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Intensive Care Management of Critical and Severe SARS-CoV-2 Infection in Pregnancy: A Retrospective Observational Study

Gebelikte Kritik ve Ağır SARS-CoV-2 Enfeksiyonunun Yoğun Bakım Yönetimi: Retrospektif Gözlemsel Çalışma

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ABSTRACT *Objective:* This study examined the clinical consequences of pregnancy coexisting with SARS-CoV-2 in the intensive care unit (ICU).
Materials and Methods: The study was designed as a retrospective observational study. After the ethical approval of the local ethics committee, the study was conducted for a period when the number of young COVID-19 cases increased in our country. The patients enrolled in the study were pregnant/puerperal patients followed up in our third-level intensive care unit.
Results: The mean age of 35 pregnant women included in the study was 29.57±4.36 years. Twenty-one of the births (80.8%) were preterm births. Twelve (34.3%) patients received invasive mechanical ventilation (IMV), and 5 (41.7%) of these patients were deceased. Twenty-six (74.3%) underwent a cesarean section (C/S). There were 5 (14.3%) patients who needed extracorporeal membrane oxygenation (ECMO) and 3 (8.5%) patients who needed continuous renal replacement therapy (CRRT). The 28-day neonatal mortality rate for 26 births was 3.8%. The maternal mortality rate in the ICU was 14.3%.
Conclusion: The preterm birth rate was high in our pregnant patients followed up in the ICU with a diagnosis of COVID-19. Because of clinical and radiological progression in pregnant women, it is difficult to indicate any gestational week in which maternal outcomes are better to undergo C/S. Invasive mechanical ventilation mortality is not higher than in non-pregnant patients, so endotracheal intubation should not be avoided in appropriate patients, whether pregnancy continues or not. The absence of fully vaccinated patients in the study group revealed the protective effect of vaccination during pregnancy.
Keywords: COVID-19, pregnancy, SARS-CoV-2, intensive care unit, extracorporeal membrane oxygenation

ÖZ *Amaç:* Bu çalışma ile yoğun bakım ünitesinde (YBÜ) SARS-CoV-2 enfeksiyonu ile gebelik birlikteliğinin klinik sonuçlarının incelenmesi amaçlandı.
Gereç ve Yöntem: Çalışma retrospektif gözlemsel bir çalışma olarak tasarlandı. Yerel etik kurulun etik onayının ardından ülkemizde genç COVID-19 vaka sayısının arttığı bir dönemde çalışma yürütüldü. Çalışmaya alınan hastalar üçüncü basamak yoğun bakım ünitemizde takip edilen gebe/lohusa hastalardır.
Bulgular: Çalışmaya alınan 35 gebenin yaş ortalaması 29,57±4,36 idi. Doğumların 21'i (%80,8) erken doğumdu. On iki (%34,3) hastaya invaziv mekanik ventilasyon (IMV) uygulandı ve bu hastaların 5'i (%41,7) kaybedildi. Yirmi altı (%74,3) hastaya sezaryen (C/S) uygulandı. Ekstrakorporeal membran oksijenasyonu (ECMO) ihtiyacı olan 5 (%14,3) hasta ve sürekli renal replasman tedavisi (CRRT) ihtiyacı olan 3 (%8,5) hasta vardı. 26 doğum için 28 günlük yenidoğan ölüm oranı %3,8'di. Yoğun bakımda anne ölüm oranı %14,3 oldu.
Sonuç: COVID-19 tanısı ile yoğun bakımda izlenen gebe hastalarımızda erken doğum oranı yüksekti. Gebe kadınlarda klinik ve radyolojik progresyon nedeniyle, C/S yaptırmak için maternal sonuçların daha iyi olduğu herhangi bir gebelik haftasını belirtmek zordur. İnvaziv mekanik ventilasyon mortalitesi gebe olmayan hastalara göre daha yüksek olmadığı için uygun hastalarda gebelik devam etse de etmese de endotrakeal entübasyondan kaçınılmamalıdır. Çalışma grubunda aşıları tam olan hastaların bulunmaması gebelikte aşılamanın koruyucu etkisini ortaya koymaktadır.
Anahtar Kelimeler: COVİD-19, gebelik, SARS-CoV-2, yoğun bakım ünitesi, ekstrakorporeal membran oksijenasyonu

Introduction

Pregnancy is a high-risk group for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Pregnancy and childbirth generally do not increase the risk of contracting SARS-CoV-2 infection but appear to worsen the clinical course of Coronavirus disease 2019 (COVID-19) compared to non-pregnant individuals of the same sex and age; however, most (> 90%) infected patients recover without giving birth [1–7]risk factors, and maternal and perinatal outcomes in pregnant and recently pregnant women with suspected or confirmed coronavirus disease 2019 (covid-19. On the other hand, there appears to be an increased incidence of preterm delivery and cesarean delivery, possibly due to severe maternal disease in infected women, particularly in severely or critically ill patients who develop pneumonia [3,6]2020. Disease severity was classified by National Institutes of Health criteria. Maternal, fetal, and neonatal outcomes were abstracted by centrally trained and certified perinatal research staff. We evaluated trends in maternal characteristics and outcomes across COVID-19 severity classes and associations between severity and outcomes by multivariable modeling. RESULTS: A total of 1,219 patients were included: 47% asymptomatic, 27% mild, 14% moderate, 8% severe, 4% critical. Overall, 53% were Hispanic; there was no trend in race-ethnicity distribution by disease severity. Those with more severe illness had older mean age, higher median body mass index, and pre-existing medical comorbidities. Four maternal deaths (0.3%. In a meta-analysis, 339 (0.02%) pregnant women with confirmed COVID-19 died from any cause, approximately 4% of pregnant women needed intensive care management due to COVID-19progression, 3% of them required invasive mechanical ventilation (IMV) support, and extracorporeal membrane oxygenation (ECMO) was applied 0.2% of the patients [1]. Admission rates to the intensive care unit (ICU) for the need for IMV support and ECMO appear to be higher in pregnant and recently pregnant women than non-pregnant women of reproductive age with COVID-19. Maternal complication rates are not different from infected nonpregnant patients. These rates are much higher than the average population [8]. There are many articles, meta-analyses, and reviews about the course and clinical results of SARS-CoV-2 in pregnancy. However, there is a need for national and international data on pregnant patients followed up in ICU. This study aims to describe the clinical characteristics, laboratory abnormalities, radiological findings, and clinical outcomes of these unique patients followed up in intensive care units.

Materials and Methods

Patients

The study included pregnant/puerperal women followed up in the third-level ICU from March to September 2021. The study was approved by the COVID-19 Scientific Research Platform of the Turkish Ministry of Health (N°: 2021-10-14T09_07_08; date: 15.10.2021) and also by the local ethics committee (Protocol number: 2021-344 date:14.12.2021). The diagnosis of SARS-CoV-2 pneumonia was based on radiological findings and microbiological results obtained by the polymerase chain reaction (PCR). Only the patients with severe and critical COVID-19 pneumonia were followed up in our intensive care unit. Severe illness is defined as; Clinical signs of pneumonia (fever, cough, dyspnea, fast breathing) and one of the followings: respiratory rate > 30 breaths/minute, severe respiratory distress; or SaO_2< 90% on room air, and critical illness; the presence of acute respiratory distress syndrome (ARDS) or respiratory failure requiring ventilation, sepsis or septic shock [9,10]000 patients annually with a mortality rate of 30% to 60% despite wide use of low tidal volume (LTV. The patients generally required high-flow nasal cannula (HFNC) or invasive/noninvasive mechanical ventilation due to respiratory failure. There were no exclusion criteria in the study. All pregnant women hospitalized in the ICU for >24 hours were included. The patients were followed up until discharge from the ICU or until they died.

Data Collection

Patient data were obtained from intensive care bedside follow-up charts and electronic records. Pregnancy, delivery, and neonatal data were obtained from electronic medical records and phone calls from patients/patient relatives.

Demographic data of patients, comorbidities, initial laboratory data, ICU scores (APACHE II, SOFA), radiological evaluations, type of respiratory support at admission and during follow-up, medical treatments for COVID-19, arterial blood gas analyses at admission and PaO_2/FiO_2 values, mechanical ventilation (MV) settings, whether they receive ECMO, continuous renal replacement therapy (CRRT), coupled plasma filtration adsorption (CPFA) treatments, complications related to the disease and pregnancy were recorded.

The venovenous ECMO (VV- ECMO) was applied according to the recommendation of The Extracorporeal Life Support Organization (ELSO) COVID-19 consensus, and the lung protective ventilation strategy was applied in all patients [11].Regarding the pregnancy; the gestational week at the time of diagnosis of COVID-19, the week of birth, the type of delivery (cesarean section (C/S), spontaneous vaginal. etc.), the form of termination of pregnancy (live birth, induced abortion, spontaneous abortion.), whether there is postpartum disease progression, the indication of C/S secondary bacterial/fungal infections of the patients were recorded. Pregnant and postpartum women were evaluated at the bedside with daily obstetrics consultations. The duration of intensive care stays, if any mechanical ventilation periods, and patient outcomes were recorded.

Statistical Analysis

Categorical variables are presented as numbers (proportions). Continuous variables are expressed as mean ± standard deviation or as median (interquartile range) and median (minimum-maximum) according to the importance of style and the distributions examined by the Kolmogorov-Smirnov test. All data were analyzed using IBM SPSS V23 (IBM, Chicago, IL, USA). The start of timings in the timeline figure and onset day was determined as a PCR-positive day with an interquartile range (IQR) of 25-75. The Sankey diagram was created in Jamovi V2.2.4.

Results

The mean age of 35 pregnant women included in the study was 29.57 ± 4.36 years. The vast majority of pregnant women's (57.1%) blood group was A Rh $^{+}$. Only 1 (2.9%) pregnant woman had a history of smoking. The median sequential organ failure assessment (SOFA) score and acute physiology and chronic health evaluation (APACHE II) score of the patients at admission to the ICU were 3 (IQR: 2-8) and 10 (IQR: 9-20), respectively. 82.9% of the patients had no history of comorbidity. None of the 35 patients were fully vaccinated, but only one was infected with COVID-19 for the second time. Bilateral infiltration was detected in chest radiography in 91.4% of the patients on anteroposterior radiographs. Laboratory values and other characteristic values are shown in Table 1.

Six (17.1%) patients were admitted to ICU with invasive mechanical ventilator (IMV) support, and in all follow-up periods, 12 (34.3%) patients received invasive mechanical ventilation support. 21 (60%) of the patients received HFNC treatment, and 8 (22.9%) of them were provided with non-invasive mechanical ventilation (NIMV). The values of the first day of IMV in intubated patients are shown in Table 2. Low dose and pulse dose methylprednisolone were given to 8 (22.9%) and 24 (68.6%) patients. Lopinavir/Ritonavir was given to 22 (62.9%) patients; tocilizumab was given to 6 (17.1%) and postpartum patients. Antibiotic treatment was given to 23 patients (62.9%). Antibiotic use was most common in respiratory and urinary tract infections in 11 (31.4%) patients. C/S was applied to 26 (74.3%) patients. There were 5 (14.3%) patients who needed VV-ECMO and 3 (8.5%) patients who needed CRRT. While CPFA was applied to 1 patient, cytokine adsorption was applied to 2 patients (Table 2). The most common complication developed in the patients was pneumothorax/pneumomediastinum, with 11 (31.4%) patients. When the patients were diagnosed with COVID-19, the median gestational week was 31 (IQR: 18 – 38). The distribution of the patients by weeks of gestation is shown in Table 3. The median week of birth was determined as 34 (IQR: 26 – 38) weeks. 21 (80.8%) of them were preterm births. All 26 deliveries were with C/S. The proportions of all patients who underwent C/Sare shown in the Sankey diagram (Figure 1). Among all C/Ss, the rates of C/S due to fetal distress and increased maternal respiratory distress were 53.8% and 80.8%, respectively. Of the 35 patients admitted to the ICU, 9 (25.7%) were discharged from ICU with ongoing pregnancy. The 28-day neonatal mortality rate for 26 deliveries was 3.8% (Table 3).

The timeline of the process from the onset of the disease is given in Figure 2. The median IMV timing of the patients was 11.5 (IQR: 2.75 – 26) days, and the median ICU stay was 6 (4 – 11) days. Of the five patients treated with ECMO, 2 (40%) were decannulated from ECMO and discharged from ICU. Thirty (85.7%) of the 35 patients were discharged from the ICU in good health (Table 4).

Discussion

SARS-CoV-2 came into our lives as an unprecedented global health problem and affected different patient groups. One of the most critical patient populations is pregnant women. Until now, the literature data included a pregnant woman with SARS-CoV-2 requiring intensive care, among all other patients, but merely very few data on homogeneous intensive care data were presented [12–14].

Table 1. Demographic, clinic and laboratory characteristics of the pregnant patients admitted to intensive care unit due to COVID-19*

Characteristics	
Age, mean ± SD-year	29.57±4.36
A rh+ blood type-no. (%)	20 (57.1)
0 rh+ blood type-no. (%)	7 (20.0)
Smoking-no. (%)	1 (2.9)
Score points (IQR)	
SOFA score	3 (2-8)
APACHE-II score	10 (9-20)
Comorbidity-no. (%)	
None	29 (82.9)
Gestational diabetes mellitus	2 (5.7)
Preeclampsia	1 (2.9)
Asthma	1 (2.9)
Hypo/Hyper thyroidism	2 (5.7)
Vaccine or infection-no. (%)	
None	34 (97.1)
One dose	1 (2.9)
Second time infection	1 (2.9)
Infiltration on X-ray-no. (%)	
Unilateral	3 (8.6)
Bilateral	32 (91.4)
Laboratory values on admission (IQR)†	
C-reactive protein-mg/L	90.3 (45.6-123.8)
Procalcitonin-µg/L	0.11 (0.07-0.26)
White blood cell-10^3 cells/mm^3	13.1 (9.25-17.08)
Lymphocyte ratio-%	6 (3.7-8.6)
Lymphocyte-10^3 cells/mm^3	0.74 (0.52-1.08)
Platelet-10^3 cells/mm^3	233 (179-286)
Haemoglobin-g/dL	10.9 (9.7-11.7)
Creatinine-mg/dL	0.43 (0.35-0.5)
Blood urea nitrogen level-mg/dL	8 (6-12)
D-dimer-mg/L	1.2 (0.92-1.8)
Fibrinogen-mg/dL	472 (387-567)
Ferritin-µg/L	85.3 (28.9-140.5)
Complications-no. (%)	
Haemothorax	2 (5.7)
Pneumothorax/pneumomediastinum	11 (31.4)
Heart failure	2 (5.7)
AKI	4 (11.4)
Secondary infection‡	18 (51.4)
Respiratory tract	11 (31.4)
Urinary tract	11 (31.4)
CRBSI	6 (17.1)
Wound side	1 (2.9)

*Percentages may not total 100 because of rounding. †Procalcitonin level was missing for 1 patient, ‡Some patients had more than one infection source
IQR: Interquartile range, SOFA: sequential organ failure assessment, APACHE-II: acute physiology and chronic health evaluation-II, AKI: acute kidney injury, CRBSI: catheter related bloodstream infection, IMV: invasive mechanical ventilation, ICU: intensive care unit, ECMO: extracorporeal membrane oxygenation, COVID-19: coronavirus disease-2019

Table 2. Treatment of the pregnant patients admitted to intensive care unit due to COVID-19*

Treatments	
Oxygen supports-no. (%)	
IMV at admission	6 (17.1)
IMV	12 (34.3)
HFNC	21 (60)
NIV	8 (22.9%)
Mechanical ventilation parameters on first day (IQR)	
FiO_2	100 (72.5-100)
PEEP-mmHg	13 (10.25-15)
Tidal volume	445 (347-480)
Respiratory rate-breath/min	23 (17-26)
Plateau pressure-mmHg	26.5 (20.75-31)
Peak pressure-mmHg	34.5 (29.5-40.25)
Medical-no. (%)†	
Low dose steroid	8 (22.9%)
Pulse steroid	24 (68.6)
Vasopressor	9 (25.7)
Tocilizumab	6 (17.1)
Lopinavir/ritonavir	22 (62.9)
Antibiotic	23 (62.9)
Prone position	4 (11.4)
Invasive/extracorporeal-no. (%)	
Cesarean section	26 (74.3)
Tube thoracostomy	8 (22.9%)
Thoracotomy	2 (5.7)
CRRT	3 (8.5)
CPFA	1 (2.8)
Cytokine adsorption	2 (5.7)
ECMO	5 (14.3)

*Percentages may not total 100 because of rounding. †Low dose steroid means 1 mg/kg methylprednisolone/day, pulse steroid 250 mg methylprednisolone/day, IQR: Interquartile range, IMV: invasive mechanical ventilation, HFNC: high flow nasal cannula, NIV: non-invasive ventilation, FiO_2: fraction of inspired oxygen, PO_2: partial pressure of oxygen, pCO_2: partial pressure of carbon dioxide, sO_2: arterial oxygen saturation, CRRT: continuous renal replacement therapy, CPFA: coupled plasma filtration adsorption, ECMO: extracorporeal membrane oxygenation, COVID-19: coronavirus disease-2019

According to existing data, about 13% of pregnant women with COVID-19 have a severe illness, and 4% of these patients need an ICU [1,15–17]. The mean age of 35 patients was 29.57 ± 4.36 years, all patients were severe or critically ill, and the mortality rate in ICU was 14.3%. While the mortality rate is 1.2% in pregnant women infected with

SARS-CoV-2, mortality can reach up to 90% in intensive care patients on MV [18].

The Centers for Disease Control and Prevention has suggested that pregnancy poses a higher risk for the need for mechanical ventilation or ECMO. Also, these patients' mortality rate appears to be increased [19,20]. 34.3% of our patients received IMV support, and 5 (14.3%) needed ECMO. While the mortality rate of the patients in mechanical ventilation was 41.7%, this rate reached 60% in patients who needed ECMO support. Two (40%) of these patients were weaned from ECMO and were discharged from the hospital. While the median ECMO time was 17 days

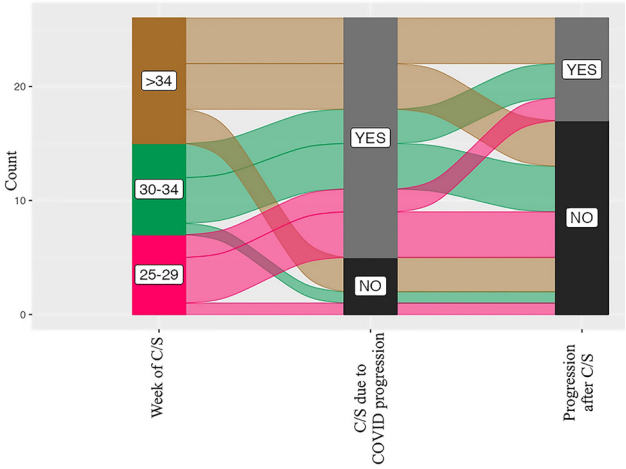

Figure 1. Ratio of C/S due to COVID progression*
*Percentages may not total 100 because of rounding. Count denotes number of cases
C/S: Cesarean section, COVID: coronavirus disease

Table 3. Details of pregnancy duration of patients admitted to intensive care unit due to COVID-19*

Diagnoses	
COVID-19 diagnosed, week-(IQR)	31 (18-38)
Diagnosed in 16-24th week-no. (%)	6 (17.1)
Diagnosed in 25-29th week-no. (%)	10 (28.6)
Diagnosed in 30-34th week-no. (%)	10 (28.6)
Diagnosed in >34th week-no. (%)	9 (25.7)
Birth-no. (%)	26 (74.3)
Week of birth-med (min-max)	34 (26-38)
Preterm births in births-no. (%)	21 (80.8)
C/S in births-no. (%)	26 (100)
C/S in births due to COVID progression-no. (%)	21 (80.8)
Progression after C/S in births-no. (%)	9 (34.6)
Indication of C/S in births-no. (%)†	
Fetal distress	14 (53.8)
Increased of maternal respiratory distress	21 (80.8)
Outcome of babies-no. (%)	
Discharge with an ongoing pregnancy	9 (25.7)
28 days of mortality in births	1 (3.8)

*Percentages may not total 100 because of rounding. †Some C/S had both indications. IQR: Interquartile range, med: median, min: minimum, max: maximum, C/S: cesarean section, COVID-19: coronavirus disease-2019

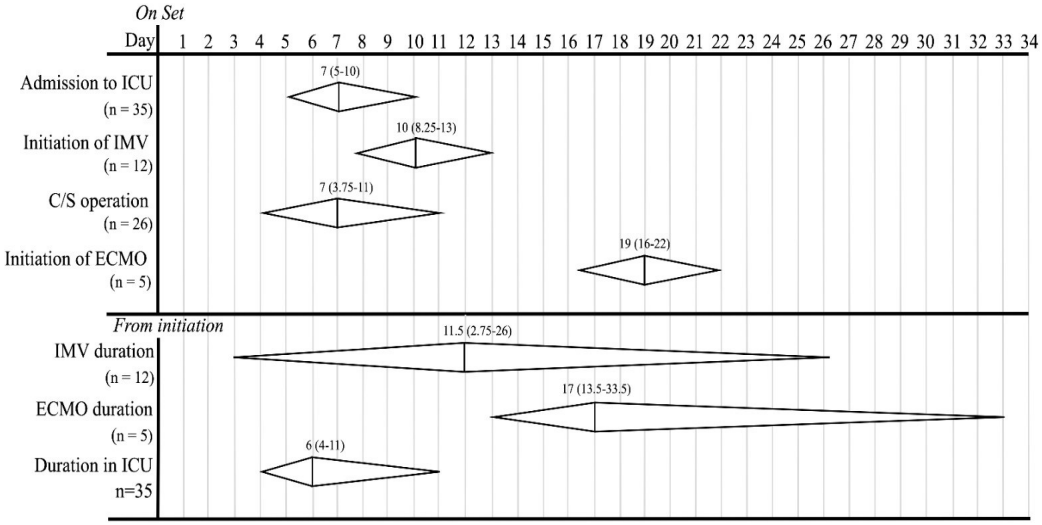

Figure 2. Timeline period of patients admitted to intensive care unit*
*On set day was determined as COVID-19 PCR positive day. Prism show median (IQR 25-75).
ICU: Donates intensive care unit, IMV: invasive mechanical ventilation, C/S: cesarean section, ECMO: extracorporeal membrane oxygenation, COVID-19: coronavirus disease-2019, PCR: polymerase chain reaction

Table 4. Outcomes of the patients admitted to intensive care unit due to COVID-19*

Duration of IMV, IQR-days	11.5 (2.75-26)
Mortality in IMV-no. (%)	5 (41.7)
Duration of ECMO treatment, IQR-days	17 (13.5-33.5)
Duration of ICU stay, IQR-days	6 (4-11)
Wean from ECMO-no. (%)	2.40
Mortality under ECMO-no. (%)	3.60
Discharge from ICU-no. (%)	30 (85.7)
Mortality in lopinavir/ritonavir givens-no. (%)	3 (13.6%)
Mortality in tocilizumab givens-no. (%)	2 (33.3)
Mortality-no. (%)	5 (14.3)

*Percentages may not total 100 because of rounding. IQR: Interquartile range, IMV: invasive mechanical ventilation, ICU: intensive care unit, ECMO: extracorporeal membrane oxygenation, COVID-19: coronavirus disease-2019

in these patients, two patients who weaned from ECMO could be decannulated on the 10th and 17th days. For patients requiring IMV or ECMO, it is increasingly approved that recovery and extubation (and/or decannulation) is often a lengthy process [21]. As a result of a study of pregnant women admitted to ICUs across the United States and 64 nonpregnant women with COVID-19, the frequency and severity of the acute respiratory failure, assessed by receipt of IMV, were similar between groups. Unlike prior viral pandemics [22–25], maternal outcomes among critically ill pregnant women with COVID-19 in this cohort were excellent, with no reported deaths [12].

In contrast to this study, a case series published in Iran reported a very high mortality rate (77.8%) in 9 critically ill pregnant women with COVID-19 [25]. Again, as a result of a study including pregnant/puerperal critically ill patients with COVID-19, 8 (42%) were intubated. All patients that were in IMV deceased [13]. When we compare our results with the literature, the results are satisfactory in terms of both pregnant/puerperal woman mortality in IMV and overall mortality.

Vaccination is the most important prognostic determinant of disease progression during pregnancy. 82.9% of our ICU patients do not have comorbidities, and 97.1% have never been vaccinated. These data reveal a theatrical public health problem. The physicians' recommendations in the follow-up of pregnant women and the press organizations strongly warn especially the pregnant woman about promoting vaccination.[26–28].

A complex medical decision-making process is involved in the intensive care management of pregnant women. The decision-making process begins with the informed consent of the patient and their relatives, in line with medical indications and possibilities. While deciding on the birth, many conditions, including preterm birth risks for the fetus, improvement/worsening of the respiratory condition of the mother with delivery, and hemodynamic, inflammatory, and surgical burden, are known to accompany significant surgeries such as C/S, should be evaluated together.

The critically-ill pregnant population has found an 88% rate of preterm delivery, with 94% of these occurring by cesarean delivery[20,29]. Similarly, preterm birth was observed in 21 (80.8%) of our patients. The median delivery time of our patients was 34 (IQR: 26 – 38) weeks of gestation. While the patients were transferred to the ICU on the median 7th day after the diagnosis, they also underwent C/S on the median 7th day and needed IMV support on the median 10th day. Similarly, a study determined the timing of intubation as the ninth day in this patient group [30]. Patients who need a high level of oxygen support should be followed up carefully in appropriate centers, especially between 7-10 days from symptom onset or diagnosis.

The top priority question to be answered by a pregnant COVID-19 woman is the timing of delivery. Guidelines on this topic are primarily derived from clinical experience, not clinical trials, and are an area currently supported by very little evidence [31,32]. According to the guidelines, an obstetrical ultrasound was performed to confirm fetal viability and gestational age for each patient admitted to ICU after initiating standard medications (antiviral, systemic steroid, and anticoagulant treatments). Afterward, the potential delivery decision is made according to the gestational week, repetitive respiratory evaluations of the mother, and daily fetal evaluations. If delivery is considered based on severe hypoxemia, and especially if the gestational age is less than 32 weeks, other options should be discussed first, including prone position, ECMO, and other advanced ventilator modalities [33]. Antenatal corticosteroids and magnesium sulfate for neuroprotection should be given to any pregnant woman with a potentially viable fetus before any preterm delivery [34].

If gestational age is < 23+0/7 to 24+0/7 weeks (pre-viable): Delivery is indicated only in the case of maternal cardiopulmonary arrest (resuscitative cesarean delivery) with a gestational age of ≥ 20 weeks.

If gestational age is between 23+0/7 to 24+0/7 and 31+6/7 weeks: Despite optimization of all treatments in

the unreliable fetal condition in the setting of refractory hypoxemia, an antenatal corticosteroid is administered.

If the gestational age is between 32+0/7 and 33+6/7 weeks: In daily fetal and maternal evaluations: if it is necessary to increase PEEP or FiO2 to maintain mothers' arterial blood gas at PaO2>70 mmHg or SaO2> 95% level, delivery should be considered in two situations; 1) In case of non-reassuring fetal status, without waiting for corticosteroid administration, 2) In case of mechanical ventilation requiring PEEP >10 cm H2O or ECMO requirement (especially if an antenatal corticosteroid course has been completed).

If gestational age is ≥34+0/7 weeks: An antenatal corticosteroid course can be applied, but it should not delay preterm delivery. In case of any permanent deterioration in maternal respiratory status, delivery is considered.

This decision protocol for birth is primarily based on limited available data and personal experience. The primary purpose is to provide an initial plan for institutions [32–34]. Considering our results, the main reason in 21 (80.8%) patients who underwent C/S was deterioration in maternal respiratory parameters due to COVID-19 progression. While the clinical condition after C/S improved in most of our patients, the clinical picture after C/S deteriorated in 9 (34.6%) patients, and all patients who died were in this group.

Relieving pressure (from the pressure because of the gravid uterus during pregnancy) may be beneficial for lung mechanics, a potential concern for immune restoration in the early post-partum period [35,36]. One of our patients was transferred to the operating room with IMV and ECMO for emergent C/S, and live birth occurred. However, the mother died under ECMO due to refractory septic shock on the 32 days of follow-up. 2 out of 5 patients admitted to VV-ECMO were successfully decannulated and discharged. Not only can ECMO be life-saving in this patient group, but it also requires experience in applying ECMO and complication management. Beforehand, rescue maneuvers such as lung protective mechanical ventilation and prone position should be tried in all patients [11]. Since mortality is known to be high in intubated patients with COVID-19 ARDS (CARDS), there is generally a tendency to avoid intubation. Our study's IMV mortality was 41.7%, which was not higher than the non-pregnant patient population. However, delaying intubation in hypoxemic pregnant women may cause fatal consequences for both the mother and fetus. During pregnancy, the chest wall and lung compliance decrease by approximately 30%, and the functional residual capacity (FRC) decreases. Because of reduced chest wall compliance caused by the gravid uterus, increased plateau airway pressures may be noted. In these patients, higher PEEP is recommended in mechanical ventilation with a plateau pressure of <35 cmH2O to prevent atelectasis and hypoxemia from developing due to compression by the gravid uterus. "Permissive hypercapnia," applied in ARDS mechanical ventilation management, should be avoided in these patients as it may cause fetal acidosis. Other approaches should be implemented in the standard ARDS protocol [37,38].

In this precious and unique patient group, the number of studies that compile only the results of intensive care patients is very few, so this study makes a significant contribution to the existing data. In other respects, the limitations of our study are; the lack of long-term follow-up data, the insufficiency to compare the data with the non-pregnant population, and the lack of obtaining SARS-CoV-2 test results of newborns.

Conclusion

As a result, 35 critically and severely ill pregnant ICU patients diagnosed with COVID-19 were screened in this study. The rate of preterm birth with cesarean delivery was found to be increased. Due to clinical and radiological progression in pregnant women, it is difficult to indicate any gestational week in which maternal outcomes are better to undergo C/S. However, pregnancy termination improves the mother's respiratory parameters by eliminating the problems caused by the uterus during pregnancy and increasing respiratory functions. There is no clear evidence that C/S delivery in the pre-viable period improves the patient's clinical condition. IMV mortality in pregnant SARS-CoV-2 patients is not higher than in nonpregnant patients, so whether or not the pregnancy continues, intubation should not be avoided in appropriate patients to avoid maternal hypoxia. However, mechanical ventilation is not an indication of delivery on its own. The absence of vaccinated and comorbid patients in our study group reveals the potential protective effect of the vaccine in this patient group. Such studies can provide valuable guidance to physicians following pregnant women with severe COVID-19.

Ethics

Ethics Committee Approval:

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: A.O.K., M.P.K., O.A., Ö.D., F.Ö., Y.B., T.Ö., Design: A.O.K., M.P.K., Data Collection and Process: A.O.K., M.P.K., A.P., O.A., Ö.D., Analysis or Interpretation: A.O.K., M.P.K., F.Ö., Literature Search: A.P., Ö.D., Writing: A.O.K., M.P.K., A.P., O.A., Ö.D., F.Ö., Y.B.

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