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Clinical and obstetric characteristics of pregnant women with Covid-19: A case series study on 26 patients

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ABSTRACT

Objective: To evaluate the clinical characteristics and outcomes of pregnant women with Covid-19.

Materials and methods: This case series study was performed to investigate demographic, clinical and obstetric characteristics of 26 pregnant women with COVID-19 referring to a university hospital of Kashan during the epidemic of COVID-19 (March to May 2020).

Results: The mean gestational age of the patients at admission and delivery was 31.8 ± 5.2 and 36.3 ± 3.4 weeks, respectively. The most common symptoms were fever (96.2%) followed by dyspnea and cough (30.8%). The findings of lung CT scan showed abnormalities confirming the pneumonia in 22 patients (84.6%). Cesarean section was performed in 69.2% of the mothers. The most common maternal–fetal outcome was preterm delivery (38%). Two mothers were transferred to the ICU due to deterioration in clinical condition and they underwent mechanical ventilation without any maternal death. The most common neonatal outcomes included prematurity (38%) and low birth weight (34.6%). No cases of confirmed COVID-19 were observed in the neonates.

Conclusion: Clinical manifestations and laboratory and radiographic findings in pregnant women with COVID-19 are similar to the general population. Common outcomes of pregnancy and delivery in mothers included increased rate of preterm delivery and cesarean section. The most prevalent neonatal outcomes included prematurity and LBW. Careful monitoring of pregnant women with COVID-19 is recommended.

Introduction

Coronaviruses as RNA viruses that belong to the family Coronaviridae have been responsible for two major epidemics (SARS and MERS) in the last two decades [1]. They mainly cause mild to severe gastrointestinal and respiratory infections in the form of pneumonia with systemic disorders [2]. In late 2019, a new gene mutation in this virus led to a severe respiratory disease called COVID-19 [3] that is mainly transmitted through airborne droplets. COVID-19 appears with clinical symptoms such as fever, cough and dyspnea, leading to pneumonia, ARDS (acute respiratory distress syndrome), renal failure and multiple organ dysfunctions. Elderly people with underlying diseases such as asthma, diabetes and heart failure and people with immunodeficiency disorders are more likely to get infected to COVID-19 [4].

Pregnancy causes immunosuppressive conditions and makes individuals more susceptible to infectious diseases. There is also the possibility of vertical transmission of the infection from mother to fetus and development of significant infections in the fetus and infant [5]. Therefore, it seems that pregnant women are at higher risk for complications of COVID-19 and its mortality due to immunological and physiological changes during pregnancy [6]. Because of the lack of sufficient information about the effects of COVID-19 during pregnancy, all pregnant women suspected of COVID-19 infection should be screened and if confirmed, both mother and fetus should be seriously monitored [7].

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1028-4559/© 2021 Taiwan Association of Obstetrics & Gynecology. Publishing services by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).
The risk of developing viral infections such as SARS, MERS and influenza has been higher in pregnant women and evidence suggests that this can lead to adverse clinical and prenatal outcomes such as abortion, stillbirth, preterm delivery, fetal distress, IUUG (Intrauterine Growth Retardation), DIC (Disseminated intravascular coagulation), hospitalization in ICU (Intensive Care Unit) and endotracheal intubation [8,9]. A systematic review of sixteen studies showed that the most common symptoms in pregnant women were fever (68%), cough (34%), lymphopenia (59%) and elevated CRP (70%). Oxygen and antiviral therapy were given to the women were fever (68%), cough (34%), lymphopenia (59%) and elevated CRP (70%). Furthermore, in a case—control study, they referred to fever and pneumonia as the main clinical symptoms in pregnant women with Covid-19. Also, their results showed that the levels of ALT, CRP, WBC and Neutrophils were lower in case group on hospital admission [11].

The results of one study revealed that pregnant women presented similar symptoms of COVID-19 to non-pregnant ones and no complications were observed in the neonates of these mothers. All mothers underwent cesarean section and the baby was born alive and here was no evidence of intrauterine or vertical transmission of the disease in pregnant women infected with COVID-19 [12]. However, another study conducted on eleven infants born to mothers with COVID-19 showed that the complications in neonates were found to be significant and included prematurity, thrombocytopenia due to hepatic dysfunction, fetal distress and respiratory distress [13]. The results of the study by Yan et al. indicated that the most common symptoms in pregnant women with COVID-19 were fever and cough, 7.8% of them had gestational diabetes, 7.7% had hypertension or preeclampsia and 23.3% of pregnant women had no symptoms. 24% of mothers were treated with antibiotics and 54.3% received antiviral therapy. Among the mothers, 6.9% of them were admitted to the ICU and two patients underwent mechanical ventilation. No maternal death was observed in their study. Based on laboratory findings, 44% of mothers had lymphopenia and an increase in CRP level; CT scan findings were normal in 3.7% of the patients. The type of delivery in most cases was cesarean section, which in 38.8% of cases was caused by pneumonia due to COVID-19. Premature delivery and PROM before 37 weeks of pregnancy were observed in 21.2% and 1.6% of cases, respectively and the rate of transfer to the NICU was 47% [14].

Due to the rapid spread of COVID-19 in Iran and especially the city of Kashan, which has a relatively high incidence rate in the province and the country and also the lack of sufficient knowledge about the maternal and neonatal outcomes of this disease, the present study aimed to investigate demographic, clinical and obstetric characteristics of pregnant women with COVID-19.

Methods

This case series study was performed to investigate demographic, clinical and obstetric characteristics of 26 pregnant women with COVID-19 referring to a university hospital of Kashan, Iran; during the epidemic of COVID-19 (March to May 2020). The diagnosis of COVID-19 infection was made by positive qRT-PCR assay performed on the throat or sputum swabs. Patients with significant clinical symptoms such as fever, O2 saturation<93% or respiratory rate >20 and/or laboratory findings such as CRP elevation or lymphopenia were considered as highly suspicious for Covid-19 in the present study. In the chest CT scan findings such as scattered multiple patchy infiltrates, mixed consolidation, pleural thickening alongside ground-glass appearance considered as COVID infection. This criterion is based on Iranian Ministry of Health, Treatment and Medical Training protocols, when COVID-19 Pandemic started. Laboratory test values were considered based on measurements of pregnancy trimesters presented in the reference book [15].

Data collection

The following data were collected using a checklist consisting of four sections:
1. Demographic and obstetric information of patients, including maternal age, gestational age at admission and delivery, parity, maternal BMI, pregnancy complications, type of delivery and cause of cesarean section.
2. Information related to COVID-19 disease, including clinical symptoms, laboratory and radiographic findings, the type of treatment and length of hospital stay.
3. Maternofetal outcomes, including abortion, preterm delivery, PROM, preeclampsia, type of delivery, oligohydramnios, vaginal bleeding, meconium stained fluid, fetal distress, IUFD, IUUG, mother’s hospitalization in ICU, fever and respiratory problems, weakness, severe weight loss and myalgia in the postpartum period.
4. Neonatal Outcomes, Including COVID-19 infection, low Apgar score, asphyxia, prematurity, LBW, infant death, NICU admission, fever, pneumonia, gastrointestinal bleeding and DIC.

Data analysis

Data were described and presented as mean and standard deviation, frequency and percentages using SPSS v16 software. Also data were presented in three categories. All patients, patients with positive qRT-PCR and patients with clinical symptoms, laboratory results and abnormal findings of CT-scan.

Ethical considerations

This study was approved by the ethics committee of Kashan University of Medical Sciences with the code of ethics IRKAUMS-REC.1399.002. Given that the data were extracted from patients' records and hospital database, so there was no need to obtain the patient's consent and the necessary permits were obtained from the authorities.

Results

Clinical manifestations

The present study was carried out on 26 pregnant women with COVID-19. The mean age of women was 30.6 ± 6.5 years. Among the participants, eight cases had positive qRT-PCR result and the rest eighteen cases underwent treatment based on laboratory or CT scan findings. The findings of lung CT scan showed abnormalities confirming the pneumonia in 22 patients (84.6%). All the patients with positive RT-PCR test result had also positive results in the CT scan that were representative of COVID-19 infection.

The results presented in Table 1 shows that the most common symptom in pregnant women was fever and chills (96.2%), followed by dyspnea and cough (30.8%). Regarding the laboratory findings, all the patients had an increase in CRP level (100%), 19 patients (73.1%) had lymphopenia and 10 cases (38.5%) had an increase in LDH. The level of platelets less than 100,000 was observed in one patient with a history of ITP. At admission all other laboratory test results, including leukocytes, hemoglobin, liver enzymes (AST-ALT), renal function tests (Creatinine and BUN) were in the normal range. The values of patients’ laboratory tests are summarized in Table 2.

Regarding the treatment, 80.8% of patients were treated with antibiotics and 19.2% of them received both antibiotics and antiviral
mean birth weight and height were 2821 ± 817 g and 48.5 ± 4.7 cm, respectively. The most common neonatal outcomes were prematurity (38%) and low birth weight (34%).

Maternofetal outcomes

The mean gestational age of the patients at admission and delivery was 31.8 ± 5.2 and 36.3 ± 3.4 weeks, respectively. 73.1% of the women were multiparous. A minority of the infected pregnant women had gestational diabetes (19.2%) and 11.5% suffered from hypertension. Regarding the type of delivery, 69.2% of the mothers had cesarean section which was the cause of cesarean section in most cases (38.8%) was repeated cesarean delivery (Table 3).

According to the results, the most common maternofetal outcome was preterm delivery (38%) followed by preeclampsia (19.2%). Fever was the most common problem after childbirth, which was reported in 46.2% of the cases (Table 4).

Among the patients, two mothers were transferred to the ICU due to deterioration in clinical condition and they underwent mechanical ventilation. Their length of ICU stay was 14 and 31 days; then they were transferred to the general ward with a stable condition and were finally discharged from the hospital.

Neonatal outcomes

More than half of the infants were boys (57.7%). The neonates’ mean birth weight and height were 2821 ± 817 g and 48.5 ± 4.7 cm, respectively. The most common neonatal outcomes were prematurity (38%) and low birth weight (34%).

Table 1
Clinical and laboratory findings of pregnant women with Covid-19.

| Symptoms          | All deliveries (n = 26) | PCR Positive (n = 8) | CT or laboratory Positive (n = 18) |
|-------------------|------------------------|---------------------|-----------------------------------|
| Symptoms          |                        |                     |                                   |
| Cough             | 8 (30.8)               | 5 (62.5)            | 3 (16.7)                          |
| Fever and Chill   | 25 (96.2)              | 8 (100)             | 17 (94.4)                         |
| Dyspnea           | 8 (30.8)               | 4 (50)              | 4 (22.2)                          |
| Shortness of Breath | 5 (19.2)             | 3 (37.5)            | 2 (11.1)                          |
| Headache          | 4 (15.4)               | 2 (25)              | 2 (11.1)                          |
| Diarrhea          | 2 (7.7)                | 2 (25)              | 0                                 |
| Laboratory Tests  |                        |                     |                                   |
| Lymphopenia (<1.1*10^9/L) | 19 (73.1)       | 5 (62.5)            | 14 (77.8)                         |
| Elevated CRP (>8 mg/L) | 26 (100)            | 8 (100)             | 18 (100)                          |
| Elevated LDH      | 10 (38.5)              | 4 (50)              | 6 (33.3)                          |
| Therapy           |                        |                     |                                   |
| Antibiotic        | 21 (80.8)              | 4 (50)              | 17 (94.4)                         |
| Antibiotic and antiviral | 5 (19.2)          | 4 (50)              | 1 (5.6)                           |
| Duration of hospitalization (day) | 7.1 ± 8.3             | 13.6 ± 12.3         | 4.2 ± 3.1                         |

Table 2
Laboratory test values in pregnant women with Covid-19.

| WBC (x10^9/L) | Neutrophil (%) | Lymphocyte (%) | ESR (mg/dL) | CRP (mg/dL) | HB (g/dL) | LDH (U/L) | ALT (U/L) | AST (U/L) | PLT (x10^9/L) | BUN (mg/dL) | Cr (mg/dL) |
|---------------|----------------|---------------|-------------|-------------|-----------|-----------|-----------|-----------|---------------|-------------|-----------|
| 10.18 ± 4.30  | 63.46 ± 20.5   | 9.27 ± 5.48   | 53.15 ± 29.2| 47.8 ± 34.2 | 11.5 ± 1.2| 519.4 ± 172| 226.6 ± 16 | 25.4 ± 18 | 204.1 ± 68.7 | 9.23 ± 3.2 | 0.79 ± 0.2 |

Table 3
Demographic and obstetric characteristics of pregnant women with Covid-19.

| Maternal Age (year) | All deliveries (n = 26) | PCR Positive (n = 8) | CT or laboratory Positive (n = 18) |
|---------------------|------------------------|---------------------|-----------------------------------|
| Fever               | 2 (25)                 | 9 (60)              |
| preeclampsia        | 5 (19.2)               | 4 (26.6)            |
| PROM                | 1 (3.8)                | 1 (6.6)             |
| Fetal Distress      | 2 (7.7)                | 2 (13.3)            |
| IUGR                | 2 (7.7)                | 0                   |
| Asphyxia            | 1 (3.8)                | 1 (6.6)             |
| ICU admission       | 2 (7.7)                | 0                   |

Of the 26 newborns, six cases were admitted to the NICU (23.1%), all of whom were tested for qRT-PCR and had negative results. Two cases of neonatal death were observed (7.7%). The first case was a boy who was born through vaginal delivery to a 31-year-old mother (G4 P1) with a 1-min Apgar score of 8 and 5-min score of 10 due to labor pains at 31 weeks of gestation. However, after giving birth, the baby developed sepsis, then kidney failure, and after that DIC and finally was died. The second case of death was a daughter born through cesarean section due to labor arrest and fetal distress from a 27-year-old mother (G4 P1) in 36 weeks of pregnancy with 1-min Apgar score of 0. The infant was expired through an unsuccessful CPR. The Apgar score less than 7 was observed in two infants. The rest of the infants were discharged with good clinical condition and no cases of confirmed COVID-19 were observed in the neonates. This finding suggests that there was no evidence of maternal–fetal vertical transmission in this set of patients (Table 5).

Discussion

This is a case series study of 26 pregnant patients with confirmed 2019-nCoV infection. The findings of this study are similar to most previous reports in terms of clinical symptoms,
which identified fever and cough as the most common symptoms at admission and postpartum period [12–14,16]. Although in the study by Yan et al., 23.3% of pregnant women had no symptoms [14].

In terms of laboratory values, the findings of this study indicate that 73.1% of women had lymphopenia, which is consistent with the findings of the study by Yu et al. [17]. However, the rate of decrease in lymphocytes reported in different studies has varied from 44% to 56% in other studies [12,14]. Furthermore, there was a rise in CRP level for all the patients of this study and this is what is also referred to in the study of Yu et al. [17]. However, in the study by Yan et al. the results indicated that only 44% of the patients had an increase in CRP [14].

In the present study, more than two-thirds of pregnant women (80.3%) were treated with antibiotics, while Chen et al. reported that all of the patients (100%) received antibiotics and the majority of them (67%) were also treated with antiviral drugs [12]. Furthermore, Yan et al. revealed that almost all of the infected patients (94%) underwent antibiotic therapy [14]. These differences can be due to the diversities in the treatment protocols of medical centers.

In this study, 69.2% of the patients underwent cesarean section. Consistent with this result, in Zhu et al.’s study, out of nine pregnant women, seven (77.7%) had cesarean delivery [13]. Although this rate has been higher in other studies, including Chen et al., (100%), Liu et al. (90%) Yu et al. (91%) and Yan et al. studies (89.5%) [12,14,16,17]. However, in the study of Yan et al. the cause of cesarean section was COVID-19 pneumonia in 38.8% of cases [14], while in our study, none of the patients underwent C/S due to the infection, and obstetric problems made this occurred. Of course, conditions such as the early onset of labor pains and termination of pregnancy in women who have had a previous cesarean section can be related to stress caused by 2019-nCoV infection.

Out of 26 patients, two cases of fetal distress and one case of PROM were observed. In the study of Zhu et al. Out of nine pregnant women, six (66%) had intrauterine distress and 3 cases (33%) developed PROM [13]. In the present study, two patients experienced a severe form of the disease (7.7%) and were transferred to the ICU, but no maternal death was observed. Comparing to this study, Yan et al. reported the rate of ICU admission as 6.2% and two patients underwent mechanical ventilation [14]. Contrary to current findings, there was no case of ICU admission in the study of Yu et al. [17].

Regarding neonatal outcomes, findings showed that 11 neonates (38%) were born premature. This rate ranges from 36.4% to 44.4% in the study of Liu et al. [16] and Chen et al. [12], to 60% in the study of Zhu et al. [13]. Finding of this study revealed that, one third of the infants (34.6%) weighed less than 2500 g (LBW). This rate was similar to reports of other studies [12,13].

According to the results, two cases of neonates had an Apgar score less than 7 and one case of fetal asphyxia and two cases of neonatal death were observed. Contrary to this finding, in several studies all the infants had an Apgar score higher than 8 and no cases developed asphyxia or death [12,16,17]. However, in two studies, one case of infant death was reported due to fetal distress [13,14]. In the present study, the NICU admission rate was 23.1%, which was lower than 47% in the study by Yan et al. [14].

In general, differences in some findings may be due to differences in the periods of the disease, symptoms and disease severity, diagnostic and treatment methods, as well as differences in the strength of immune systems of mother and infant.

In our study, most patients were diagnosed based on CT scan and laboratory findings and this can be acceptable in such a critical condition of COVID-19 epidemic because there is not enough time to wait for the confirmative result of qRT-PCR test. When we confronted with COVID-19 disease, we started treatment immediately and the care was provided by a multidisciplinary team including obstetricians, infectious disease specialists, anesthesiologists and intensive care specialists.

To the best of our knowledge, this is the first case series study conducted on pregnant women infected with 2019-nCoV in Iran. In this study, we also included the cases that were diagnosed based on clinical and laboratory findings that are classified as suspected cases according to the WHO definition. Given that the possible diagnosis of cases is based on CT scan and other laboratory findings. It seems that the presentation of these cases can be useful.

One of the limitations of this study is that, the sampling of the vaginal discharge and amniotic fluid and placenta were not performed to detect 2019-nCoV infection and it is necessary to be considered in future studies. Also in the current study, all mothers were infected with coronavirus in the third trimester of pregnancy; therefore it was not possible to evaluate the early pregnancy outcomes such as abortion.

Conclusion

Clinical manifestations and laboratory and radiographic findings in pregnant women with COVID-19 are similar to non-pregnant women. Common outcomes of pregnancy and delivery in mothers included increased rate of preterm delivery and cesarean section. The most prevalent neonatal outcomes included prematurity and LBW. The maternofetal outcomes of 2019-nCoV infection are different and may have negative effects on mothers and neonates, but the main reason is not clear and it makes it impossible to determine the possible association between maternofetal disorders with the COVID-19 disease. Therefore, cohort studies are recommended to determine the cause–effect relationship more accurately.

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Declaration of competing interest

The authors declare that they have no conflict of interest.

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