

Original Article

Clinical, Laboratory, and Obstetrics Features of Novel Coronavirus Disease 2019 (COVID-19) during Pregnancy

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Received: 16 September, 2021; Accepted: 05 February, 2022

Abstract

Background: The novel coronavirus disease 2019 (COVID-19) remains a new entity; the data on its clinical features, complications, and adverse outcomes during pregnancy are still to be identified and described. Several studies have reported a series of COVID-19 infections in pregnancy, the maternal and the neonatal outcome from different ethnicities and geographical regions.

Materials and Methods: This retrospective cross-sectional study was conducted in the obstetrics department of Mahdijeh Hospital of Tehran, Iran, between February and April 2020. We included a series of 23 singleton pregnancies presenting to our department with fever and dry cough. All patients were tested for COVID-19 infection using nasopharyngeal swabs.

Results: We included 23 singleton pregnant patients with a mean age of 28.1 ± 6.16 (ranging from 15 to 39) years and gestational age of 29.96 ± 10.2 [ranging from 7 to 40] weeks. Of these patients, 7 (30.4%) tested positive for the SARS-CoV-2. Among the total patient population, 16 (69.5%) had elevated serum levels of C-reactive protein (CRP), 1 [4.3%] had lymphopenia, and 8 (34.7%) had elevated erythrocyte sedimentation rate (ESR). Only 2 (8.7%) patients had positive findings of chest CT-scan. Most newborns had acceptable Apgar and birth weight, and only 4 (17.4%) required NICU admission.

Conclusion: The clinical characteristics of the COVID-19 infection in pregnant patients were comparable to those of non-pregnant patients. We did not record a high frequency of lymphopenia and leukopenia, probably due to leukocytosis during pregnancy. CRP was a sensitive marker for COVID-19 pneumonia in pregnant patients.

Keywords: Novel coronavirus 2019 (COVID-19), Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), Pregnancy, Features, Obstetric outcome

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Please cite this article as Parsa Y, Shokri N, Rafiee F, Naeiji Z, Jahedbozorgan T, Zadehmodares Sh, et al. Clinical, Laboratory, and Obstetrics Features of Novel Coronavirus Disease 2019 (COVID-19) during Pregnancy. Novel Biomed. 2022;10(2):93-100.

Introduction

The novel coronavirus disease 2019 (COVID-19)

caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first appeared in Wuhan, China, in late December 2019^{1,2}. It was rapidly

spread worldwide, being announced as a pandemic on March 11th, 2020, by the World Health Organization (WHO)³. Approaching the end of June, approximately 98 million people are infected worldwide, and 500,000 have died due to the infection and its complications⁴. The virus causes respiratory illness and involves the upper and lower respiratory tract and the gastrointestinal tract, hepatic, neurologic, and renal systems⁵. COVID-19 disease ranges from asymptomatic to severe respiratory illness and can cause respiratory failure requiring mechanical ventilation⁶.

As the COVID-19 disease remains a new entity, the data on its clinical features, complications, and adverse outcomes during pregnancy are still to be identified and described while the data are scarce⁷. Several have reported a series of COVID-19 infections in pregnancy, the maternal and the neonatal outcomes, and the treatment strategies from different ethnicities and geographical regions⁸⁻¹⁴. None of the studies except one article reported vertical transmission of the virus from the mother to the newborn; however, the evidence is scarce and needs further investigation^{7,8}. The pregnancy-specific characteristics of the disease are not well-described as there is a shortage of published studies. Pregnant women had a higher mortality rate and tendency to severe illness during SARS and H1N1 epidemics¹⁵, while the current data for COVID-19 does not support this fact. The present study aimed to report the clinical characteristics and the maternal outcome of a series of Iranian pregnant women with COVID-19 infection.

Methods

Study population: This retrospective cross-sectional study was conducted in the obstetrics department of Mahdiah Hospital, a tertiary obstetrics referral center affiliated with Shahid Beheshti University of Medical Sciences, Tehran, Iran, between February and April 2020. We included 23 pregnant women in the current study who were suspected of having COVID-19 as they presented to our department with fever and dry cough. We have excluded patients with inadequate medical chart information and those with symptoms that were not typical for the COVID-19 disease. The study protocol was approved by the institutional review board (IRB) and medical ethics committee of

Shahid Beheshti University of Medical Sciences. As this was a retrospective medical chart review, the IRB and the medical ethics committee waived the need for informed written consent.

Ethical approval: All methods used in the present study are based on the principles of Helsinki Human Studies. Patients' information will be kept entirely confidential during and after the study. The study's methodology was approved before by the ethics committee of Shahid Beheshti University of Medical Sciences with the ethics code of IR.SBMU.RETECH.REC.1399.731.

Study protocol: The medical charts of the included patients were reviewed, and the demographic information, obstetrics history, clinical characteristics, and outcomes were recorded. After the frame checklist, we reviewed demographic and clinical records, laboratory findings (CBC, ESR, CRP), chest radiography, and computerized tomography (CT)-scan for all 23 pregnant patients. All information was obtained and curated with a customized data collection, and one investigator reviewed the data collection forms to verify their accuracy.

All the included patients have been tested for SARS-CoV-2 through direct sampling of the upper respiratory tract via nasopharyngeal swabs. The samples were sent to Masih Daneshvari hospital, the central laboratory for isolation and diagnosis of the COVID-19 disease, affiliated with Shahid Beheshti University of Medical Sciences. The tests were all conducted according to the standard WHO protocol. Briefly, nucleic acid was extracted from the samples with the Qiasymphony system (QIAGEN, Hilden, Germany). All oligonucleotides were synthesized. Thermal cycling was performed at 55°C for 10 min for reverse transcription, followed by 95°C for 3 min, and then 45 cycles of 95°C for 15 s, 58°C for 30 s. SARS-CoV-2 RNA was detected using primer and probe sequences for screening and confirmation based on the line described by Victor M Corman et al.¹⁶.

Statistical analysis: All the data were entered into a computerized database and analyzed using the statistical package for social sciences (SPSS Inc., Chicago, Illinois, USA) version 22.0. Data are presented as mean±SD and proportions as appropriate. Chi-square and Fisher's exact tests compared the proportions between those testing positive and negative

for SARS-CoV-2. Independent t-test was used to compare the parametric variables between groups. A two-sided p-value of less than 0.05 was considered statistically significant.

Results

We have included 23 singleton pregnant patients referring to our center with signs and symptoms of COVID-19 disease. The mean age of the patients was 28.1 ± 6.16 (ranging from 15 to 39) years, and the gestational age was 29.96 ± 10.2 (ranging from 7 to 40) weeks. Of these patients, 7 (30.4%) tested positive for the SARS-CoV-2. None of the patients had a high-grade fever, and the temperature ranged from 37.0 to

40.3°C. None of the patients had gastrointestinal symptoms, and none required mechanical ventilation. The baseline characteristics of the included patients are summarized in Table 1.

All patients were treated with hydroxychloroquine and wide-spectrum antibiotics. Among the patients, 16 (69.5%) had elevated serum levels of C-reactive protein (CRP), 1 (4.3%) had lymphopenia, and 8 (34.7%) had elevated erythrocyte sedimentation rate (ESR). All the patients had normal white blood cell (WBC) counts. The radiological signs of COVID-19 disease were detected in 2 (8.7%) patients, while they were unremarkable in 21 (91.3%) of the patients. 16 (69.4%)

Table 1: The clinical and pregnancy characteristics of 23 singleton pregnancies with suspected COVID-19 disease.

Variables	Value
Age (years)	28.1 ± 6.16
Gestational age (weeks)	29.96 ± 10.2
Ethnicity	
Iranian (%)	15 (65.2%)
Afghan (%)	8 (34.8%)
Gravid	
1 (%)	10 (43.5%)
2 (%)	8 (34.8%)
>3 (%)	5 (21.7%)
Parity	
0 (%)	11 (47.8%)
1 (%)	10 (43.5%)
≥2 (%)	2 (8.7%)
Abortion	
0 (%)	19 (82.6%)
≥1 (%)	4 (17.3%)
Comorbidities	
Minor thalassemia (%)	1 (4.3%)
Gestational diabetes mellitus (%)	1 (4.3%)
Sign and Symptoms	
Fever (%)	23 (100%)
Dry cough (%)	6 (26.1%)
Dyspnea (%)	2 (8.7%)
Chest radiography or HRCT	
Normal (%)	21 (91.3%)
Abnormal (%)	2 (8.7%)
COVID-19 test	
Negative (%)	16 (69.6%)
Positive (%)	7 (30.4%)
IUGR (%)	1 (4.3%)
Preeclampsia (%)	1 (4.3%)
Delivery	
Normal vaginal delivery (%)	9 (39.1%)
Cesarean section (%)	7 (30.4%)
Neonatal outcome	
Birth weight (grams)	2607.33 ± 823.9
Apgar	8.56 ± 3.36
NICU admission (%)	4 (17.4%)

HRCT: High resolution computerized tomography; **IUGR:** Intrauterine growth retardation; **NICU:** Neonatal intensive care unit

Table 2: The laboratory findings of 23 singleton pregnancies with suspected COVID-19 disease.

Variables	Value
Creatinine (mg/dL)	0.781 ± 0.098
Lactate dehydrogenase (U/L)	536.40 ± 152.8
Aspartate transaminase (U/L)	18.43 ± 4.96
Alanine transaminase (U/L)	36.98 ± 32.5
Erythrocyte sedimentation rate (sec)	46.73 ± 18.2
C-Reactive Protein	36.98 ± 32.5
WBC (×10 ⁶ /mL)	12.13 ± 4.94
Lymph (×10 ³ /mL)	1747.3 ± 658.4
Platelet (×10 ⁶ /mL)	204.08 ± 57.1
Hemoglobin (mg/dL)	10.67 ± 1.03
O ₂ Saturation (%)	96.7 ± 2.5
Oral temperature (°C)	37.80 ± 0.91
Pulse rate (per min)	100.7 ± 10.1
Respiratory rate (per min)	18.52 ± 4.43

WBC: White Blood Cell

women delivered through normal vaginal delivery (NVD) route. Most newborns had acceptable Apgar and birthweight, and only 4 (17.4%) required NICU admission. Table 2 summarizes the laboratory findings of the patients.

We have also compared the clinical characteristics, laboratory findings, and the pregnancy outcome of those who tested positive and negative for SARS-CoV-2. As shown in Table 3, there was no significant difference between these two study groups regarding the baseline characteristics, clinical characteristics, and pregnancy outcome. Those with COVID-19 disease had higher rates of cough and dyspnea than those who tested negative, while this difference did not reach a statistically significant level ($p=0.068$). Regarding the laboratory information, as demonstrated in Table 4, the two study groups were comparable except for CRP, which was significantly higher in those who tested positive for SARS-CoV-2 compared to negative cases ($p=0.004$). The vital signs and the temperature were also comparable between the study groups.

Discussion

In these retrospective case series, we reported the clinical, laboratory, and pregnancy characteristics of 23 singleton pregnancies suspected of having COVID-19 disease. The clinical, laboratory, and outcome features of those who tested positive for COVID-19 pneumonia were similar to patients with negative test results. In addition, pregnant women with COVID-19 disease had similar characteristics compared to non-

pregnant individuals. There was no maternal and neonatal mortality in this series, and none of the morbidities were attributable to the COVID-19 disease. We also did not observe any sign of vertical transmission in this series. The results are comparable with those previously reported^{7, 10, 12, 13}, while some authors have reported increased preterm birth rates and maternal morbidity for COVID-19 patients^{9, 11, 14}.

Some clinicians believe that pregnant women suffer from a suppressed immune system and thus will experience more severe respiratory illness and a higher mortality rate^{17, 18}. Some previous series have demonstrated that those with COVID-19 disease experience more severe respiratory illness and higher morbidity and mortality^{9, 11, 19}. However, we did not record higher mortality and morbidity rates in either mothers or newborns in the current series. Chen et al.²⁰ reported the first series of pregnant women with COVID-19 pneumonia in China. They demonstrated that the clinical characteristics of COVID-19 pneumonia in pregnant women were similar to those reported for non-pregnant adult patients who developed COVID-19 pneumonia. Findings from this small group of cases suggest that there is currently no evidence for intrauterine infection caused by vertical transmission in women who develop COVID-19 pneumonia in late pregnancy²⁰.

It is postulated that in pregnant patients with COVID-

Table 3: Comparing the clinical and pregnancy characteristics between those with positive and negative SARS-CoV-2 test.

	Positive (n=7)	Negative (n=16)	p-value
Age (years)	29.57 ± 5.44	27.31 ± 6.49	0.432
Gestational age (weeks)	24.86 ± 12.32	32.19 ± 8.62	0.115
Ethnicity			
Iranian (%)	5 (71.4%)	10 (62.5%)	0.998
Afghan (%)	2 (29.6%)	6 (37.5%)	
Gravid			
1 (%)	4 (57.1%)	6 (37.5%)	0.568
2 (%)	1 (14.3%)	7 (43.8%)	
>3 (%)	2 (28.6%)	3 (18.8%)	
Parity			
0 (%)	4 (57.1%)	7 (43.8%)	0.081
1 (%)	1 (14.3%)	9 (56.3%)	
≥2 (%)	2 (28.6%)	0 (0.0%)	
Abortion			
0 (%)	7 (100.0%)	12 (75.0%)	0.347
≥1 (%)	0 (0.0%)	3 (18.8%)	
Comorbidities			
Minor thalassemia (%)	0 (0.0%)	1 (6.3%)	0.619
GDM (%)	0 (0.0%)	1 (6.3%)	
Sign and Symptoms			
Fever (%)	7 (100.0%)	16 (100.0%)	0.068
Dry cough (%)	2 (28.6%)	4 (25.0%)	
Dyspnea (%)	2 (28.6%)	0 (0.0%)	
Chest radiography or HRCT			
Normal (%)	6 (85.7%)	15 (93.8%)	0.526
Abnormal (%)	1 (14.3%)	1 (6.3%)	
IUGR (%)	0 (0.0%)	1 (6.3%)	0.998
Preeclampsia (%)	1 (14.3%)	0 (0.0%)	0.304
Delivery			
Normal vaginal delivery (%)	2 (50.0%)	7 (58.3%)	0.998
Cesarean section (%)	2 (50.0%)	5 (41.7%)	
Neonatal outcome			
Birth weight (grams)	2910.0 ± 425.7	2531.6 ± 894.3	0.497
Apgar	7.25 ± 4.8	9.00 ± 2.86	0.386
NICU admission (%)	1 (14.3%)	3 (18.8%)	0.996

HRCT: High resolution computerized tomography; **IUGR:** Intrauterine growth retardation; **NICU:** Neonatal intensive care unit

19, respiratory symptoms are more common than those of non-pregnant patients due to elevated diaphragms. Other risk factors that make pregnant patients prone to respiratory diseases are basal atelectasis from the enlarged uterus, reduced functional residual capacity, and increased oxygen consumption^{12, 17}. However, in the present study, we demonstrated that the frequency of the respiratory symptoms was as high as in non-pregnant patients, and the O₂ saturation was comparable between COVID-19 positive and negative patients. However, Chen et al.²⁰ reported a higher frequency of respiratory symptoms as well as lower levels of oxygen saturation in patients with COVID-19 pneumonia. All the patients in the reported series have delivered within a short interval after COVID-19 pneumonia diagnosis²¹.

Report of the WHO-China joint mission on 147 pregnant patients with COVID-19 pneumonia, reported 1% severe illness where patients needed mechanical ventilation, experienced shock and were admitted in intensive care units (ICU)²². Breslin et al.⁹ reported seven COVID-19 positive pregnant patients, of whom, four were admitted to the hospital, including two who required supportive care with intravenous hydration. The other two admitted patients, asymptomatic on admission to the hospital, presenting instead for obstetrically indicated labor inductions, became symptomatic after delivery, each requiring ICU admission¹⁰. Yu et al.²³ described the clinical features of 7 pregnant patients with COVID-19 infection admitted to a single center in China. All the patients had a cesarean section within three days of clinical

Table 4: Comparing the laboratory characteristics between those with positive and negative SARS-CoV-2 test.

	Positive (n=7)	Negative (n=16)	p-value
Creatinine (mg/dL)	0.78 ± 0.8	0.78 ± 0.11	0.959
Lactate dehydrogenase (U/L)	580.0 ± 163.8	525.5 ± 174.2	0.798
Aspartate transaminase (U/L)	17.67 ± 2.51	19.00 ± 6.63	0.759
Alanine transaminase (U/L)	15.33 ± 3.05	11.50 ± 2.38	0.119
ESR (sec)	51.33 ± 23.4	45.00 ± 16.4	0.481
C-Reactive Protein	64.99 ± 44.25	24.73 ± 15.74	0.004
WBC (×10 ⁶ /mL)	9.38 ± 4.41	13.34 ± 4.80	0.077
Lymph (×10 ³ /mL)	1.51 ± 0.56	1.85 ± 0.70	0.342
Platelet (×10 ⁶ /mL)	190.14 ± 48.03	210.18 ± 61.06	0.451
Hemoglobin (mg/dL)	10.84 ± 1.05	10.60 ± 1.05	0.616
O ₂ Saturation (%)	93.6 ± 2.36	98.0 ± 2.14	0.825
Oral temperature (°C)	38.04 ± 1.06	37.70 ± 0.85	0.420
Pulse rate (per min)	101.71 ± 8.3	100.25 ± 10.9	0.509
Respiratory rate (per min)	17.57 ± 2.44	18.94 ± 5.07	0.756

ESR: Erythrocyte sedimentation rate; WBC: White blood cell

presentation. The outcomes for pregnant women and neonates were good. Three neonates were tested for SARS-CoV-2, and one neonate was infected with SARS-CoV-2 36 h after birth²³. In a series by Rasmussen et al.,¹² common symptoms and signs of COVID-19 in non-pregnant patients were fever (88-100%), cough (59-82%), myalgia (11-35%), headache (7-8%) and diarrhea (2-10%). All the patients had abnormalities on radiographic imaging of the chest. However, in our series, all the patients had fever on presentation (100.0%). About half of them had cough and dyspnea, but none had myalgia or diarrhea. Only two patients had abnormal chest imaging. Most of the studies reported that pregnant women have a similar scenario compared to non-pregnant patients and the clinical characteristics are similar^{10, 12, 14, 22, 24}.

The most common laboratory findings have been reported to be lymphopenia, leukopenia, and elevated serum CRP and ESR¹. In our series, however, none of the patients had leukopenia, and only 1 had lymphopenia, which is probably due to reactive leukocytosis during pregnancy. Some other studies confirm our results as well^{7-10, 20}. Thus, in pregnancy, lymphopenia is not a reliable factor to predict COVID-19 infection. A recent systematic review and meta-analysis by Rodriguez-Morales et al.²⁵ demonstrated that serum levels of CRP and ESR were among the most sensitive and reliable markers of COVID-19 disease. As demonstrated in our series, CRP and ESR were increased in most patients. We have also demonstrated that serum level of CRP was significantly higher in patients with positive test

results than in negative ones. Finally, our series' neonatal outcome was good, and none experienced severe complications. As reported by Khan et al.²⁶, those delivering through the NVD route are at higher risk of intrapartum transmission of the virus to the newborn. The neonatal outcomes reported in their series were acceptable, with no severe complication recorded²⁶. Schwartz et al.²⁷ reviewed the neonatal outcome of 38 neonates born to mothers who had COVID-19 pneumonia. Their analysis revealed that unlike coronavirus infections of pregnant women caused by SARS and MERS, in these 38 pregnant women, COVID-19 did not lead to maternal deaths. Importantly, and similar to pregnancies with SARS and MERS, there were no confirmed intrauterine transmission of SARS-CoV-2 from mothers with COVID-19 to their fetuses²⁷. The results of our study confirm the findings of this review.

We note some limitations to the current study. First, the study had a small sample size due to the limited cases available. We have included all the pregnant patients with symptoms similar to COVID-19 who presented to our center. The number of COVID-19 positive cases is comparable to other series from other centers. However, a systematic review or meta-analysis is required to gather all the issues. The second limitation was the study's retrospective nature, leading to missing some information. Moreover, last, we could not evaluate whether COVID-19 pneumonia affected the route of delivery as the database could not be used to evaluate the cause and effect relationship. Taking it all together, this is the first report of COVID-19 infection

during pregnancy from the Iranian population.

Conclusion

The clinical characteristics of the COVID-19 infection in pregnant patients were comparable to those of non-pregnant patients. We did not record a high frequency of lymphopenia and leukopenia, probably due to leukocytosis during pregnancy. CRP was a sensitive marker for COVID-19 pneumonia in pregnant patients.

Acknowledgment

We want to thank all the patients and their families who participated in the current study. We would also like to acknowledge the editorial assistance of the Diba Negar Research Institute to improve the manuscript's English and style.

Conflict of interest

The authors further declare that they have no conflict of interest.

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