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Characteristics and outcomes of COVID-19 pneumonia in pregnancy compared with infected nonpregnant women

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Abstract

Objective: To compare the clinical and paraclinical features and outcomes of pregnant and nonpregnant women with COVID-19.

Methods: A multicenter retrospective cohort study of pregnant and nonpregnant women of reproductive age hospitalized between March and October 2020 in Tehran, Iran. Medical records were reviewed and women who tested positive for SARS-CoV-2 on RT-PCR were included. Extracted data were compared and logistic regression performed.

Results: A total of 110 pregnant and 234 nonpregnant COVID-19-positive women were included. Frequency of severe disease was higher in nonpregnant women than pregnant women (29% vs 11.8%; P < 0.001). Symptoms including cough, dyspnea, chill, fatigue, and headache were more frequent in nonpregnant women (P < 0.05). Pregnant women had higher oxygen saturation levels and lower lymphocyte count (P = 0.001). Six (5.5%) pregnant and 12 (5.1%) nonpregnant women died (P = 0.80). No significant differences between the groups were found for ICU admission and end organ failure. Significantly more nonpregnant women had acute respiratory distress syndrome (ARDS, 9.4% vs 0%; P = 0.001). Univariate regression indicated association between hypertension and death; oxygen saturation and ARDS; and body mass index and ICU admission. No association was found between pregnancy and death, ICU admission, or ARDS.

Conclusion: Pregnant women with COVID-19 are not at higher risk of adverse outcomes compared with nonpregnant women.

KEYWORDS

COVID-19, pneumonia, pregnancy, pregnancy outcomes, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)

1 | INTRODUCTION

Coronavirus disease 2019 (COVID-19) caused by severe acute respiratory distress syndrome coronavirus 2 (SARS-CoV-2) was declared a public health emergency of international concern and a pandemic by the World Health Organization on March 11, 2020.¹ Pregnancy is characterized by a special immunological adaptation to improve the tolerance of the fetal semi-allograft. This state makes pregnant women more susceptible to infectious diseases.² Moreover, the physiological changes to the cardiovascular and pulmonary systems

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of pregnant women may deteriorate the outcomes of viral infections.³ Previous studies on the 2009 H1 N1 influenza virus, severe acute respiratory syndrome (SARS), and Middle East respiratory syndrome (MERS) showed that compared with nonpregnant women of reproductive age, pregnancy was associated with a higher risk of severe pneumonia, acute respiratory distress syndrome (ARDS), mechanical ventilation, and death.^{3,4}

It is logical therefore to consider that pregnant women infected by SARS-CoV-2 are also at a higher risk of severe disease, morbidity, and mortality compared with nonpregnant women. Nevertheless, primary data have suggested that pregnancy is not a risk factor for severe COVID-19 and might not aggravate the clinical figures and outcomes of COVID-19 when compared with nonpregnant agematched individuals.⁵

More studies are needed to conclude whether pregnant women with COVID-19 have a similar clinical course and outcomes to nonpregnant women. Therefore, the aim of the present study was to conduct a retrospective cohort study assessing the medical records of pregnant and nonpregnant women with COVID-19 to compare their clinical and paraclinical characteristics, outcomes, neonatal outcomes, and the vertical transmission potential of COVID-19.

2 | MATERIALS AND METHODS

A retrospective cohort study of hospitalized women across three hospitals—Arash, Imam Khomeini, and Shariati (all affiliated with Tehran University of Medical Sciences, Tehran, Iran)—was conducted between March 2020 and October 2020. The study sample comprised pregnant and nonpregnant women of reproductive age (defined as 15–45 years old) who tested positive for COVID-19. Given that a higher rate of mortality and morbidity due to COVID-19 is expected with advanced age, we included nonpregnant women of reproductive age to control for age as a confounding factor.⁶ SARS-CoV-2 infection was confirmed by real-time polymerase chain reaction (RT-PCR).⁷

The study was approved by the Ethics Committee of the Deputy of Research Affairs, Tehran University of Medical Sciences, Tehran, Iran (IR.TUMS.MEDICINE.REC.1399.393). Given the retrospective design of the study, informed consent from the participants was not required.

All patients admitted to the three hospitals over the study period were considered. After excluding male patients, only pregnant mothers and women of reproductive age were included in the study. Necessary information was selected from electronic medical records. Extracted data included demographic characteristics, pregnancy status, information on neonates, clinical signs and symptoms, paraclinical characteristics, comorbidities, treatments, and outcomes. In addition, clinical symptoms, prescribed medications, duration of hospitalization, management and outcomes, recovery or death, as well as demographic and medical risk factors were evaluated. Maternal, fetal, and neonatal outcomes, and neonatal infection were also assessed. 🛞-WILEY-

Quantitative variables are described using mean \pm SD or median. Categorical variables are summarized as frequency and percentage. Pregnant and nonpregnant women of reproductive age were compared using the *t* test for continuous variables and χ^2 or Fisher exact test for categorical variables. Logistic regression was performed to examine the relationship between pregnancy, underlying diseases, age, and COVID-19 outcomes. Statistical analyses were performed using SPSS version 21.0 (IBM Corp., Armonk, NY, USA). *P* < 0.05 was considered statistically significant.

3 | RESULTS

A total of 4391 COVID-19 patients were admitted to the three hospitals over the study period. After excluding male patients, women older than 45 years, and women younger than 15 years, 344 women were included, of whom 110 were pregnant and 234 were nonpregnant women of reproductive age (31.98% vs 68.02%).

The mean age of pregnant and nonpregnant women was similar (32.02 \pm 6.1 [IQR, 17-45] vs 32.88 \pm 6.3 [IQR 15-45]; *P* = 0.241) (Table 1). For pregnant women, mean gestational age was 32 weeks plus 1 day (range, 6 weeks to 41 weeks plus 1 day). Although high in both groups, prevalence of comorbidities was higher in pregnant women (51.8% vs 22.2%; *P* < 0.001) (Table 1).

For clinical findings, in both groups most patients had moderate disease (Table 1). The frequency of severe disease was higher in nonpregnant women compared with pregnant women (29% vs 11.8%; P < 0.001). The two groups did not differ significantly in length of time from onset of symptoms to hospitalization (5.26 ± 4.19 days vs 6.19 ± 4.79 days; P = 0.244). Data for this variable were only available for 49 pregnant and 107 nonpregnant patients.

The most frequent symptom reported by pregnant women was fever (n = 60, 54.5%), followed by cough (n = 42, 38.2%) and myalgia (n = 30, 27.3%). In nonpregnant women the most common symptom was cough (n = 164, 70.1%), followed by dyspnea (n = 140, 59.8%) and fever (n = 110, 47%). Cough, dyspnea, chill, fatigue, headache, vomiting, loss of appetite, and chest pain were significantly more frequent in nonpregnant women compared with pregnant women (P < 0.05). In contrast, anosmia and runny nose were significantly more frequent in pregnant women compared with nonpregnant women (P = 0.001). There were no differences between the groups for frequency of fever, myalgia, weakness, diarrhea, and nausea (Table 1).

Heart rate (101.81 ± 15.84 vs 91.80 ± 14.76 bpm; P = 0.001) and peripheral oxygen saturation (95.69 ± 3.31 vs 93.50 ± 5.63; P = 0.001) were significantly higher in pregnant women compared with nonpregnant women. Mean temperature was not significantly different between the two groups (P = 0.163); however, a higher percentage of pregnant women experienced temperature above 38°C compared with nonpregnant women (27.3% vs 11.1%; P = 0.001) (Table 1).

In 16 (14.5%) pregnant women, COVID-19 symptoms were revealed after admission to hospital. Mean duration of hospitalization -WILEY- GINECOLOGY OBSTETRICS

TABLE 1 Characteristics of pregnant and nonpregnant women of reproductive age with COVID-19^a

Characteristics	Pregnant women (n = 110)	Nonpregnant women (n = 234)	P value
Age, y	32.02 ± 6.1	32.88 ± 6.3	0.241
Onset of symptoms to hospitalization, d	5.26 ± 4.19	6.19 ± 4.79	0.244
Severity of disease			
Mild	47 (42.7)	77 (32.9)	0.001
Moderate	50 (45.5)	89 (38.0)	0.001
Severe	13 (11.8)	68 (29.1)	0.001
Presence of comorbidities	57 (51.8)	52 (22.2)	<0.001
Hypertension	4 (3.6)	15 (6.4)	0.2
Diabetes	9 (8.2)	15 (6.4)	0.5
Hypothyroidism	30 (27.3)	10 (4.3)	<0.001
Drug history			
ASA	14 (12.7)	O (O)	<0.001
Enoxaparin	11 (10.0)	2 (0.7)	<0.001
Levothyroxine	29 (26.4)	11 (4.7)	<0.001
Insulin	9 (8.2)	1 (0.4)	<0.001
Common symptoms at onset			
Fever	60 (54.5)	110 (47.0)	0.20
Cough	42 (38.2)	164 (70.1)	<0.001
Myalgia	30 (27.3)	77 (32.9)	0.29
Dyspnea	26 (23.6)	140 (59.8)	<0.001
Chill	10 (9.1)	60 (25.6)	<0.001
Anosmia	11 (10.0)	3 (1.3)	<0.001
Weakness	9 (8.2)	18 (7.7)	0.87
Fatigue	9 (8.2)	46 (19.7)	0.007
Headache	6 (5.5)	32 (13.7)	0.023
Diarrhea	7 (6.4)	20 (8.5)	0.483
Nausea	9 (8.2)	37 (15.8)	0.52
Vomiting	1 (0.9)	21 (9.0)	0.004
Loss of appetite	2 (1.8)	21 (9.0)	0.013
Runny nose	8 (7.3)	2 (0.9)	0.001
Chest pain	2 (1.8)	25 (10.7)	0.004
Clinical signs			
Respiratory rate, breaths per minute	19.08 ± 3.31	19.31 ± 3.05	0.70
Peripheral oxygen saturation, %	95.69 ± 3.31	93.50 ± 5.63	0.001
Temperature, °C	37.40 ± 0.77	37.21 ± 0.74	0.163
Temperature >38°C	30 (27.3)	27 (11.1)	0.001
Systolic blood pressure, mm Hg	112 ± 10.66	120 ± 18.26	0.002
Diastolic blood pressure, mm Hg	70.81 ± 9.42	76.60 ± 13.36	0.006
Heart rate, bpm	101.81 ± 15.84	91.80 ± 14.76	0.001
ength of hospital stay, d	6.36 ± 4.49 (median: 5)	12.87 ± 7.91 (median: 12)	<0.001
CU admission	10 (9.1)	19 (8.1)	0.76
End organ failure	0 (0)	7 (3.0)	0.061
Acute respiratory distress syndrome	0 (0)	22 (9.4)	0.001
Death	6 (5.5)	12 (5.1)	0.80

 $^{\rm a}\mbox{Values}$ given as mean \pm SD or number (percentage) unless otherwise indicated.

for pregnant women was significantly shorter than for nonpregnant women ($6.32 \pm 4.49 \text{ vs } 12.87 \pm 7.91 \text{ days}; P < 0.001$). Of the nonpregnant women ($6.32 \pm 4.49 \text{ vs } 12.87 \pm 7.91 \text{ days}; P < 0.001$). Of the nonpregnant women, 19 (8.1%) patients needed ICU-level care. Although a higher percentage of pregnant women (n = 10, 9.1%) received ICU care, the difference was not significant (P = 0.76). While none of the pregnant women developed end organ failure, this occurred in 7 (3.0%) nonpregnant patients (P = 0.061). The mortality rate in both groups was similar, comprising 6 (5.5%) deaths among pregnant women and 12 (5.1%) in the nonpregnant group (P = 0.8). Of six deaths in the pregnant group, 3 (50.0%) were in the postpartum period. Frequency of ARDS was significantly higher in nonpregnant compared with pregnant women (9.4% vs 0%; P = 0.001).

For paraclinical presentation, neutrophil count was lower in nonpregnant women compared with pregnant women (66.64 ± 20.46 vs 77.5 ± 10.85; *P* = 0.001), whereas lymphocyte count was lower in pregnant women compared with the nonpregnant group (18.48 ± 9.18 vs 24.43 ± 12.3; *P* < 0.001). Erythrocyte sedimentation rate and C-reactive protein levels were elevated in both groups, with significantly higher levels in nonpregnant women (*P* = 0.010 and *P* < 0.001, respectively) compared with pregnant women. A higher percentage of pregnant women showed abnormal CT and chest Xray compared with nonpregnant women (39.1% vs 14.5%, *P* = 0.007; 26.4% vs 1.7%, *P* < 0.001, respectively) (Table 2).

Of the 110 pregnant women, 5 (4.5%) were in the postpartum period. The remaining 105 women had a gestational age of between 6 weeks and 40 weeks +1 day with a median of 32 weeks +1 day. The majority (n = 67, 60.9%) were in the third trimester (Table 3). The chief complaint in 29 (26.4%) pregnant women admitted to hospital was symptoms related to COVID-19; in the rest of them it was delivery in 13 (11.8%), decreased fetal movements in 5 (4.5%), decreased amniotic fluid in 2 (1.8%), preeclampsia in 4 (3.6%), preterm labor in one (0.9%), and postpartum illness in 3 (2.7%) women. Data were missing for 53 pregnant women (48.2%). Pregnancy continued in 49 (44.5%) women and 48 (43.6%) women

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delivered their babies, resulting in 51 neonates (three were twin pregnancies). Of 48 deliveries, a total of 40 (83.3%) women underwent cesarean section and 8 (16.7%) delivered vaginally. The most common indications for cesarean were COVID-19 (15.0%), previous history of cesarean (35.0%), and fetal distress (22.5%). Moreover, 8 (7.3%) pregnancies led to spontaneous abortion. Among 110 pregnant women, a total of 13 (11.81%) deliveries were premature, 12 (10.9%) were low birth weight, and 1 (0.9%) was intrauterine growth restriction. Premature rupture of membranes occurred in 5 (4.54%) pregnancies (Table 3).

SARS-CoV-2 test results were positive in 8 (15.7%) neonates, including one set of twins. Except for one, all infected neonates were born by cesarean. The two neonatal deaths were from two different twin pregnancies and both neonates tested positive for SARS-CoV-2. The gestational age range of infected neonates was between 26 weeks +5 days and 35 weeks +3 days; the two neonates that died were 26 weeks +5 days and 29 weeks +1 day. Three of the infected neonates were delivered by mothers who died owing to COVID-19. A total of 15 (29.4%) neonates were admitted to the neonatal intensive care unit. Respiratory complications were observed in 7 (13.7%) neonates and 1 (2.0%) neonate had gastrointestinal complications. Apgar score at 1 min ranged from 3–9 and from 7–10 at 5 min (Table 3).

Based on the recommendations for treatment of COVID-19 at the time, various combinations of hydroxychloroquine and chloroquine, especially in the beginning of the pandemic, and antiviral treatments, antibiotics, and corticosteroids were administrated to both pregnant and nonpregnant patients.

Univariate regression indicated an association between hypertension and death (OR 0.18; 95% CI, 0.050–0.711; P = 0.014); oxygen saturation and ARDS (OR 1.09; 95% CI, 1.02–1.16; P < 0.001); and body mass index and ICU admission (OR 1.28; 95% CI, 1.04–1.57; P = 0.01). No association was found between pregnancy and death (OR 0.58; 95% CI, 0.17–1.94; P = 0.381); pregnancy and ICU admission (OR 1.13; P = 0.381); pregnancy and ICU admission (OR 1.13; P = 0.381); pregnancy and ICU admission (OR 1.13; P = 0.381); pregnancy and ICU admission (OR 1.13; P = 0.381); pregnancy and ICU admission (OR 1.28; P = 0.381); pregnancy and ICU admission (OR 1.28; P = 0.381); pregnancy and ICU admission (OR 1.28; P = 0.381); pregnancy and ICU admission (OR 1.28; P = 0.381); pregnancy and ICU admission (OR 1.28; P = 0.381); pregnancy and ICU admission (OR 1.28; P = 0.381); pregnancy and ICU admission (OR 1.28; P = 0.381); pregnancy and ICU admission (OR 1.28; P = 0.381); pregnancy and ICU admission (OR 1.28; P = 0.381); pregnancy and ICU admission (OR 1.28; P = 0.381); pregnancy and ICU admission (OR 1.28; P = 0.381); pregnancy and ICU admission (OR 1.28; P = 0.381); pregnancy admission (OR 1.28; P = 0.

TABLE 2 Paraclinical analysis of pregnant and nonpregnant women of reproductive age with COVID-19^a

Characteristics	Pregnant women (n=110)	Nonpregnant women (n=234)	P value
Hemoglobin, g/L	11.56 ± 1.52	11.42 ± 2.36	0.66
Neutrophils, %	77.5 ± 10.85	66.64 ± 20.46	0.001
Lymphocytes, %	18.48 ± 9.18	24.43 ± 12.3	<0.001
Urea, mg/dl	8.78 ± 0.48	16.81 ± 1.34	<0.001
Creatinine, mg/dl	0.77 ± 0.58	0.95 ± 0.82	0.111
Erythrocyte sedimentation rate, mm/h	40.15 ± 2.36	53.27 ± 4.87	0.010
C-reactive protein, (mg/L)	22.29 ± 2.59	50.45 ± 6.86	<0.001
Platelets, (×10 ³ /ml)	222.40 ± 10.64	207.27 ± 6.67	0.228
CT scan			
Abnormal	43 (39.1)	34 (14.5)	0.007
Chest X-ray			
Abnormal	29 (26.4)	4 (1.7)	<0.001

^aValues given as mean ± SD or number (percentage) unless otherwise indicated.

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TABLE 3 Maternal and neonatal outcomes in pregnant women with COVID-19 (n = 110)^a

Characteristics	
Gestational age on admission, wk	6-40.1 (median: 32.01)
First trimester (weeks 1–13w, 6d)	6 (5.5%)
Second trimester (weeks 13w, 6d–27w, 6d)	32 (29.1%)
Third trimester (weeks 28-42)	67 (60.9%)
Postpartum	5 (4.5%)
Delivery	48 (43.6%)
Continued pregnancy	49 (44.5%)
Spontaneous abortion	8 (7.3%)
Gestational diabetes mellitus	5 (4.5%)
Pre-eclampsia	5 (4.5%)
Mode of delivery	
Vaginal delivery	8 (16.7%)
Cesarean	40 (83.3%)
Indication for cesarean	
COVID-19	6 (15.0%)
Previous history of cesarean	14 (35.0%)
Fetal distress	9 (22.5%)
Pre-eclampsia	3 (7.5%)
Other	8 (20.0%)
Neonates (n=51)	
Apgar score (1 minute)	3-9 (median: 8)
Apgar score (5 minutes)	7–10 (median: 9)
Fetal weight, g	1300-4020 (median: 2970)
Low birth weight, <2500 g	12 (10.9%)
Preterm labor	13 (11.8%)
Premature rupture of membranes	5 (4.54%)
Neonatal intensive care unit admission	15 (29.4%)
Respiratory complications	7 (13.7%)
Neonatal positive SARS-CoV-2 result	8 (15.7%)
Neonatal death	2 (3.9%)

^aValues are given as number (percentage) unless otherwise indicated.

95% Cl, 0.50–2.52; P = 0.76); and pregnancy and ARDS (OR 0.97; 95% Cl, 0.93–1.01; P = 0.22).

4 | DISCUSSION

Given the lack of data on the effect of COVID-19 on pregnancy outcomes,⁸ the present study investigated the clinical and paraclinical features and outcomes of pregnant and nonpregnant women of reproductive age with COVID-19.

The results of the present study showed that initial symptoms in pregnant women are different compared with nonpregnant women.

Fever was the most observed symptom in pregnant women compared with cough in nonpregnant women. Higher peripheral oxygen saturation level and lymphopenia at the time of admission were more common in pregnant women. Duration of hospitalization was significantly shorter in pregnant women. Although the rate of underlying disease in both groups was significant, death in both groups was similar. The most common adverse pregnancy outcomes were increased cesarean section, fetal distress, preterm labor, low birth weight, and neonatal intensive care unit admission.

The results of the present study show some differences and similarities with previous studies. In contrast to our findings, the large sample-size study by Ellington et al.⁹ reported fever as the most common symptom in both pregnant and nonpregnant women. Moreover, other studies have reported that fever was not underpinned as a common symptom in pregnant women.¹⁰ One possible reason is that, although fever was the most frequent symptom in pregnant women in the present study, there was no difference between temperature at admission between the two groups. Although 60 (54.5%) pregnant and 110 (47.0%) nonpregnant women complained of fever, only 30 (27.3%) pregnant and 27 (11.1%) nonpregnant women had a temperature higher than 38°C.

Similar to the results of the present study, obstetric complications such as fetal distress, preterm labor, and premature rupture of membranes were frequently reported.¹⁰ In a systematic review of 89 pregnant women and their neonates, fetal distress, premature rupture of membranes, and preterm labor were the main prenatal complications.¹¹ In our study, 83.3% of deliveries were performed by cesarean section. Similarly, a significant rise in cesarean section rate was also observed in other studies.¹² This increase was at first due to fear of vertical transmission of infection to the neonate during vaginal delivery.¹³ However, another primary reason is frequent obstetric complications, including fetal distress, premature rupture of membranes, and decreased fetal movement, all leading to need for emergency termination of pregnancy. Although the adverse pregnancy outcomes in our study were significant, these results should be interpreted with caution as we did not have a control group of noninfected pregnant women to compare between the two groups.

Eight neonates were positive for SARS-CoV-2, of which two were from twin pregnancies. In Iran, assessing vertical transmission of infection through examination of abortion specimen, breastmilk samples, amniotic fluid, or cord blood is not performed. Strict prevention approaches have been implemented during the delivery of infected mothers to minimize the possibility of neonatal infection, and the first PCR test is performed 2 h after birth. Therefore, the possibility of vertical transmission cannot be ruled out. Although primary data have suggested that SARS-CoV-2 cannot transmit vertically, updated studies with larger sample sizes have reported various cases of infection in neonates. This is possibly because the first cases of COVID-19 were mostly in pregnant women in late pregnancy.¹¹ In a preliminary review of 155 PCR tests on neonates born to mothers with COVID-19, three had positive results-almost 2%.¹⁴ Furthermore, in some large-scale studies, the rate of positive SARS-CoV-2 tests for neonates ranged between 5% and 8%.^{12,15} In

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our study, just one of eight infected neonates delivered vaginally. Therefore, we cannot answer whether it was possible to get the infection during vaginal delivery. However, it provides support to restrict cesarean section to obstetric indications.

Studies from China with high COVID-19 cases reported a higher rate of cesarean section, no association between pregnancy and severity of disease and length of hospital stay,¹⁶ more frequent abnormal CT scan, and similar outcomes compared with nonpregnant women.¹⁷ A large study of 326 335 women of reproductive age (15– 44 years), of which 8207 (9.0%) were pregnant, concluded that pregnant women are more likely to be admitted to the ICU or receive mechanical ventilation, but the risk of mortality is not increased.⁹ A study from Sweden reported that the risk of admission to the ICU is higher in pregnant women than nonpregnant women.¹⁸ In the present study, the rate of ICU admission was higher in pregnant women although the difference between the groups was not significant. We believe these results should be interpreted cautiously. In many areas with a high incidence of infection or inadequate supplies, such as Iran, only patients with severe or critical disease would be hospitalized. At the same time, given pregnant women's specific situation and the hypothesis that a pregnant patient with SARS-COV-2 infection may experience rapid onset of critical complications and deterioration, all infected patients should be examined closely.¹⁹ Therefore, it may be that pregnant patients with less adverse clinical and paraclinical presentations are hospitalized compared with nonpregnant women.

In the present study, half of the deaths in the pregnant group occurred in the postpartum period. The rate of maternal mortality in the postpartum period was considerable in other studies. Of 20 maternal deaths reported in a study from Brazil, 16 occurred in the postpartum period (range 2–12 days after delivery).²⁰ Naturally, family members and friends come to visit a new mother and her baby. These people may transmit the infection to new mothers. It is important to remind all pregnant women and new mothers to consider quarantine and social distancing after discharge from hospital.

In our study, 14.5% of pregnant patients presented symptoms after admission to the hospital for other reasons. However, since universal screening at the time of admission is not performed in Iran, we cannot conclude whether these patients were infected before hospitalization or contracted SARS-CoV-2 in hospital. Nevertheless, this demonstrates the importance of the use of personal protective equipment by medical staff and hospital patients. Universal screening of pregnant women presenting in labor or to hospital for obstetric complaints may be beneficial in diagnosing infected women in the maternity ward and starting medical care for COVID-19 earlier, therefore reducing transmission of infection to other individuals in the hospital.²¹

The present study highlights some crucial points for managing pregnant women in the era of the COVID-19 pandemic. Studies have revealed that a sizable number of pregnant mothers with positive results for SARS-COV-2 show no symptoms at admission.²² A universal screening strategy to recognize asymptomatic or pre-symptomatic pregnant women admitted to the labor ward has a pivotal role in early diagnosis and the isolation of infected mothers and their newborns. Furthermore, the obstetric consequences of COVID-19 are

considerable. Pregnant women should be informed and encouraged to maintain personal and social hygiene very strictly. Social distancing and avoiding family gatherings in the postpartum period should be emphasized for women after discharge from hospital as the mortality rate in the postpartum period is considerable. In addition, because many infected mothers have delivered their babies vaginally without neonatal infection, considering cesarean section just to avoid the possibility of vertical transmission of infection is not feasible.

The present study has some strengths and limitations. In contrast to many previous studies that included pregnant women only in late pregnancy, our study included women in all trimesters. Furthermore, most studies had a small sample size. A limitation of the present study is its retrospective design, which exposes our results to potential bias. Another limitation is that we did not include patients who were not hospitalized, which may generate bias in generalizability of findings.

In conclusion, the clinical and paraclinical presentations of pregnant women are different from nonpregnant women. Although there were no significant differences between the two groups for mortality, ICU admission, and end organ failure, the rate of ARDS in pregnant women was lower. Moreover, a considerable rate of obstetric complications and neonatal consequences was observed.

CONFLICTS OF INTEREST

The authors have no conflicts of interest.

AUTHOR CONTRIBUTIONS

MV, SM, and AT contributed to study concept and design and manuscript writing. FA, ZM, FB, HH, and AA contributed to acquisition, analysis, or interpretation of data. All authors approved the final version of manuscript.

REFERENCES

- 1. Cucinotta D, Vanelli M. WHO declares COVID-19 a pandemic. Acta Bio Medica: Atenei Parmensis. 2020;91(1):157-160.
- Jamieson DJ, Theiler RN, Rasmussen SA. Emerging infections and pregnancy. *Emerg Infect Dis.* 2006;12(11):1638-1643.
- Rasmussen SA, Smulian JC, Lednicky JA, Wen TS, Jamieson DJ. Coronavirus disease 2019 (COVID-19) and pregnancy: what obstetricians need to know. *Am J Obstet Gynecol*. 2020;222(5):415-426.
- Schwartz DA, Graham AL. Potential maternal and infant outcomes from (Wuhan) coronavirus 2019-nCoV infecting pregnant women: lessons from SARS, MERS, and other human coronavirus infections. *Viruses*. 2020;12(2):194.
- Yang Z, Wang M, Zhu Z, Liu Y. Coronavirus disease 2019 (COVID-19) and pregnancy: a systematic review. J Matern Fetal Neonatal Med. 2020;1-4 [Epub ahead of print].
- Mohr-Sasson A, Chayo J, Bart Y, et al. Laboratory characteristics of pregnant compared to non-pregnant women infected with SARS-CoV-2. Arch Gynecol Obstet. 2020;302(3):629-634.
- Tian S, Hu N, Lou J, et al. Characteristics of COVID-19 infection in Beijing. J Infect. 2020;80(4):401-406.
- Di Mascio D, Khalil A, Saccone G, et al. Outcome of coronavirus spectrum infections (SARS, MERS, COVID-19) during pregnancy: a systematic review and meta-analysis. *Am J Obstet Gynecol MFM*. 2020;2(2):100107.

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- Ellington S, Strid P, Tong VT, et al. Characteristics of women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status—United States, January 22–June 7, 2020. MMWR Morb Mortal Wkly Rep. 2020;69(25):769-775.
- Liu F, Liu H, Hou L, et al. Clinico-radiological features and outcomes in pregnant women with COVID-19 pneumonia compared with age-matched non-pregnant women. *Infect Drug Resist*. 2020;13:2845-2854.
- Muhidin S, Behboodi Moghadam Z, Vizheh M. Analysis of maternal coronavirus infections and neonates born to mothers with 2019nCoV; a systematic review. Arch Acad Emerg Med. 2020;8(1):e49.
- 12. Jafari M, Pormohammad A, Sheikh Neshin SA, et al. Clinical characteristics and outcomes of pregnant women with COVID-19 and comparison with control patients: a systematic review and metaanalysis. *Rev Med Virol.* 2021;e2208.
- Li NA, Han L, Peng M, et al. Maternal and neonatal outcomes of pregnant women with coronavirus disease 2019 (COVID-19) pneumonia: a case-control study. *Clin Infect Dis.* 2020;71(16):2035-2041.
- Juan J, Gil MM, Rong Z, Zhang Y, Yang H, Poon LC. Effect of coronavirus disease 2019 (COVID-19) on maternal, perinatal and neonatal outcome: systematic review. Ultrasound Obstet Gynecol. 2020;56(1):15-27.
- Knight M, Bunch K, Vousden N, et al. Characteristics and outcomes of pregnant women hospitalised with confirmed SARS-CoV-2 infection in the UK: a national cohort study using the UK Obstetric Surveillance System (UKOSS). *BMJ*. 2020;369:m2107.
- 16. Qiancheng XU, Jian S, Lingling P, et al. Coronavirus disease 2019 in pregnancy. *Int J Infect Dis*. 2020;95:376-383.
- 17. Liu F, Liu H, Li J, Hou L, Lan W, Wang D. Clinico-radiological features and outcomes in pregnant women with COVID-19:

compared with age-matched non-pregnant women. *Infect Drug Resist*. 2020;13:2845-2854.

- Collin J, Byström E, Carnahan A, Ahrne M. Public Health Agency of Sweden's Brief Report: pregnant and postpartum women with severe acute respiratory syndrome coronavirus 2 infection in intensive care in Sweden. Acta Obstet Gynecol Scand. 2020;99(7):819-822.
- Vallejo V, Ilagan JG. A postpartum death due to coronavirus disease 2019 (COVID-19) in the United States. Obstet Gynecol. 2020;136(1):52-55.
- Takemoto MLS, Menezes MO, Andreucci CB, et al. Maternal mortality and COVID-19. J Matern Fetal Neonatal Med. 2020;1-7 [Epub ahead of print].
- 21. Muhidin S, Vizheh M, Behboodi MZ. Asymptomatic coronavirus infection among pregnant women: a necessity for universal screening of COVID-19 in pregnant women admitted to labor. *J Matern Fetal Neonatal Med.* 2020;1-2.[Epub ahead of print].
- 22. Breslin N, Baptiste C, Gyamfi-Bannerman C, et al. Coronavirus disease 2019 infection among asymptomatic and symptomatic pregnant women: two weeks of confirmed presentations to an affiliated pair of New York City hospitals. *Am J Obstet Gynecol MFM*. 2020;2(2):100118.

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