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Demographic, clinical and laboratory characteristics of pregnant women hospitalized with COVID-19 in the intensive care: a retrospective cohort study

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ABSTRACT

Background: The COVID-19 disease is linked with several maternal and infant complications. Here, we conducted a study to examine the characteristics and outcomes of pregnant women who were admitted to the intensive care unit (ICU) due to COVID-19 complications.

Methods: We performed a retrospective cohort study of symptomatic pregnant women with COVID-19 who were hospitalized at Ayatollah Rouhani Hospital, in Babol, northern Iran, from March 2019 to September 2021. We used a checklist to collect data from patient records, including maternal characteristics (age, body mass, gestational age, parity, blood type, residence, education, and comorbidities), disease symptoms, and laboratory criteria at admission and then compared these variables between pregnant women who required intensive care unit (ICU) admission and those who did not. We used SPSS 20 for data analysis and considered P<0.05 as significant.

Results: We included 215 symptomatic PCR-positive pregnant women with COVID-19 who were hospitalized. The mean age of the women was 30.63±6.09 years and the mean gestational age was 27.77±9.96 weeks. The mean hospital stay was 5.38±5.20 days, and 21 (9.8%) women were admitted to the ICU for a mean of 6.28 ± 5.84 days. The levels of LDH and D-Dimer were significantly higher in the ICU group than in the non-ICU group (P-value<0.000 and P-value=0.024, respectively). The ICU group also had a higher rate of cesarean section (P-value<0.000). There were no significant differences between the groups in terms of clinical symptoms, demographic characteristics, Moreover, none of the women hospitalized with COVID-19 had renal, hepatic, or cardiac disease. None of the infants tested positive for COVID-19 by PCR.

Conclusion: Our findings suggest that pregnant women with COVID-19 are not at increased risk of disease progression or ICU admission. Furthermore, we propose that monitoring the levels of D-Dimer and LDH in pregnant women with COVID-19 could be useful for predicting the severity of the disease and the need for ICU care, which may have implications for maternal and fetal outcomes.

Keywords: Pregnant, Women, Covid-19, Intensive-care unit.

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Introduction

COVID-19 infection is considered one of the greatest threats to public health in recent years (1). Most studies have focused on nonpregnant women, and there are very few studies on the effects of COVID-19 on pregnancy and childbirth (2). In addition, the consequences of COVID-19 in pregnant women and infants are not entirely clear (3). It appears that pregnant women are more susceptible to infectious diseases than the general population due to their weaker immune systems and hormonal changes during pregnancy, and they are particularly more susceptible to respiratory illness and pneumonia (4). However, preliminary reports indicate that pregnant women are at increased risk of contracting COVID-19, but they are at no greater risk of sever disease if they do contract it (5, 6). In the results published by the Centers for Disease Control and Prevention (CDC), it has pointed out that the risk of hospitalization of more pregnant women in the hospital and ICU and eventually the need for mechanical ventilation of these patients increases (7), while some believe that the hospitalization rate of pregnant women with COVID-19 or even admission to the ICU is not increased compared to nonpregnant women with COVID-19 (8). In one study, the hospitalization rate of pregnant women with COVID-19 was reported to be 7%, and 2.8% of pregnant women who were hospitalized for obstetric reasons also had COVID-19 symptoms and mild respiratory symptoms (9). The main clinical manifestations of COVID-19 in pregnant women include fever, cough, and muscle pain, and the most common laboratory results are a decrease in lymphocytes and an increase in CRP, but there is no mention of the need for intensive care or respiratory support in these pregnant women (10).

Since there are few studies on the effects of COVID-19 during pregnancy (11) and there is no study comparing the characteristics pregnant women with COVID-19 in the ICU in Iran, the aim of this study was to investigate the characteristics of pregnant women who required to hospitalize in the intensive care unit (ICU) and their outcomes from March 2019 to September 2021.

Methods

Study design and population

This retrospective cohort study was conducted on all symptomatic pregnant women hospitalized with COVID-19 via census at Ayatollah Rouhani Hospital, affiliated with Babol University of Medical Sciences, with the ethical code of IR.MUBABOL.REC.1400.257 from March 2019 to September 2021.

The inclusion criteria for the pregnant women with COVID-19 were the need for hospitalization with the opinion of an infectious disease expert, a positive pregnancy test or ultrasound based on pregnancy and polymerase chain reaction (PCR), or a positive CT scan related to COVID-19. Criteria for admission to the ICU included: the patient was in the critical phase of illness: respiratory failure; hypoxia that could not be treated invasively; respiratory fatigue; hypotension; impaired consciousness; hemodynamic instability; renal, hepatic, or cardiac disease in the opinion of an anesthesiologist. Exclusion criteria were COVID-19 pregnant women with miscarriage, mole, or ectopic pregnancy and those with incomplete information in the record.

Sample collection

The sample size was determined using the formula: $\frac{Z_{1-a/2}^2 P(1-P)}{d^2}$

Here, P=0.1 was considered as the proportion of pregnant women admitted to the ICU (9). Considering d=0.05 and an error level of 0.05, the minimum number of samples required for this study was 139 pregnant women.

Babol Ayatollah Rouhani Hospital was the only center that admitted all COVID-19 pregnant women during the COVID-19 pandemic. The information about pregnant women with COVID-19 was obtained from patient records using a checklist. Then, the characteristics of these mothers such as age, body mass,

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gestational age, number of pregnancies and deliveries and miscarriages, blood type, place of residence and education, underlying diseases, and symptoms of the disease (fever and chills, cough, shortness of breath, gastrointestinal symptoms, muscle pain), the level of leukocyte, lymphocyte, ESR, CRP, platelet, IL6, Pro-BNP, LDH, and D-Dimer at the time of admission were compared with those of pregnant women with COVID-19 hospitalized in the ICU. Subsequently, the length of stay in the hospital, the number of pregnant women who had to be admitted to the ICU, the length of stay in the ICU, the need for mechanical ventilation (intubation) or noninvasive ventilation (NIV), and organ dysfunction (renal, cardiac, coagulation) in the form of increased creatinine, positivity of troponin and decrease or increase in platelets and, finally, the mortality rate of pregnant women with COVID-19 were collected and statistically analyzed.

Statistical analysis

After data collection, in the first phase, the baseline clinical and demographic variables of pregnant women with COVID-19 admitted to the hospital were described and then compared with the variables of pregnant women with COVID-19 admitted to the ICU. To describe the continuous quantitative variables, if they were normal, the mean (standard deviation) was used and if they were not normal, the median (IQF) was used. In addition, qualitative variables were expressed as absolute frequency (relative frequency). The data were analyzed using SPSS 20 and a value of $P<0.05$ was considered significant. The t-test (Mann-Whitney test if not normal) and chi-square test (Fisher exact test if needed) were used to verify the relationships required by the tests. Multivariable logistic regression was used to examine factors related to hospitalization in the ICU.

Results

In this study, 215 symptomatic PCR-positive pregnant women with a mean age of 30.63±6.09 years (16-46 years old) and a mean gestational age of 27.77±9.96 weeks were hospitalized, of whom 7 (3.3%) had twin pregnancies and 85 (39.5%) were primiparous pregnancies. Moreover, 55.4% of these patients had a hospital stay of 5 days on average (from 1 to 42 days), of whom 78 (36.2%) were initially hospitalized for obstetric problems only. In addition, 34 (15.8%) patients had both a positive PCR and a chest CT scan. Among women hospitalized in the ICU, 9 (57.1%) had positive chest CT scans, whereas 50 (26.3%) women with COVID-19 hospitalized in non-ICU had positive chest CT scans, indicating a statistically significant difference (P-value=0.003).

Further, 21 (9.8%) of these patients were admitted to the ICU, of whom 5 (23.8%) were intubated and 8 (38%) required NIV, representing a statistically significant difference between the two groups in the need for NIV (P-value<0.000). Additionally, 75 (34.9%) of all pregnant women hospitalized with COVID-19 required oxygen with mask (28.8%), nasal cannula (1.4%), and oxygen with reservation bag (4.7%), which was found more in the group hospitalized in the ICU with a statistically significant difference (P value=0.003, P value=0.004, (P value<0.000), respectively. About 28% of pregnant women in both groups had underlying diseases such as thyroid disorders, diabetes, hypertension, heart disease, etc. No statistically significant difference was found between the demographic characteristics of COVID-19 pregnant women hospitalized in the ICU and those hospitalized in the non-ICU. Table 1 illustrates the comparison of demographic characteristics between the two groups. Although the percentage of fever and chills, shortness of breath, and cough was higher in pregnant women who required ICU treatment, this difference between the two groups was not statistically significant. Table 2 represents the comparison of clinical symptoms related to COVID-19 between the two groups. For laboratory criteria between the two groups, LDH and D-Dimer were significantly higher in pregnant women hospitalized in the ICU (P value<0.000) (P value=0.024). Table 3 indicates the comparison of laboratory criteria.

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We only had access to the blood group of 113 pregnant women. 20.5% of COVID-19 pregnant women had blood type O positive, but blood type showed no statistically significant difference between the two groups (P value=0.953). Of all pregnant women hospitalized with COVID-19 (both groups), 70 (32.5%) women delivered during hospitalization, of whom 58 (82.85%) delivered by cesarean section. Pregnant women hospitalized in the ICU were significantly more likely to undergo cesarean section (P-value<0.000) and no positive PCR was observed in the infants. Moreover, none of the women hospitalized with COVID-19 had renal, hepatic, or cardiac disease.

In the peak of the COVID delta (fifth wave), there were two cases of maternal death (0.93%) due to COVID-19, both were primiparous pregnancies. One of them was a 24-year-old woman with a gestational age of 40 weeks, drug abuse, O_2SAT=35%, and IUFD (intrauterine fetal death) and in a state of reduced consciousness and in need of resuscitation, who was referred to the hospital, whereupon resuscitation was performed immediately. The other case was a 27-year-old pregnant woman with a gestational age of 36 weeks, O_2SAT=80%, and pulmonary involvement of 90%, whose baby was born alive by cesarean section. Both mothers were intubated and died in the ICU.

Table 1. Comparison maternal characteristics from 215 pregnancies hospitalities with COVID-19 (Admission in ICU and Not admission in ICU)

Characteristics	Pregnancies with COVID-19 admission in ICU(n=21) mean± SD number(percent)	Pregnancies with COVID-19 Not admission in ICU(n=194) mean± SD number(percent)	P value
Age, year	31.38±4.95	30.54±6.21	0.087
BMI, Kg/m2	26.25±3.15	29.18±6.07	0.079
G.A, weeks	29.52±9.39	27.57±10.02	0.228
Gravid	2.28±1.55	1.89±1.00	0.124
Parity	1.04±1.16	0.83±1.10	0.826
Abortion	0.38±0.80	0.34±0.60	0.358
Time of admission, days	12.14±10.05	4.40±3.06	0.000
Underlying disease	6(28.6%)	54(28.3%)	0.846
Place of life **city** **Village**	12(55%) 9(45%)	77(39.1%) 117(60.9%)	0.167
Education **Under diploma** **Diploma** **University**	13(61.9%) 5(23.8%) 3(1.7%)	114(58.7%) 49(25.2%) 31(16.1%)	0.875
Cause of hospitalization **Covid-19** **Obstetric problem**	12(60%) 8(40%)	125(65.4%) 65(34.6%)	0.830

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Table 2. Comparison clinical symptoms from 215 pregnancies hospitalities with COVID-19 (Admission in ICU and Not admission in ICU)

Characteristics	Pregnancies with COVID-19 admission in ICU(n=21) mean± SD number(percent)	Pregnancies with COVID-19 Not admission in ICU(n=194) mean± SD number(percent)	P value
Fever	13(65%)	109(56.8%)	0.479
Shivering	10(50%)	70(36.5%)	0.234
Myalgia	5(25%)	64(33.3%)	0.449
Dyspnea	8(40%)	51(26.6%)	0.202
Cough	12(60%)	79(41.1%)	0.105
Vomiting	0(0%)	7(3.6%)	0.385
Diarrhea	0(0%)	11(5.7%)	0.272
Abdominal pain	0(0%)	2(1%)	0.647
Taste disorder	0(0%)	1(0.5%)	0.746
Smell disorder	0(0%)	2(1%)	0.647

Table 3. Comparison Laboratory criteria from 215 pregnancies hospitalities with COVID-19 (Admission in ICU and Not admission in ICU)

Characteristics	Pregnancies with COVID-19 admission in ICU(n=21) mean± SD number(percent)	Pregnancies with COVID-19 Not admission in ICU(n=194) mean± SD number(percent)	P value
WBC	10245.00±6388.95	8266.58±5640.04	0.072
Lymphocyte	2023.00±1698.32	1468.87±1440.52	0.188
Platelet	188436.33±92162.82	185689.50±76353.48	0.793
LDH	1233.93±1295.76	489.02±209.13	0.000
ESR	46.61±89.05	38.18±25.90	0.817
CRP	64.12±40.68	45.19±71.66	0.801
D-Dimer	1767.57±1626.87	411.60±939.77	0.024
Pro-BNP	132.85±100.55	83.47±182.7	0.880
IL6	250.02±514.50	105.87±329.35	0.205
BG-RH (N=113) **A negative** **A positive** **B negative** **B positive** **AB negative** **AB positive** **O negative** **O positive**	N=113 0(0%) 3(14.3%) 0(0%) 3(14.3%) 0(0%) 0(0%) 0(0%) 5(23.8%)	N=10 2(1%) 24(12.4%) 2(1%) 15(7.7%) 1(0.5%) 3(1.5%) 5(2.6%) 39(20.1%)	0.953

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Discussion

The current study showed that 9.8% of COVID-19 pregnant women required ICU hospitalization, whereas the rate of ICU hospitalization in the general population with COVID-19 was 20.4% in Larsson's study in Sweden (12). In the 2020 study by Blitz et al. in New York, the hospitalization rate was 9.8% in 82 of women with COVID -19, suggesting that pregnant women with COVID-19 were not at higher risk for ICU hospitalization (15.1%) or more severe disease compared with nonpregnant women with COVID -19 (9). In a meta-analysis of 24 articles on pregnant women with COVID-19 conducted by Italian Di Toro et al. in 2020, the rate of ICU hospitalization in pregnant women with COVID-19 was 8%. They also stated that pregnancy may not be a reason for more severe illness in pregnant women (13).

In Lissa et al.'s meta-analysis of the study of 31,016 pregnant women with COVID-19 from 62 studies, about half had no clinical symptoms and 7% were hospitalized in the ICU (14). However, in the 2020 study by Sitter et al. and the 2020-2021 study by Kalafat et al., pregnant women with COVID-19 were found to require ICU hospitalization at the rate of 4% and 5.5%, respectively, which was lower than that in the present study (15, 16). In Sitter's study on 101 pregnant women with COVID-19, in Germany, 34% were from the Middle East and 8% were from South Asia, highlighting the role of race in severity of illness and need for ICU. In addition, the women in their study did not include all 5 waves of the COVID-19 epidemic. Their study suggested that the pregnant women with COVID-19 did not present with more severe diseases requiring intensive care (15). Kalafat et al. could indicate the role of race in disease severity because they selected 793 pregnant women with COVID-19 from 4 countries including England, Turkey, Australia, and Greece (16). A report published by the CDC in 2021 found that pregnant women with COVID-19 were 5.4 times more likely to be hospitalized than nonpregnant women with COVID-19 and 1.5 times more likely to be hospitalized in the ICU and 1.7 times more likely to require mechanical ventilation. They note that the mortality rate was the same in both groups (0.2%) (12). The differences between the present study and some studies may be related to the limitation of the present study in terms of access to data from pregnant women with COVID, which was limited to only one region and one race.

We found no study comparing the demographic, clinical, and laboratory characteristics of COVID-19 pregnant women admitted to the ICU, and most studies compared pregnant women with nonpregnant women with COVID-19. In the current study, as in some other studies, the age of the pregnant woman was not found to play a role in the severity of illness or the need for ICU hospitalization (9, 13, 15-17). However, one of the studies indicated that pregnant women with COVID-19 who were older than 35 years were 1.5 times more likely to have more severe disease, and in fact, pregnant women with severe symptoms were 3.7 years older (14).

Although in the present study, the presence of an underlying disease did not make a significant difference in the rate of ICU hospitalization in pregnant women with COVID-19, the meta-analysis by Khan et al. (2021) demonstrated that blood pressure (2.07 times), respiratory disease (1.64 times), and obesity (1.37 times) increased the likelihood of symptomatic COVID-19 in these women. Asian women were 1.64 times more likely to have symptomatic COVID-19 than white women. In their study, women with symptoms were 13.25 times more likely to be hospitalized in the ICU and 15.65 times more likely to require mechanical ventilation. The aforementioned study highlighted the role of race in the occurrence and outcomes of COVID-19 in pregnancy (18).

The present study demonstrated that clinical and demographic criteria alone cannot predict whether pregnant women need to be hospitalized in the ICU (10). Although, as in many studies, more attention should be paid to symptoms such as fever, chills, cough, and shortness of breath in pregnant women (10, 12, 13, 15, 19, 20), these symptoms did not show a statistically significant difference in the group hospitalized in the ICU in the current study.

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Furthermore, pregnant women with elevated LDH and D-Dimer levels should be monitored more closely for the severity of clinical symptoms and the need for ICU treatment. Another study investigated the role of D-Dimer in pregnant women hospitalized in the ICU (16). Although lymphocyte counts and CRP levels were not statistically different in COVID-19 pregnant women who required intensive care, the role of lymphopenia and high CRP in pregnant women with COVID-19 should not be forgotten (10, 16, 20).

In the present study, as in some other studies, the rate of cesarean deliveries was higher than that of natural deliveries in COVID-19 pregnant women (10, 13, 15, 20), which may save the life of the fetus in case of worsening of the patient's respiratory problems during delivery or further hospitalization. The need to intubate pregnant women or the maternal mortality rate varied from 8% to 42% (14, 15) and from 0.2% to 2% in different studies, respectively (12-14). In various studies, in addition to the effect of the medical team and the equipment available in different centers, the role of the physician in terms of the time required for intubation is considered very important. For example, in the meta-analysis by Lissa et al., the rate of hospitalization of COVID-19 pregnant women in the ICU and intubation was found to be lower compared with the present study or some studies, but the rate of maternal deaths was higher (14). The limitation of this study was that it only had access to data from COVID -19 pregnant women in one city and was unable to investigate the impact of COVID -19 on other Iranian races and ethnicities.

Conclusion

The current study suggests that attention to and monitoring of some laboratory criteria (LDH and D-Dimer) in COVID-19 pregnant women may help predict the severity of disease in pregnant women with COVID-19 and their need for intensive care in the future, which may have a positive impact on pregnancy outcome and maternal and fetal health. Pregnant women at any gestational age and in any physical condition have the possibility of being infected with COVID-19 and the severity of COVID-19, but they are not more likely to be hospitalized in the ICU or to experience higher mortality and exacerbation of disease. However, more attention should be paid to racial differences in COVID-19 pregnant women in different climates. Respiratory support such as NIV should be considered when COVID-19 pregnant women are admitted to the ICU. For this reason, the high rate of cesarean section in COVID-19 pregnant women, especially those admitted to the ICU, seems to be due to the fear of worsening respiratory problems during delivery. It is suggested that future studies compare the characteristics of pregnant and nonpregnant women with COVID-19 in the ICU.

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