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CLINICAL ARTICLE

Obstetrics

The severity of COVID-19 among pregnant women and the risk of adverse maternal outcomes

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Abstract

Objective: To evaluate the relationship between the severity of coronavirus disease 2019 (COVID-19) during pregnancy and the risk of adverse maternal outcomes.

Methods: A descriptive-analytical cross-sectional study conducted on 258 pregnant women who were hospitalized due to confirmed COVID-19 from March 2020 to January 2021 at the Forghani Hospital in Qom, Iran. Demographic and obstetric characteristics, laboratory findings, and adverse maternal outcomes were recorded from the patients' medical records. The Fisher exact test, one-way analysis of variance, and regression logistics were used to assess the relationship between variables.

Results: Of the total study population, 206 (79.8%) pregnant women had mild to moderate disease, 43 (16.7%) had severe disease, and 9 (3.5%) were in the critical stage of the disease. Eight women (3.1%) died and 33 (12.8%) were admitted to the intensive care unit (ICU). The most important demographic factors associated with the severity of the disease were ethnicity, underlying conditions, maternal age, and parity. The severity of the disease was significantly associated with increased cesarean delivery and admission to the ICU.

Conclusion: Pregnant women with severe and critical disease had a high rate of cesarean delivery and admission to the ICU. There were eight cases of maternal mortality.

KEYWORDS
adverse maternal outcomes, coronavirus disease 2019, COVID-19, pregnant women, severity

1 | INTRODUCTION

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) caused a coronavirus disease 2019 (COVID-19) pandemic and recently emerged as a major threat to human health.[1] By February 21, 2021, there were more than 107 856 160 cases confirmed worldwide and more than 2 364 980 deaths.[2] In addition, COVID-19 is associated with a wide range of clinical manifestations, from an asymptomatic or mild illness to severe pneumonia and death. Most people have only mild to moderate disease (80%), 15% have severe disease, and 5% reach a critical stage with complications such as respiratory failure, acute respiratory distress syndrome, sepsis and septic shock, thromboembolism, and experience multiple organic failures, including acute kidney injury and heart failure.[1] The overall rate of mortality is reported at 2.3%.[3] A systematic review study shows that the COVID-19 disease spectrum was mild in 95.6% pregnant women, severe in 3.6%, and critical in 0.8%.[4] Research shows that in different populations, the clinical spectrum of COVID-19 can be varied and may be affected by several factors, including underlying conditions, such as diabetes, hypertension, heart disease, chronic lung disease, and cancer. History of underlying diseases are disproportionately affected by COVID-19 and are at higher risk of severe disease and death.[5–7] Pregnancy is also considered a risk factor for severe pneumonia due to its unique "immunological" conditions

and physiological cardiopulmonary changes (diaphragm elevation, increased consumption of oxygen, and respiratory tract mucosal edema).[8] Therefore, pregnant women are a vulnerable population, and there are many challenges to deciding how to deal with, prevent, and treat infectious diseases.[9] Studies in pregnant women on other coronavirus epidemics, such as Middle East respiratory syndrome (MERS) and severe acute respiratory syndrome (SARS), have also been associated with increased maternal morbidity, mortality, and adverse pregnancy and delivery outcomes. The influenza pandemic of 1918 killed 2.6% of the total population, but the mortality rate for pregnant women was 37%.[10] Regarding the relationship between COVID-19 and pregnancy outcomes, the results of a systematic review showed that 69.4% were delivered by cesarean section and 30.6% by vaginal delivery. Out of 256 newborns, four were positive on reverse transcriptase-reverse polymerase chain reaction (RT-PCR) test and there were two stillbirths and one neonatal death.[3] Maternal complications such as severe pneumonia also occurred in 14% of pregnant women, and most cases required admission to the intensive care unit (ICU) and invasive mechanical ventilation, with one reported maternal death.[4] Given that viral epidemics threaten the general population, including pregnant women, and pregnancy is a unique immune condition that is modulated but not suppressed,[9] and given that there are still many unanswered questions about the clinical course of COVID-19 in pregnant women,[5–7] understanding the correct concept of the severity of coronavirus disease in pregnancy and its impact on pregnancy and childbirth outcomes allows caregivers and policymakers to make valid recommendations for the treatment of pregnant women during the coronavirus pandemic. Therefore, the aim of the present descriptive-analytical cross-sectional study was to evaluate relationship between the severity of COVID-19 during pregnancy and adverse maternal outcomes.

2 | MATERIALS AND METHODS

2.1 | Setting and sample

A descriptive-analytical cross-sectional study was conducted on women who were at 5–42 weeks of pregnancy who were hospitalized due to confirmed COVID-19 from March 15, 2020 to January 30, 2021 at the Forghani Hospital in Qom, a tertiary referral hospital, to assess the relationship between the severity of coronavirus disease and adverse pregnancy outcomes. The present study was approved by the Ethics Committee of Qom University of Medical Sciences (no. IR.MUQ.REC.1399.152).

2.2 | Data collection

In the present study, the inclusion criteria were all women at 5–42 weeks of pregnancy who had COVID-19 confirmed by viral RNA detection in a PCR test or the presence of marked changes in computed tomography (CT) scans of the lungs or both. Data collection was performed by a reproductive health specialist. The demographic characteristics of pregnant women with COVID-19 and history of underlying diseases such as gestational diabetes, chronic diabetes, chronic hypertension and pre-eclampsia, kidney and liver disease, cancer, and body mass index (BMI, calculated as weight in kilograms divided by the square of height in meters) were recorded according to the patients' medical records. Gestational age was also calculated based on the ultrasound reported in the patients' medical records. Drugs used to treat COVID-19, including hydroxychloroquine, azithromycin, ceftriaxone, or other research drugs (e.g. RemedSiver and plasma injections) were recorded from the patients' medical records.

In addition, laboratory findings such as lymphopenia, leukopenia, thrombocytopenia, erythrocyte sedimentation rate, concentration of C-reactive protein (CRP), alanine aminotransferase, aspartate aminotransferase, white blood cell count, and concentration of hemoglobin were recorded from the patients' medical records.

Pregnancy and childbirth outcomes include: rate of abortion, prolonged labor, method of delivery (normal vaginal delivery, emergency cesarean delivery due to fetal distress, emergency cesarean delivery due to complications of COVID-19 in the mother); postpartum complications such as placental abruption, abscess at the site of a cesarean delivery or episiotomy, hematoma, and postpartum hemorrhage. In addition, length of hospital stay, duration of hospitalization in the ICU, and maternal deaths were recorded according to the patients' medical records.

Information was obtained through telephone interviews if some of the required information was not included in a patient's medical records.

2.3 | Severity of the disease

The severity of COVID-19 in pregnancy was classified according to the guidelines of the Society for Maternal and Fetal Medical Association as follows: mild illness was categorized by symptoms such as fever, fatigue, cough, and the less common features of COVID-19; severe illness was categorized as tachypnea (respiration rate >30 breaths per minute), hypoxia (oxygen saturation in room air of 93% or PaO_2/FiO_2 <300 mm Hg), or >50% lung involvement on imaging; and the critical stage of the disease was characterized by respiratory failure, shock, or the dysfunction of several organs.[11,12] Other studies also categorized the clinical manifestations from mild to severe and critical.[3] In a systematic review, the severity of disease in pregnant women was also as reported mild, severe, and critical.[4] In the present study, all pregnant women were hospitalized with symptomatic COVID-19; therefore, asymptomatic individuals were not included in the study. To define severe COVID-19 in the present study, "dyspnea" was defined as shortness of breath reported by the patient at rest. The critical stage of COVID-19 was defined as respiratory failure requiring mechanical ventilation, septic shock, or dysfunction or multiple organ failure.[13,14] Respiratory failure is also defined as the need for invasive mechanical ventilation.[15]

The sample size in the present study, according to a similar study[15] and based on $\alpha = 0.05$ and $\beta = 0.1$, was 120 people and the sample size was increased according to the period and spread of disease to increase the accuracy of the study.

2.4 | Statistical analysis

In the present study, the χ^2 test, Fisher exact test, and one-way analysis of variance (ANOVA) were used to assess the relationship between demographic characteristics, obstetrics, and laboratory findings with the severity of COVID-19, and the relationship between disease severity and pregnancy and childbirth outcomes (Tables 1–3).

Regression logistics were used to examine the predictors of adverse pregnancy outcomes, which were two-state, and confounding variables simultaneously entered into regression analysis. These relationships were adjusted for ethnicity, maternal age, underlying disease, and severity of COVID-19 (Table 4). SPSS version 22 (IBM Corp., Armonk, NY, USA) statistical software was used to perform statistical calculations in the present study. The level of significance was considered to be <0.05.

3 | RESULTS

From March 15, 2020, to January 30, 2021, 567 pregnant women were admitted to the Forghani Hospital in Qom with confirmed

TABLE 1 Relationships between characteristics and obstetric findings of pregnant women and severity of COVID-19[a]

Characteristics	Overall (*n* = 258)	Mild and moderate (*n* = 206)	Severe (*n* = 43)	Critical (*n* = 9)	*P*
Maternal age (years)	29.5 ± 6.03	29.1 ± 6.1	31.57 ± 5.2	29.6 ± 5.0	0.03
Gestational age at symptom onset (weeks)	28.4 ± 9.2	27.9 ± 9.6	30.2 ± 7. 3	32.5 ± 4.2	0.15
BMI					
Normal	207 (80.2)	171 (83.0)	29 (67.4)	7 (77.7)	0.05
Overweight	18 (7.0)	15 (7.3)	3 (7.0)	0 (0.0)	
Obese	33 (12.8)	20 (9.7)	11 (25.6)	2 (22.2)	
Race/Ethnicity					
Iranian	213 (82.6)	180 (87.4)	28 (65.1)	5 (55.6)	0.001
Afghan	44 (17.1)	25 (12.1)	15 (34.9)	4 (44.4)	
Indian	1 (0.5)	0 (0.0)	0 (0.0)	1 (0.4)	
Parity					
Nulliparous	62 (24.0)	56 (27.2)	5 (11.6)	1 (11.1)	0.05
Multiparous	196 (76.0)	150 (72.8)	38 (88.4)	8 (88.9)	
Pregnancy					
Single	6 (2.3)	3 (1.5)	3 (7.0)	0 (0.0)	0.08
Twins	252 (97.7)	203 (98.5)	40 (93.0)	9 (100.0)	
Underlying conditions					
No medical problems	171 (66.3)	151 (73.3)	19 (44.2)	1 (11.1)	0.001
Asthma	2 (0.8)	2 (1.0)	0 (0.0)	0 (0.0)	
Hypertension	18 (7.0)	13 (6.3)	4 (9.3)	1 (11.1)	
GDM	46 (17.8)	25 (12.1)	15 (34.9)	6 (66.7)	
Diabetes	3 (1.2)	2 (1.0)	1 (2.3)	0 (0.0)	
Liver disease	2 (0.8)	2 (1.0)	0 (0.0)	0 (0.0)	
Anemia	4 (1.6)	4 (1.9)	0 (0.0)	0 (0.0)	
Renal disease	1 (0.4)	0 (0.0)	0 (0.0)	1 (11.1)	
Heart disease	5 (1.9)	4 (1.9)	1 (2.3)	0 (0.0)	
Severe pre-eclampsia	2 (0.8)	1 (0.5)	1 (2.3)	0 (0.0)	
GDM and hypertension	4 (1.6)	2 (1.0)	2 (4.7)	0 (0.0)	

Abbreviations: BMI, body mass index; GDM, gestational diabetes mellitus.

[a]Values are given as number (percentage) or mean ± SD.

TABLE 2 Relationship between laboratory findings of pregnant women and severity of COVID-19[a]

Laboratory findings	Overall (*n* = 258)	Mild and moderate (*n* = 206)	Severe (*n* = 43)	Critical (*n* = 9)	*P*
Hemoglobin levels	11.1 ± 1.6	11.09 ± 1.7	11.8 ± 1.3	10.35 ± 1.2	0.01
SpO_2	95.1 ± 3.6	96.6 ± 1.1	91.5 ± 4.2	83.0 ± 5.8	0.001
Leukopenia					
Yes	23 (8.9)	17 (8.3)	4 (9.3)	2 (22.2)	0.3
No	235 (91.1)	189 (91.7)	39 (90.7)	7 (77.8)	
Lymphopenia					
Yes	78 (30.6)	55 (27.1)	16 (37.2)	7 (77.8	0.003
No	177 (69.4)	148 (72.9)	27 (62.8)	2 (22.2)	
Thrombocytopenia					
Yes	49 (19.1)	40 (19.6)	6 (14.0)	3 (33.3)	0.3
No	207 (80.9)	164 (80.4)	37 (86)	6 (66.7)	
Elevated ALT (>45 U/L)					
Yes	77 (30.2)	47 (23.0)	24 (57.1)	6 (66.7)	0.001
No	178 (69.8)	157 (77.0)	18 (42.9)	3 (33.3)	
Elevated AST (>35 U/L)					
Yes	57 (22.4)	37 (18.1)	17 (40.5)	3 (33.3)	0.005
No	198 (87.6)	167 (81.9)	25 (59.5)	6 (66.7)	
ESR (mm/h; normal range 0·0–15·0)					
Normal	6 (2.6)	5 (2.8)	1 (2.4)	0 (0.0)	0.9
Increased	224 (97.4)	175 (97.2)	40 (97.6)	9 (100.0)	
CRP (mg/L; normal range 0.0–5.0)					
Normal	24 (10.3)	21 (11.3)	3 (7.9)	0 (0.0)	0.001
Increased	209 (89.7)	165 (88.7)	35 (92.1)	9 (100.0)	
Confirmatory test done (SARS-CoV-2 quantitative RT-PCR)					
Positive	240 (93.0)	192 (93.2)	39 (90.7)	9 (100.0)	0.8
Not detected	3 (1.2)	3 (1.5)	0 (0.0)	0 (0.0)	
Suspected	11 (4.3)	8 (3.9)	3 (7.0)	0 (0.0)	
Not done	4 (1.6)	3 (1.5)	1 (2.3)	0 (0.0)	
CT findings					
Ground-glass opacities	58 (22.5)	28 (13.6)	21 (48.8)	9 (100.0)	0.001
Normal	17 (6.6)	17 (8.3)	0 (0.0)	0 (0.0)	
Not done	183 (70.9)	161 (78.2)	22 (51.2)	0 (0.0)	
COVID-19 investigational treatments					
Remdesivir					
Yes	43 (16.7)	17 (8.3)	19 (44.2)	7 (77.8)	0.001
No	215 (83.3)	189 (91.7)	24 (55.8)	2 (22.2)	
Azithromycin					
Yes	95 (36.8)	60 (29.1)	26 (60.5)	9 (100.0)	0.001
No	163 (63.2)	146 (70.9)	17 (39.5)	0 (0.0)	
Ceftriaxone					
Yes	125 (48.4)	84 (40.8)	32 (74.4)	9 (100.0)	0.001
No	133 (51.6)	122 (59.2)	11 (25.6)	0 (0.0)	
Hydroxychloroquine					
Yes	34 (13.2)	25 (12.1)	3 (7.0)	6 (66.7)	0.001
No	224 (86.8)	18 (87.9)	40 (93.0)	3 (33.3)	

(Continues)

TABLE 2 (Continued)

Laboratory findings	Overall (*n* = 258)	Mild and moderate (*n* = 206)	Severe (*n* = 43)	Critical (*n* = 9)	*P*
Convalescent plasma					
Yes	6 (2.3)	0 (0.0)	3 (7.0)	3 (33.3)	0.001
No	252 (97.7)	206 (100.0)	40 (93.0)	6 (66.7)	

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; CT, computed tomography; ESR, erythrocyte sedimentation rate; RT-PCR, reverse transcriptase-reverse polymerase chain reaction.

[a]Values are given as number (percentage) or mean ± SD.

TABLE 3 Relationships between severity of COVID-19[a] and adverse maternal outcomes

Pregnancy and delivery outcomes	Overall (*n* = 258)	Mild and moderate (*n* = 206)	Severe (*n* = 43)	Critical (*n* = 9)	*P*
Hospital length of stay	4.7 ± 3.3	3.8 ± 1.8	7.07 ± 4.5	13.3 ± 4.7	0.0001
Abortion					
Yes	1 (0.4)	1 (0.5)	0 (0.0)	0 (0.0)	0.1
No	257 (99.6)	205 (99.5)	43 (100.0)	9 (100.0)	
Method of delivery according to maternal and fetal outcome					
NVD	23 (8.9)	17 (8.3)	4 (9.3)	2 (22.2)	0.001
Cesarean delivery due to other indications	235 (91.1)	189 (91.7)	39 (90.7)	7 (77.8)	
Cesarean delivery due to COVID-199 complications in the mother	17 (18.1)	2 (3.5)	7 (36.8)	8 (100.0)	
Cesarean delivery due to fetal complications	20 (21.3)	14 (20.9)	6 (31.6)	0 (0.0)	
Prolonged labor					
Yes	4 (4.3)	1 (1.5)	2 (10.5)	1 (12.5)	0.8
No	225 (87.2)	66 (98.5)	17 (89.5)	7 (87.5)	
Postpartum compliance					
No compliance	251 (97.3)	203 (88.5)	41 (95.3)	7 (77.8)	0.006
Placental abruption	3 (1.2)	0 (0.0)	1 (2.3)	2 (22.2)	
Hematoma	2 (0.8.)	2 (1.0)	0 (0.0)	0 (0.0)	
Episiotomy abscess	1 (0.4)	0 (0.0)	1 (2.3)	0 (0.0)	
Postpartum hemorrhage	93 (98.9)	66 (98.5)	19 (100.0)	8 (100.0)	
Hospitalized in the ICU					
Yes	33 (12.8)	0 (0.0)	24 (55.8)	9 (100.0)	0.001
No	225 (87.2)	206 (100.0)	19 (44.2)	0 (0.0)	
Maternal mortality					
Yes	8 (3.1)	0 (0.0)	0 (0.0)	8 (88.9)	0.001
No	198 (87.6)	206 (100.0)	43 (100.0)	1 (11.1)	

Abbreviations: ICU, intensive care unit; NVD, normal vaginal delivery.

[a]Values are given as number (percentage) or mean ± SD.

SARS-CoV-2 infection by RT-PCR test or lung CT scan or both. The available medical records of the patients were reviewed.

Of the total study population, 206 (79.8%) pregnant women had mild to moderate disease, 43 (16.7%) had severe disease, and 9 (3.5%) were in the critical stage of the disease. Eight women (3.1%) died and 33 (12.8%) were admitted to the ICU. Of the total number of women with COVID-19, 94 (36.4%) gave birth: 58 (61.7%) had a cesarean delivery and 36 (38.3%) had a normal vaginal delivery. Most of the caesarean births occurred for indications of maternal compromise due to SARS-CoV-2 infection (Table 3). The most common symptoms reported by women with COVID-19 were dry cough (*n* = 165, 64%), shortness of breath (*n* = 162, 62.8%), fever (*n* = 96, 37.2%), muscle aches (*n* = 77, 29.1%), headache (*n* = 64, 24%), and weakness and lethargy.

Information about the time onset of symptoms to hospitalization was not recorded in the medical records of all pregnant women.

TABLE 4 Regression model testing the association between severity of COVID-19 and adverse maternal outcomes

	B	SE	Adjusted OR	*P*	95% CI
Method of delivery					
Severity of COVID-19	87.259	3.049	16.3	0.001	0.856–2.792
Admitted to the ICU					
Severity of COVID-19	0.44	0.002	0.010	0.000	0.781 to −4.653
Pre-existing medical problems	9.415	0.977	3.032	0.05	0.578–1.109

Abbreviations: CI, 95% confidence interval; ICU, intensive care unit; OR, odds ratio.

However, a comparison of the three groups in terms of blood oxygen saturation in room air showed that pregnant women who were hospitalized with a lower percentage of oxygen saturation had significantly higher rates of severe and critical illness. ANOVA showed that the mean percentage of SpO_2 was significantly different between the three groups in terms of severity of disease in pregnant women ($P = 0.001$) (Table 2).

Examination of the relationship between demographic and obstetric characteristics with the severity of coronavirus did not show a significant difference in maternal and gestational age among the three groups ($P = 0.10$). However, after Tukey's *b* test and comparison of the three groups, the results showed that after controlling the level of error of simultaneous tests, the mean maternal and gestational ages of the critical stage of the disease were significantly different from the mean maternal and gestational ages in the mild and moderate disease group ($P < 0.05$). Pregnant women are more likely to develop a critical stage of the disease with increasing maternal and gestational age (Table 1).

The results showed that maternal BMI and parity were significantly associated with disease severity ($P = 0.05$), and mothers with higher BMI and multiparity may develop more severe coronavirus disease.

The results showed that ethnicity and underlying conditions of pregnant women were significantly associated with an increased risk of severity of disease (Table 1). Regarding the relationship between the severity of coronavirus disease in pregnancy and laboratory findings, the results of the ANOVA are reported in Table 2.

The results of the ANOVA showed that the mean length of stay in hospital and hospitalization in the ICU of pregnant women with COVID-19 were significantly different between the three groups in terms of severity of disease ($P = 0.001$). The results showed that with the increasing severity of disease, the probability of the length of stay in hospital and hospitalization in the ICU increased ($P = 0.001$) (Table 4).

In the study of the relationship between the severity of coronavirus disease and delivery outcomes, the results of the χ^2 test showed that the severity of the disease is significantly associated with cesarean delivery ($P = 0.001$).

Logistic regression for qualitative variables was used to investigate the factors predicting adverse maternal outcomes. In the present study, the variables of maternal age, ethnicity, underlying diseases, and severity of COVID-19 were entered into the test simultaneously as confounding variables in the severity of COVID-19. After adjusting the confounding variables, the only factor that was effective in increasing the rate of cesarean delivery was the severity of coronavirus disease (odds ratio 16.3, 95% confidence interval 3.04–87.25) ($P < 0.001$).

4 | DISCUSSION

A descriptive-analytical cross-sectional study was performed on 258 pregnant women with confirmed SARS-CoV-2 infection: 79.8% had mild to moderate disease; 16.7% had severe disease; and 3.5% were critical. Of the women, 12.8% were admitted to the ICU and 3.1% died. In other studies, clinical manifestations ranged from mild in 81% to severe disease in 14%, and the critical stage was reported in 5%; the mortality rate was 2.3%.[3]

The most common clinical symptoms reported by pregnant women with COVID-19 were dry cough, shortness of breath, fever, muscle aches, and headache. "It was noted that some clinical manifestations of COVID-19 overlapped with symptoms of pregnancy (e.g. fatigue, shortness of breath, nasal congestion, nausea/vomiting), so these should be considered in the evaluation of pregnant women".[16]

In the present study, the most important demographic factors associated with the severity of disease were Afghan ethnicity, underlying conditions, maternal age, and parity. Labratory findings also showed that in severe and critical cases of the disease, lymphopenia occurred and liver enzymes increased significantly. In addition, maternal outcomes that had a significant relationship with the severity of disease were increase in cesarean delivery and admission to the ICU. Other studies have reported that the proportion of pregnant women of different ethnicities, such as black and Hispanic women with COVID-19, was higher than the overall proportion of pregnant women aged 15–49 years.[17–19] The results of other studies show that racial and ethnic differences increased both the risk of infection and the risk of severity of COVID-19 in pregnant women, which may indicate the need to address potential risk factors such as long-term inequalities in social health factors such as employment and housing conditions, and social distance in these populations.[17–19] The present study showed that 33.7% of pregnant women with coronavirus have underlying conditions, the most common of which was gestational diabetes mellitus (GDM) (17.7%). The severity of COVID-19 was significantly associated with underlying conditions so that in the group with severe and critical COVID-19, 34.9% and 66.7% of

pregnant women had GDM, respectively. The results of other studies also showed that one-third of pregnant women hospitalized with SARS-CoV-2 infection had underlying diseases in pregnancy[19] and a history of underlying conditions accompanied by the severity of COVID-19.[20]

Other findings of that study showed a significant relationship between maternal age and BMI and severity of COVID-19. The results showed that with increasing maternal age and BMI, the likelihood severity of COVID-19 disease increased. Allotey et al[20] reported that increasing maternal age and BMI may be associated with the severity of COVID-19 disease. Knight et al[19] also reported that 40% of pregnant women hospitalized with SARS-CoV-2 infection were aged 35 years or older.[19]

In terms of the relationship between laboratory findings and the severity of COVID-19, the results of the present study showed that a decrease in the levels of lymphocytes and an increase in liver enzymes and CRP were significantly associated with disease severity. Other studies reported that 35% of pregnant women with COVID-19 had lymphopenia and increased CRP.[16,20] Evidence suggests that viral infections may cause a syndrome known as secondary lymphohistiocytosis. It has also shown that patients with severe and critical COVID-19 may develop cytokine syndrome, and that patients with severe COVID-19 who develop hypercytokinemia and multiple organ failure ultimately die.[3] The results of the present study also showed that 77.8% of people who were in the critical stage of the disease developed lymphopenia and died.

In examining the relationship between the severity of coronavirus disease and the rate of hospitalization, the results of the present study showed that 12.8% were admitted to the ICU. In these women, the underlying disease had tripled the relative risk of being admitted to the ICU. Allotey et al[20] also reported in a systematic review that 13% of pregnant women with COVID-19 were admitted to the ICU, and that a history of GDM and hypertension in pregnant women increased admission to the ICU or invasive ventilation.

Further, the results of the present study showed that the severity of COVID-19 was significantly associated with cesarean delivery: 89.5% of pregnant women who were in the severe disease group and 100% of women who were in the critical stage of the disease underwent cesarean delivery. Of these women, 90% of cesarean deliveries in the severe disease group were due to complications of COVID-19 in the mother. In addition, all cesarean deliveries in the critical group were performed to save the mother's life. Pierce-Williams et al.,[15] who specifically looked at the relationship between maternal outcomes and severity of COVID-19, reported that 32 of 64 pregnant women were hospitalized with severe or critical COVID-19. Nine of 44 women with severe disease and 13 of 20 women in the critical stage due to maternal conditions underwent cesarean delivery, while only three deliveries were due to fetal conditions.[15] The results of other systematic reviews showed that 86% and 69.4% of pregnant women with COVID-19 were delivered by cesarean section.[3,21]

In the present study, 3.1% of the mothers died. Most of these mothers had underlying diseases such as uncontrolled diabetes and nephritic syndrome. Various studies have reported maternal mortality from COVID-19 from non-mortality to high prevalence. In their systematic review, Di Mascio et al[21] reported that 11.4% of mothers died, while Mullins et al[22] and Pierce-Williams et al[15] did not report any maternal deaths. The studies were different in terms of populations studied, underlying diseases, maternal age, and other underlying characteristics, and it seems that these factors affect the severity of the disease and the rate of maternal mortality and need further study.

The strengths of the present study are that only pregnant women with confirmed COVID-19 infection by CT scan or PCR or both were included in the study. In addition, because patients were divided into three groups, it was possible to compare maternal outcomes according to the severity of the disease. One of the limitations of the present study was that less than half of the pregnant women gave birth during this period and the delivery outcomes of many infected women were not available. Further, due to the lack of access to some medical records, not all pregnant women with COVID-19 were examined during pregnancy.

5 | CONCLUSION

The most important demographic factors related to the severity of disease were ethnicity, underlying conditions, maternal age, and parity. Adverse outcomes such as admission to the ICU and the need for cesarean delivery occurred in pregnant women with severe COVID-19.

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CONFLICTS OF INTEREST

The authors have no conflicts of interest.

AUTHOR CONTRIBUTIONS

Study concept and design: ZA, PS; drafting of the manuscript: ZA, PS, MG; critical revision of the manuscript for important intellectual content: ZA, RA, and PS.

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