, with small sample sizes; this suggests that the effects of COVID-19 in pregnancy warrant further studies.

Another vital question regarding COVID-19 in pregnancy is whether it could be transmitted vertically from mother to neonate – or not, as previously reported for SARS (Lam et al., 2004). A recent review assessed 38 pregnant women and their newborns in China, and no evidence for vertical transmission was identified (Schwartz, 2020). Among the included literature, one study enrolled nine pregnant women with COVID-19 in the late stage of pregnancy (Chen et al., 2020a). These researchers tested SARS-CoV-2 in amniotic fluid, cord blood, neonatal throat swab, and breastmilk samples, and all results were negative. However, the study failed to answer whether it was possible to get the infection during vaginal delivery, because all the neonates were born by cesarean section. Our study included five neonates who were born vaginally, and none of these had evidence of COVID-19, which added clinical support for the safety of vaginal delivery. However, another study investigated 19 neonates born to mothers with COVID-19 in Wuhan, of which three were reported as SARS-CoV-2 positive (Zeng et al., 2020). Because strict infection control and prevention procedures were implemented during the delivery, and all infants with COVID-19 were confirmed early on the second day of life, the authors concluded that potential vertical transmission still cannot be ruled out. Moreover, it is important to note that evidence for no vertical transmission to date is all based on the late stages of pregnancy; whether intrauterine vertical transmission could happen during the first or second trimester is still unclear.

Pregnant patients with COVID-19 received less treatment compared with non-pregnant women in our study. This reluctant therapy might be explained by concern about adverse effects in the fetus that could be generated by certain drugs, such as interferon-alpha (Hiratsuka et al., 2000; Liang and Acharya, 2020). Aside from the four cases of pregnant women who underwent a medical abortion, all other pregnant women received medications after delivery. Twenty out of 21 pregnant patients used ribavirin as an antiviral for the treatment of COVID-19. Although this was prudently used after delivery or after the decision to terminate the pregnancy, the long-term reproductive toxicity of ribavirin should also be taken into consideration (Narayana et al., 2005).

Regarding antivirus treatment in non-pregnant women, there seems to have been no standardized approach using the four

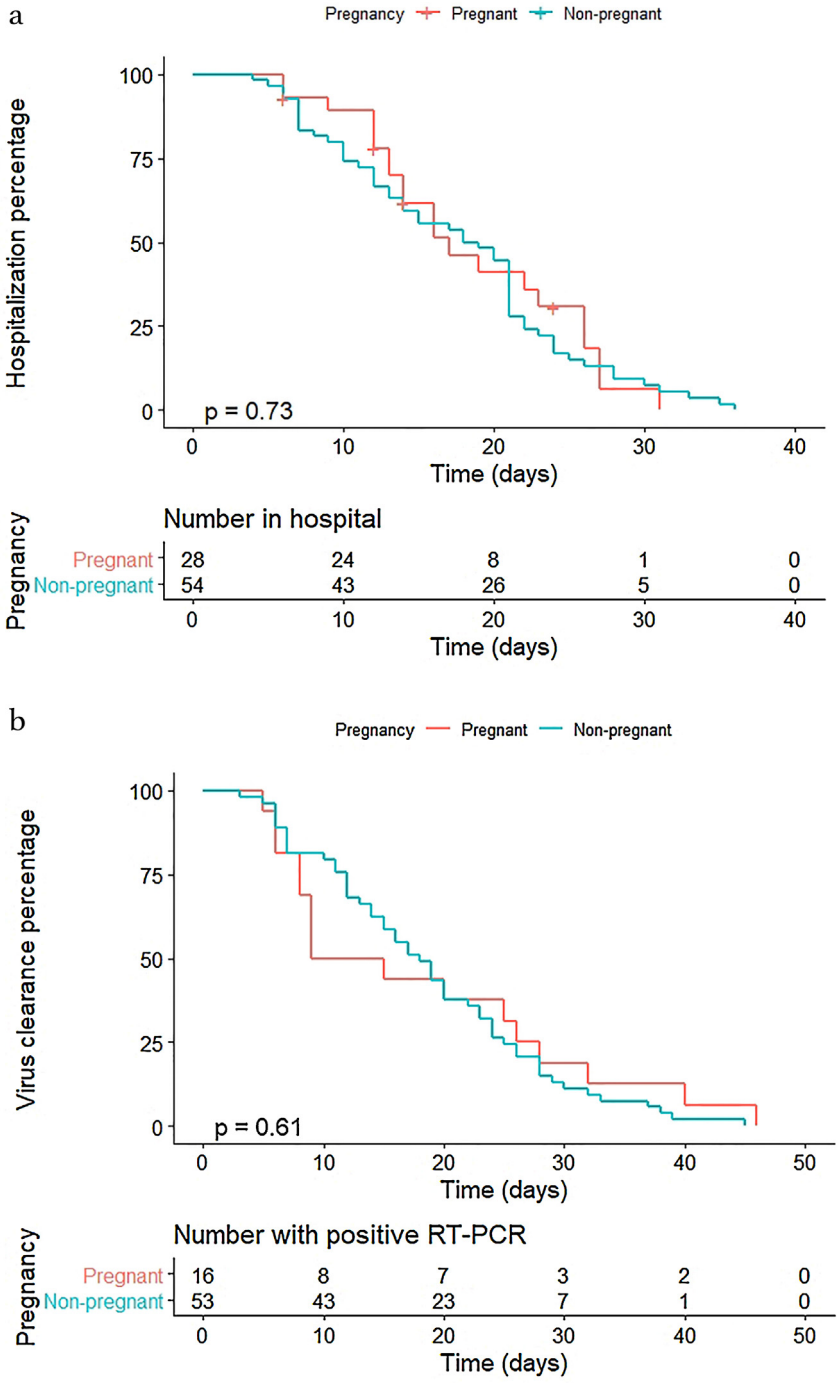

Fig. 2. Kaplan-Meier curves and log-rank tests for length of hospital stay and virus clearance time in pregnant and reproductive-aged non-pregnant women with coronavirus disease 2019 (COVID-19).

antiviral regimens. This phenomenon could be explained by the frequent updating of recommendations issued by the National Health Commission of China during the study period. Within 2 months, there were seven versions of the recommendations. Regarding corticosteroids, aside from one pregnant woman who received dexamethasone for fetal lung maturity at 35 gestational weeks, the other three pregnant women all received methylprednisolone due to complaints of dyspnea and rapid progressions on chest radiography. By contrast, most reproductive-aged non-pregnant women received methylprednisolone without clear clinical indications. Although the Chinese Thoracic Society recommended using corticosteroids prudently during the outbreak of COVID-19 (Zhao et al., 2020b), the rate of corticosteroid use remained high even with a lack of indications, as reported in previous studies (Wang Dawei et al., 2020; Zha et al., 2020). Moreover, virus clearance time was not associated with corticosteroid use in our study (HR 0.69, 95% CI 0.42–1.14; $p = 0.15$), which is consistent with a recently published study (Zha et al., 2020).

In general, decisions regarding treatment for COVID-19 in pregnant women should be more prudent until sufficient clinical evidence has been presented.

There are several limitations in our study. First, the majority of the included patients presented as mild to moderate, which limited the interpretation of results. Moreover, there were five

Table 3
Maternal and neonatal characteristics and outcomes

Characteristics and outcomes	
Maternal (*n* = 28)	*n* (%) or median (IQR)
Gestational age on admission (weeks)	38 (36.5–39)
First trimester	3 (10.7)
Second trimester	1 (3.6)
Third trimester	24 (85.7)
From admission to delivery (days)	1 (1–6)
Outcome of pregnancy	
Cesarean section	17 (60.7)
Vaginal delivery	5 (17.9)
Medical abortion	4 (14.3)
Continued pregnancy	2 (7.1)
Neonatal (*n* = 23)	*n* (%) or median (IQR)
SARS-CoV-2 infection	0 (0)
Premature delivery	1 (4.35)
Birthweight (g)	3130 (2915–3390)
Low birthweight (< 2500 g)	1 (4.35)
Apgar score (1 minute)	10 (10–10)
Apgar score (5 minute)	10 (10–10)
Severe neonatal asphyxia	0 (0)
Live birth	10 (100)
Neonatal intensive care unit admission	0 (0)
Neonatal death	0 (0)

hospitals in Wuhan designated to accommodate pregnant women with COVID-19 during the outbreak, which might have generated selection bias if more severe patients were admitted to hospitals other than the study hospital. Although a recent epidemiological study including 118 pregnant women reported similar results to ours, comprehensive research of pregnant women with COVID-19 is still warranted. Second, for some of the patients in our study the clinical diagnoses were confirmed using the specific antibody (IgM). Although the reported sensitivity and specificity were good enough, the potential for introducing selection bias should still be taken into consideration, because the test might have excluded true COVID-19 patients due to a low concentration of antibody. Moreover, in the beginning, due to the limited supply of test agents, only those with clinical diagnoses were able to receive the serological test, while those without obvious abnormalities on chest radiology or clinical symptoms were excluded, consequently generating selection bias. Third, all the delivered pregnant women were infected with SARS-CoV-2 in the late stages of pregnancy, which did not allow us to assess the probability of vertical transmission during the early trimesters. Additionally, due to the nature of the retrospective study, we were unable to test samples of the placenta, amniotic fluid, and vaginal mucosa, which weakened our conclusion of no vertical transmission potential. Finally, we used virus clearance time as one of the clinical outcomes, but RT-PCR testing for SARS-CoV-2 from respiratory samples was not routinely performed due to the lack of available agents at the beginning of the outbreak. Testing by RT-PCR for SARS-CoV-2 was ordered by attending physicians only if there were signs of improvement in COVID-19 patients according to symptoms and examination results. Subsequent tests for patients with a positive result were scheduled 2–3 days later, which might have resulted in documented virus clearance times being longer than reality. However, both groups were under the same conditions, which meant that virus clearance time was still comparable. In spite of these limitations, a study comparing pregnant women with reproductive-aged non-pregnant women is necessary and valuable, and can contribute important new information for doctors during the COVID-19 pandemic.

In conclusion, in this observational study, both pregnant and non-pregnant women infected with SARS-CoV-2 had good outcomes. There were no associations between pregnancy and severity of COVID-19, virus clearance time, and LOS. Regarding vertical transmission, in this small group of cases there was no evidence supporting vertical transmission of COVID-19 in the late stages of pregnancy, including vaginal delivery. However, due to the limited data, the potential for vertical transmission is still uncertain and warrants further study.

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Conflicts of interest

None to declare

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