Chronic Diseases Journal

DOI: 10.22122/cdj.v10i3.665 Published by Vesnu Publications

Clinical features and consequences of COVID-19 infection in pregnant women undergoing delivery in Kurdistan Province, Iran

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Original Article

Abstract

BACKGROUND: With the increasing prevalence of coronavirus disease 2019 (COVID-19), the number of pregnant women with this virus who give birth is also increasing. This study evaluates the clinical features and consequences of COVID-19 infection in pregnant women undergoing delivery in Kurdistan Province, Iran.

METHODS: In this descriptive study, we analyzed the clinical characteristics and delivery outcomes of pregnant women with laboratory-confirmed COVID-19 disease admitted to Besat Hospital of Kurdistan University of Medical Sciences, Sanandaj, Iran, from February 25, 2020, to August 21, 2020.

RESULTS: Among 192 pregnant women with laboratory-confirmed COVID-19 infection during the study period, 37 were admitted for delivery. Out of the 37 patients, 15 patients had a normal vaginal delivery, and 22 patients were delivered by cesarean. Fever and cough (32.40%) and shortness of breath (11.37%) were the main symptoms of the pregnant women in our study. None of our patients needed ventilator support or died.

CONCLUSION: Based on the results of our survey, pregnancy augments neither the signs and symptoms of COVID-19 nor the mortality rate. However, the rate of cesarean and preterm delivery increased.

KEYWORDS: Pregnancy; COVID-19; SARS-CoV-2; Cesarean

Date of submission: 07 Dec. 2021, ***Date of acceptance:*** 06 Mar. 2022

Citation: Zare S, Mahdavian Naghash Zargar S, Arianejad A, Zokaie M, Shahgheibi S, Rahimi E, et al. **Clinical features and consequences of COVID-19 infection in pregnant women undergoing delivery in Kurdistan Province, Iran.** Chron Dis J 2022; 10(3): 164-70.

Introduction

During pregnancy, the pregnant mother undergoes significant anatomical and physiological changes to provide a suitable environment for the development of a fetus. The changes begin as early as the first trimester and peak in the delivery and return to pre-pregnancy levels a few weeks after

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delivery. These changes begin after gestation and affect all body systems.[1]

Pregnant women are at increased risk of some infections due to the physiologic changes of pregnancy. Infections may cause complications during the pregnancy and some maternal infections are transmissible to the fetus.[2]

During pregnancy, the potential effects of the infection on the mother and fetus should be considered. Pregnant women may be more susceptible to the acquisition of certain infections, such as malaria, human immunodeficiency virus (HIV), listeriosis, influenza, and hepatitis E.[3] These results reinforce the importance of infection prevention as well as the importance of early identification and treatment of the infections during pregnancy. Indeed, due to lower immunity and high levels of estrogen and progesterone, pregnant women are particularly more liable to severe respiratory disease and pneumonia.[4] Moreover, changes in physiological conditions during pregnancy, such as elevated diaphragm, increased oxygen demand, and respiratory mucosal edema causes hypoxia intolerance.[4] Together, these factors make pregnant women and their fetuses more liable to respiratory disease outbreaks.[5]

In late December 2019, China reported many cases of pneumonia due to an unknown virus in Wuhan, China. On January 20, 2020, the World Health Organization (WHO) nominated this kind of virus as the new coronavirus-2019 and the disease caused by it as coronavirus disease 2019 (COVID-19), and then as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2),[6] which led to a massive pandemic around the world with millions of infections and deaths. COVID-19 could result in a wide range of diseases alternating from asymptomatic to severe respiratory disorder and death.[7] The most common symptoms of COVID-19 infection include fever, cough, myalgia, headache, fatigue, and diarrhea.[8]

Pregnant women and their fetuses are considered high-risk populations for COVID-19 infection which may enhance the risk of adverse pregnancy outcomes.[9] There is little evidence of an effect of COVID-19 in early pregnancy (up to 12 weeks of gestation). Seasonal flu has been associated with higher abortion rates and population monitoring and community-based testing are needed to determine if this is the case with COVID-19 as well. The COVID-19 infection could cause increased rates of adverse pregnancy outcomes such as fetal growth restriction, preterm birth, and perinatal mortality.[10,11]

There are high levels of circulating coagulation and fibrinolytic factors, such as plasmin, during pregnancy that may be involved in the pathogenesis of SARS-CoV-2 infection.

Pregnant women with COVID-19 may have increased risk factors for thrombosis.[12,13] This hypothesis is confirmed by a case report describing the mortality of a 29-week gestation with COVID-19 due to large pulmonary embolism and basilar artery embolism.[14]

In a study conducted to investigate the effect of COVID-19 on pregnant women and infants in China, fever (87.5%) and cough (53.8%) were the most common symptoms reported, followed by fatigue (22.5%), diarrhea (8.8%), shortness of breath (11.3%), sore throat (7.5%), and myalgia (16.3%).[15]

The clinical features of pregnant women with COVID-19 are similar to those of non-pregnant adults. Fetal and neonatal outcomes look good in most cases.[15]

In a study conducted on COVID-19-positive pregnant women in Shiraz, Iran, the result showed that 78% suffered from mild or moderate COVID-19, 99.9% had successful termination, 86% had a cough, and 68% had a fever. The overall ratios of vertical transmission, stillbirth, and neonatal mortality were zero.[16]

Despite numerous studies on the clinical features of COVID-19 since the onset of the disease, at the present, the consequences of

COVID-19 in pregnant women and their infants are not quite understood.

Due to the special importance of pregnant women's health, it is important to identify the features and complications of COVID-19 in pregnant women, to make the necessary planning and policies for the health system. Accordingly, this descriptive study aimed to evaluate the clinical features and consequences of COVID-19 in pregnant women who have undergone delivery in Kurdistan Province, Iran.

Methods

After approval of this descriptive study by the Ethics Committee of Kurdistan University of Medical Sciences, Sanandaj, Iran (IR.MUK.REC.1399.047), we reviewed clinical characteristics and delivery outcomes of pregnant women with laboratory-confirmed COVID-19 disease admitted to Besat Hospital of Kurdistan Province, from February 25, 2020, to August 21, 2020. All deliveries were performed in centers considered for pregnant women with COVID-19 that were equipped with isolation rooms. Inclusion criteria included: pregnant women of all age groups, admission to the hospitals for any reason one week before delivery until 36 hours later, having a positive test for COVID-19 confirmed by real-time polymerase chain reaction (RT-PCR), and giving birth within the time allocated for this study. Since we did a simple descriptive study, the sample size calculation was not necessary. However, the studied population was all the patients who matched the inclusion criteria and filled out the informed consent form.

Clinical screening and triage were performed in terms of COVID-19 based on WHO guidelines.[17] Additionally, diagnosis of COVID-19 using the obtained results from maternal and neonatal discharge tests with a swab sample was performed according to the guidelines of the Ministry of Health of Iran. All participating women were treated according to the national guidelines of COVID-19 during pregnancy and personalized treatment continued regarding clinical and laboratory findings for each participant.[18] Additional obstetric interventions were not performed in these patients.

Fetal growth and fetal status stability were assessed at admission and fetal heart rate was monitored continuously during labor and delivery. Breastfeeding was performed according to the international guidelines while the COVID-19 test results were positive for a pregnant woman during labor.[19] The correct method of wearing and removing the mask and frequent hand washing with alcohol-based hand sanitizers as well as soap and water was taught to all women participating in the study at the beginning of the study, during labor, and after delivery. The information required for the study was extracted through medical records, including the history of any obstetric or medical morbidity, clinical signs and symptoms of the disease at the time of admission and at the time of diagnosis, treatments used for COVID-19, diagnostic test results, delivery process information, neonatal and breastfeeding data, skin-to-skin contact between mother and infant, COVID-19 test results of infants, positive time, and neonatal results. Women and their babies were followed up for up to two weeks after discharge from the hospital. Data analyses were performed using SPSS software (version 20, IBM Corporation, Armonk, NY, USA). The mean and variance were calculated for the considered variables.

All patient information was kept confidential and their information was not shared with other persons in any way. In addition, all ethical protocols in this study have been observed and patients' privacy has been preserved.

All procedures performed in studies involving human participants were following the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later

amendments or comparable ethical standards.

Informed consent was obtained from all individual participants included.

Results

Among 192 pregnant women with positive RT-PCR during the study period, 37 were in delivery status and admitted to the delivery ward. Diagnosis of COVID-19 was made before admission to the hospital in 20, during the delivery period in 6, and during 36 hours of postpartum in 11 cases. Out of 37 patients, 15 patients had a normal vaginal delivery, 22 patients delivered by elective cesarean, and one patient underwent emergency cesarean due to COVID19 complications.

Demographic data, patients' signs and symptoms, interventions for the treatment of COVID-19 infection, and delivery methods are given in tables 1-4.

Table 1. Demographic data of patients

Variable	Min	Max	Mean ± SD
Age (year)	20.0	48.0	30.11 ± 6.24
BMI (kg/m^2)	21.0	42.1	29.35 ± 4.53
Gestational age (year)	32.0	40.0	37.49 ± 1.96
Birth weight (g)	1100.0	4000.0	3043.51 ± 555.20

SD: Standard deviation; BMI: Body mass index

The mean age of the subjects was 30 years, mean body mass index (BMI) was 29 kg/m^2, and mean gestational age was 37 years (Table 1). 75.6% were employed and 81% were educated. None of them had background diseases (Table 2).

Table 2. Socio-economic data of patients

Variable	Yes [n (%)]	No [n (%)]
Presence of background diseases	0 (0)	37 (100)
Residence in the urban area	22 (59.5)	15 (40.5)
Employed	9 (24.4)	28 (75.6)
Academic education	7 (19.0)	30 (81.0)

Fever and cough were the main symptoms of pregnant women in our study (25/37, 67.6%). Another common symptom was shortness of breath which was presented in 11 out of 37 patients (29.7%), of which 2 (5.4%) needed supportive oxygen therapy. Dyspnea, anosmia, taste agnosia, and nausea were among the less common symptoms. Spontaneous preterm labor occurred in seven participants. Premature rupture of embryonic membranes fell out in 5.4% of cases. None of the patients or neonates required hospitalization in the intensive care unit (ICU) in terms of severe COVID-19 infection (Table 3).

Table 3. Clinical symptoms of patients

Variable	n (%)
Cough	25 (67.6)
Fever	25 (67.6)
Dyspnea	11 (29.7)
Myalgia	8 (21.6)
Spontaneous preterm labor	7 (18.9)
Loss of smile	5 (13.5)
Diarrhea	4 (10.8)
Loss of taste	3 (8.1)
Supportive oxygen therapy	2 (5.4)
Premature rupture of embryonic membranes	2 (5.4)
Nausea	2 (5.4)
Tachycardia	1 (2.7)
Skin rash	1 (2.7)
Tachypnea	1 (2.7)
Lack of appetite	1 (2.7)
Mother administration in the ICU ward	0 (0)
Neonate administration in the ICU ward	0 (0)

ICU: Intensive care unit

Cesarean section was 18.9%, and normal vaginal delivery was 81%. Most patients gave birth normally and there were few neonates with positive polymerase chain reaction (PCR) (Table 4).

Table 4. Delivery method and pregnancy results

Variable	Number/total (%)
Cesarean section	7/37 (18.9)
Normal vaginal delivery	30/37 (81.0)
Neonates with positive PCR in NVD	2/30 (6.6)
Neonates with positive PCR in CS	1/7 (14.0)

PCR: Polymerase chain reaction; NVD: Normal vaginal delivery; CS: Cesarean section

Discussion

In this descriptive study, we report the clinical characteristics, method of delivery, and neonatal outcomes of 37 pregnant women with laboratory-confirmed COVID-19 infection. All of the patients had mild to moderate forms of the disease. The most common symptoms in our study were fever and cough. Lechien et al. reported 1420 non-pregnant patients with COVID-19 with mild to moderate disease from 18 European hospitals. In this study, the most common symptoms were headache, anosmia, weakness, cough, muscle pain, sore throat, and fever. The clinical characteristics of our patients with COVID-19 infection during pregnancy were different and less severe than the Lechien et al. study.[20]

Pneumonia or death did not occur in 37 pregnant patients in our study. Chen et al. reported nine pregnant patients without pneumonia or death.[25]

Elwood et al. also reported that all 23 positive pregnant women for COVID-19 infection revealed mild or asymptomatic disease and none of the symptomatic patients required hospitalization for their infection.[21] These findings are consistent with our results.

Due to physiological adaptive modifications during pregnancy like diaphragm elevation, enlarged oxygen consumption, and respiratory tract mucosal edema, pregnant women are theoretically vulnerable to respiratory problems and pneumonia.[22]

There is currently no evidence to suggest that the development of COVID-19 pneumonia in the third trimester of pregnancy could lead to the occurrence of severe adverse outcomes in neonates and fetal infection that might be caused by intrauterine vertical transmission.

More than 80% of the subjects were delivered vaginally. Post-partum radiological findings confirmed the presence of pneumonia in 10 individuals; none of them required respiratory support.

Lymphopenia and elevated blood C-reactive protein (CRP), persistent fever, and worsening maternal dyspnea were findings that persuaded us to select cesarean section.

Despite the high rate of cesarean delivery in this study and the presence of some other pregnancy complications such as preterm delivery and premature rupture of membranes, it may not be concluded that viral infection alone causes these complications because the study includes no concurrent control group with healthy pregnant women. Hence, the psychological pressures of the epidemic of COVID-19 may not have been ignored in the clinical decisions.

Vertical transmission is one of the most serious risks of viral diseases including Zika virus, varicella zoster virus (VZV), HIV, rubella virus, human cytomegalovirus (HCMV), and herpes simplex virus (HSV) that threaten the life of the fetus and baby.[23]

Studies that have focused on vertical transmission of COVID-19 so far have found that even if the newborn's RT-PCR test is positive, there is no evidence of viral nucleic acid in amniotic fluid, breast milk, placenta, umbilical cord blood, and vaginal discharge. However, it still cannot be concluded that the vertical transfer of COVID-19 has been definitively ruled out.

In this study, a total number of three infants became infected with COVID-19, of which two were born vaginally and one was delivered by cesarean section. One of the babies was probably infected in the postpartum ward. For the second one, the infection probably occurred during childbirth; however, other sources of infection and transmission immediately after delivery may not be ignored. Besides, in one case, the RT-PCR test was reported positive due to postpartum fever. It may be concluded that skin-to-skin and close contact with the mother is accompanied by breastfeeding without the mask, making the baby's RT-PCR test positive 3 days after birth. However, since these tests were not

performed immediately after the delivery, the vertical transmission from mother to baby could not be ruled out.

More follow-up of neonates born in this cohort study also showed that RT-PCR test for two neonates was positive in the period of discharge up to two weeks after delivery, which can be attributed to non-observance with postnatal contraceptive protocols; however, lack of diagnosis test shortly after delivery prevented identifying the main source of infection.

In most studies of neonatal outcomes, no serious adverse outcomes have been observed in infants born to SARS-CoV-2-positive mothers.[24,25]

Among thirteen studies that tested neonates for SARS-CoV-2, only three studies identified positive cases. Even when neonates tested positive for SARS-CoV-2, they were largely asymptomatic or had mild self-limiting symptoms.[9,11,26]

Our study also confirms the findings of previous studies in this field that the severity of COVID-19 disease in pregnancy mostly includes a range of mild to moderate symptoms.[17,18] It is also very likely that a large number of pregnant women with the disease are completely asymptomatic or symptoms appear after delivery.

Data from centers in London, United Kingdom, and New York, United States, where all pregnant women admitted to giving birth had routine nasal/throat swab PCR testing, found that of the women who tested positive, 88% were asymptomatic.[27,28]

These findings further confirm that the use of personal protective equipment is critical for caregivers, midwives, and physicians in maternity wards. It is also necessary to use personal protective equipment and proper education in accompanying mothers' personal hygiene to prevent any possible transmission of the disease to their babies.

The main limitation of the study is the lack of access to details of patients' lifestyles and events and experiences during pregnancy, which was due to the nature of the study.

It is suggested for future studies to follow up with the patients for a longer period (before and after delivery), do more detailed para-clinical assessments on mother and infant, and study the maternal post-medical records.

Conclusion

SARS-CoV-2 is a novel human pathogen that may uniquely interact with host antiviral defenses, especially in pregnant women**.** Based on the results of our survey, pregnancy does not augment the signs and symptoms of COVID-19 and the resulting morbidity and mortality. However, the rate of cesarean section and preterm delivery increased.

Current studies do not support the vertical transfer of COVID-19 in the fetus, but the effect of disease consequences on fetal development cannot be ruled out. The lack of information about early pregnancy does not rule out the long-term persistence of placental inflammation. Such inflammatory conditions during pregnancy can affect various aspects of fetal brain development and compensate for a wide range of neurological and behavioral disorders later in the postnatal life of the offspring.

Conflict of Interests

Authors have no conflict of interests.

Acknowledgments

We thank the Vice Chancellor's Office for Research Affairs of Kurdistan University of Medical Sciences for financial support.

Financials support and sponsorship

This work was supported by a grant from Kurdistan University of Medical Sciences to Ezatollah Rahimi.

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