original article

Evaluation of critically ill obstetric patients treated in an intensive care unit during the COVID-19 pandemic

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Citation: Arslan K, Arslan HC, Sahin AS. Evaluation of critically ill obstetric patients treated in an ıntensive care unit during the COVID-19 pandemic. Ann Saudi Med 2023; 43(1):10-16 DOI: 10.5144/0256-4947.2023.10

Received: August 29, 2022

Accepted: October 15, 2022

Published: February 2, 2023

Funding: None.

BACKGROUND: Although obstetric morbidity and mortality have decreased recently, rates are still high enough to constitute a significant health problem. With the COVID-19 pandemic, many obstetric patients have required treatment in intensive care units (ICU).

OBJECTIVES: Evaluate critical obstetric patients who were treated in an ICU for COVID-19 and followed up for 90 days.

DESIGN: Medical record review

SETTING: Intensıve care unit

PATİENTS AND METHODS: Obstetric patients admitted to the ICU between 15 March 2020 and 15 March 2022 and followed up for at least 90 days were evaluated retrospectively. Patients with and without COVID-19 were compared by gestational week, indications, comorbidities, length of stay in the hospital and ICU, requirement for mechanical ventilation, blood transfusion, renal replacement therapy (RRT), plasmapheresis, ICU scores, and mortality.

MAIN OUTCOME MEASURES: Clinical outcomes and mortality.

SAMPLE SIZE AND CHARACTERISTICS: 102 patients with a mean (SD) maternal age of 29.1 (6.3) years, and median (IQR) length of gestation of 35.0 (7.8) weeks.

RESULTS: About 30% (n=31) of the patients were positive for COVID-19. Most (87.2%) were cesarean deliveries; 4.9% vaginal (8.7% did not deliver). COVID-19, eclampsia/preeclampsia, and postpartum hemorrhage were the most common ICU indications. While the 28-day mortality was 19.3% (n=6) in the COVID-19 group, it was 1.4% (n=1) in the non-COVID-19 group (*P*<.001). The gestational period was significantly shorter in the COVID-19 group (*P*=.01) while the duration of stay in ICU (*P*<.001) and mechanical ventilation (*P*=.03), lactate (*P*=.002), blood transfusions (*P*=.001), plasmapheresis requirements (*P*=.02), and 28-day mortality were significantly higher (*P*<.001). APACHE-2 scores (*P*=.007), duration of stay in ICU (*P*<.001) and mechanical ventilation (*P*<.001), RRT (*P*=.007), and plasmapheresis requirements (*P*=.005) were significantly higher in patients who died than in those who were discharged.

CONCLUSION: The most common indication for ICU admission was COVID-19. The APACHE-2 scoring was helpful in predicting mortality. We think multicenter studies with larger sample sizes are needed for COVID-19 obstetric patients. In addition to greater mortality and morbidity, the infection may affect newborn outcomes by causing premature birth.

LIMITATIONS: Retrospectıve, single-center, small population size.

CONFLICT OF INTEREST: None.

Critical obstetric patients are generally young individuals without a history of systemic disease. Physiological changes in pregnancy and systemic diseases that occur during or after pregnancy require close follow-up of obstetric patients. Peripartum hemorrhage, hypertensive disorders of pregnancy such as preeclampsia and eclampsia, HELLP syndrome (hemolysis, elevated liver enzymes, and low platelet count), embolic events, and infections are responsible for 75% of maternal deaths.[1] Early recognition of these problems and effective treatment and follow-up of obstetric patients in intensive care units are vital for mothers and babies.

Although maternal mortality has decreased recently, it is a significant health problem that can devastate developing or underdeveloped countries. In the 2018 report of the World Health Organization, the maternal mortality rate in developing countries was 239 per 100 000 births, while it was 12 per 100000 births in developed countries.[1] In Turkey, it was reported as 13.1 per 100000 live births, according to the 2019 data of the Ministry of Health.[2] These patients are lost due to complications in the antenatal period. Many complications occur during pregnancy, and most are preventable or treatable.

The COVID-19 pandemic has placed an unprecedented burden on healthcare around the world. Critical obstetric patients were followed in ICUs for obstetric and non-obstetric reasons due to the multisystemic effects of the COVID-19 pandemic in the peripartum period.[3] There are few studies in the literature evaluating critical obstetric patients followed in the ICU. This study aimed to evaluate critical obstetric patients who were treated in the ICU of a tertiary center during the first two years of the COVID-19 pandemic and followed up for 90 days.

PATIENTS AND METHODS

For this retrospective observational study, approval was obtained from the Clinical Research Ethics Committee of the University of University of Health Sciences, Kanuni Sultan Süleyman Training and Research Hospital, Istanbul, Turkey (date:30.06.2021 number:200). The investigation complied with the principles of the Declaration of Helsinki of 1964. We evaluated obstetric patients who were treated in the first two years of the COVID-19 pandemic between 15 March 2020 and 15 March 2022 in the hospital intensive care unit (ICU) and followed up for 90 days. Patients were followed up and treated in two separate ICUs with a capacity of 50 beds by the Anesthesiology and Reanimation Clinic. The study included all obstetric patients aged 18 years and older who stayed in the ICU for more than 24 hours and were without deficiencies in scoring systems, or clinical and laboratory results. In this retrospective observational study, a statistical determination of sample size was not calculated; all eligible obstetric patients were included.

We recorded patient age, gestational week, indications for admission to the ICU, type of birth, comorbidities, length of stay in the ICU, use of mechanical ventilation and hospital length of hospital stay, blood products, and fibrinogen transfusions during follow-up, renal replacement therapy (RRT), plasmapheresis requirements, tracheostomy opening status, Glasgow Coma Score (GCS) in the first 24 hours, APACHE-2 (Acute Physiology and Chronic Health Assessment-2) score, lactate levels, and 28- and 90-day mortality. Patients with positive real-time COVID-19 polymerase chain reaction (PCR) test or negative PCR with tomography imaging and a clinical status compatible with COVID-19 were considered COVID-19 positive. Patients whose PCR test was negative and whose clinical status was not suggestive of COVID-19 were considered COVID-19 negative. Risk factors affecting mortality were investigated.

IBM SPSS version 22.0 (Armonk, New York, United States: IBM Corp) was used to analyze the data. Descriptive data are expressed as the number of patients and percentage, or median, interquartile range and minimum and maximum. The conformity of the variables to the normal distribution was evaluated analytically (Shapiro-Wilks test) and visually (histogram). The Mann-Whitney U test was used to analyze the quantitative variables that were not normally distributed among the groups. The Chi-square and Fisher exact tests were used to evaluate qualitative data. The statistical significance limit was accepted as $P<.05$.

RESULTS

During the two years after the start of the COVID-19 pandemic, a total of 2784 patients were followed up and treated in our hospital's ICU; 3.6% of the patients (n=102) were critically ill obstetric patients. A few patients (3.9%, n=4) were referred to our hospital from an external center after delivery. Of the critical patients, 23% (n=24) had a history of systemic disease (such as asthma, hypothyroidism, and myasthenia gravis). COVID-19 positivity was detected in 30.3% of the obstetric patients (n=31) and was the most common reason for admission of obstetric patients. None of the continuous variables except age were normally distributed. The gestation period was significantly lower in the COVID-19 group (P=.01) (**Table 1**). Duration of hospital, ICU stay and duration of mechanical ventilation were longer in COVID-19 patients.

Delivery was cesarean in 87.2% (n=89) and standard spontaneous vaginal delivery in 4.9% of the patients (n=5). The severe respiratory distress of the COVID-19-positive patients followed in the ICU, and the decision for intubation was the primary consideration in making the emergency decision for cesarean delivery. Patients in the non-COVID-19 group were hospitalized in the ICU after cesarean delivery with diagnoses such as eclampsia/preeclampsia, placental invasion anomalies, and HELLP syndrome, which we thought were the reasons for the high rate of cesarean delivery.

Blood products were transfused (erythrocyte suspension, fresh frozen plasma, and thrombocyte suspension) into 50% of the patients (n=51), and fibrinogen was administered to 35.2% of the patients (n=36). While RRT was applied to 8.8% of the patients (n=9), plasmapheresis was applied to 13.7% (n=14). Differences in GCS in the first 24 hours and APACHE-2 scores were not statistically significant. Lactate levels were lower in the COVID-19 patients (*P*=.002). The discharge rate from the ICU was 91.2%.

The 28-day and 90-day mortality of all patients were 6.8% (n=7) and 8.8% (n=9), respectively, and fewer COVID-19 patients survived (*P*<.001). COVID-19 in 25% of the patients, eclampsia/preeclampsia in 20%, and postpartum bleeding in 16% of the patients were the most common reasons for hospitalization (**Table 2**). Cardiomyopathies such as new-onset myocarditis and pericarditis were observed in 19.3% of 31 patients (n=6) in the COVID-19 group. One patient was referred to an external center for ECMO. Spontaneous pneumothorax was observed in 9.6% of patients due to pulmo-

Table 1. Demographic and clinical data.

	Total (n=102)	COVID-19 (n=31)	Non-COVID-19 (n=71)	*P* value
Maternal age (years)	29.2 (6.4)	29.1 (5.3)	29.2 (6.9)	.89
Gestation (weeks)	35.0 (7.8. 6-42)	33 (4, 22-38)	36 (7.5, 6-42)	**.01**
Birth type				
Vaginal birth	5 (4.9)	1 (3.2)	4 (5.6)	
Cesarean delivery	89 (87.2)	26 (83.8)	63 (88.7)	.41
Did not give birth	8 (7.8)	4 (12.9)	4 (5.6)	
Comorbidity	24 (23.5)	8 (25.8)	16 (26.7)	.37
Duration of ICU (days)	3.0 (3.0, 1-40)	6 (10, 1-40)	2 (2, 1-12)	**<.001**
Mechanical ventilation	53 (51.9)	17 (54.8)	36 (50.7)	.70
Duration of mechanical ventilation (days)	1.0 (2.0. 0-38)	1 (7, 0-38)	0 (1, 0-6)	**.03**
Duration of hospital (days)	8 (8.8, 2-65)	14 (9, 4-45)	7 (4, 2-65)	**<.001**
Renal replacement therapy	9 (8.8)	5 (16.1)	4 (5.6)	.08
Plasmapheresis	14 (13.7)	8 (25.8)	6 (8.4)	**.02**
Blood transfusion	51 (50)	8 (25.8)	43 (60.5)	**<.001**
Fibrinogen	36 (35.2)	5 (16.1)	31 (43.6)	**<.007**
Vasopressor	15 (14.7)	12 (38.7)	3 (4.2)	**<.001**
Glasgow coma scale score	13 (8, 7-15)	13 (4.5, 6-15)	12 (8, 3-15)	.10
APACHE-2 score	12 (7.8, 5-32)	12 (8.5, 5-30)	12 (7, 5-32)	.95
Lactate (mmol/L)	1.9 (1.5, 0.8-24.7)	1.5 (0.9, 0.8-3.3)	2.1 (1.8, 0.8-24.7)	**.002**
Mortality (28-day)	7 (6.8)	6 (19.3)	1 (1.4)	**<.001**
Mortality (90-day)	9 (8.8)	8 (25.8)	1 (1.4)	**<.001**

Values are number of patients (percentage) or median (interquartile range) except for age (mean, standard deviation).

Table 2. Indications for admission to the intensive care unit (n=102).

COVID-19	26 (25.4)
Eclampsia/preeclampsia	21 (20.5)
Postpartum bleeding	16 (15.6)
Placental invasion anomaly	9 (8.8)
HELLP syndrome	9 (8.8)
Disseminated intravascular coagulation	5 (4.9)
Anesthesia complications	4 (3.9)
Ectopic pregnancy rupture	4 (3.9)
COVID-19 + Eclampsia/preeclampsia	2 (1.9)
Fatty liver of pregnancy	1 (0.9)
Pulmonary embolism	1 (0.9)
Sinus vein thrombosis	1 (0.9)
COVID-19 + Postpartum bleeding	1 (0.9)
COVID-19 + HELLP syndrome	1 (0.9)

Values are number of patients (percentage). HELLP: hemolysis, elevated liver enzymes, and low platelet count

nary complications of COVID-19. Eight (88.8%) of the patients who died were COVID-19 patients.. Only one patient died in the non-COVID-19 group. The patient was referred to our hospital after spontaneous vaginal delivery from an external center with the diagnosis of DIC (disseminated intravascular coagulation) and hemorrhagic shock. When the patients were evaluated by mortality (**Table 3**), the APACHE-2 score in the first 24 hours, the length of stay in the ICU, duration of mechanical ventilation, the application of RRT and plasmapheresis differed significantly in COVID-19 vs non-COVID-19 patients.

DISCUSSION

The rate of obstetric patients admitted to the ICU varies between 0.7-16%, depending on the development level of the country.[4-6] In developed countries, the rate of obstetric patients in the ICU has been reported to be less than 2%.[4-6] In our tertiary center hospital, patients are followed up and treated by the Anesthesiology and Reanimation Clinic, with 50 beds in two separate ICUs. In the first two years of the COVID-19 pandemic, 3.6% of the patients (n=102) who were followed up and treated in the ICU were critical obstetric patients. The rate of obstetric patients admitted in our ICU was approximately between that of developing and developed countries

Obstetric patients are admitted to the ICU primarily because of postpartum bleeding and hypertension complications.[7,8] Singh et al reported that 43% of obstetric patients were hospitalized in the ICU due to postpartum bleeding and 31% due to preeclampsia/eclampsia.[9] Sevdi et al said that obstetric bleeding in 25% of the patients and preeclampsia/eclampsia in 19% were the most common reasons for admission.[2] In our study, 26% of the patients were hospitalized due to problems related to COVID-19. Apart from this, following the literature, eclampsia/preeclampsia in 20% of patients and postpartum bleeding in 15% are the most common indications for hospitalization.

Table 3. Demographic and clinical characteristics of patients by mortality.

Variable	Survived (n=93)	Died (n=9)	*P* value
Maternal age (years)	29.2 (6.5)	29.2 (5.5)	.89
Gestational week	35 (8, 6-42)	34 (3, 28-38)	.48
COVID-19 positivity	23 (24.7)	8 (88.9)	**<.001**
GCS score	14 (8, 3-15)	10 (2, 3-13)	.07
APACHE-2 score	12 (7, 5-32)	22 (14, 9-30)	.007
Lactate (mmol/L)	1.9 (1.5, 0.8-14.2)	1.8 (0.8, 1.1-24.7)	.86
Duration of ICU (days)	3 (3, 1-25)	13 (10, 5-40)	**<.001**
Duration of mechanical ventilation (days)	0 (1, 0-12)	14.1 (11.2)	**<.001**
Comorbidity	21 (22.5)	3 (33.3)	.09
Renal replacement therapy	6 (16.1)	3 (33.3)	.007
Plasmapheresis	10 (10.7)	4 (44.4)	**.005**

Values are number of patients (percentage) or median (interquartile range) except for age (mean, standard deviation).

Mortality rates in obstetric intensive care patients also vary from country to country. In Canada, mortality in obstetric patients was reported as 2.3%.[10] Zwart et al in the Netherlands found obstetric mortality to be 3.5%.[11] Ashraf et al from India reported obstetric mortality of 13%.[12] In our study, the 90-day mortality was 8.8%, 22.5% in the COVID-19 group, and 1.4% in the non-COVID-19 group. Newly developed cardiomyopathies such as myocarditis, pericarditis, and heart failure were observed in 19.3% of the patients (n=6) in the COVID-19 group during their ICU follow-up. One of the patients was referred to an external center for application of ECMO. Spontaneous pneumothorax was observed in 9.6% of these patients (n=3). The pulmonary, cardiac, and metabolic effects of COVID-19 increase mortality.In our study, the mortality rates of pregnant women in the non-COVID-19 group were as low as in developed countries (28-day mortality, 1/70 [1.4%]). However, the mortality rates of pregnant women in the COVID-19 group were significantly higher than in the non-COVID-19 group (28-day mortality 86/31 [19.4%] % vs. 1/71 [1.4%], *P*<.001).

In a study from Turkey, maternal age did not affect mortality.[2] However, the gestational week was significantly lower in deceased obstetric patients.[2] In our study, while the gestational week was significantly lower in the COVID-19 group with significantly higher mortality (*P*=.03), no significant difference was observed in maternal age (*P*=.89). Since the patients in the COVID-19 group were admitted to the ICU earlier in the gestation period, the median value for gestational weeks was significantly lower. COVID-19-positive patients were generally not admitted on admission to the ICU, but 54.8% of the patients in this group needed mechanical ventilation support and were intubated. Emergency cesarean delivery was performed in intubated COVID-19-positive pregnant women when admitted to the ICU. When intubation was required, delivery was performed by emergency cesarean delivery.

Complicated pregnant women are referred to more advanced tertiary hospitals during prepartum and postpartum periods. In data from the Australian and New Zealand Intensive Care Society Adult Patient Database, mortality was higher in complicated obstetric patients referred to other hospitals compared to emergency departments.[13] However, the studies on referred obstetric patients and the sample numbers in these studies are limited. In another study, 34% of patients in the ICU were referred from other hospitals in Turkey; the mortaily in those patients was three times higher in the transferred patients.[6]

Mechanical ventilatory support is generally needed in critical obstetric patients admitted to the ICU because of pregnancy-related complications. In studies before the COVID-19 pandemic, the need for mechanical ventilation was reported to be between 19% and 80%.[2,6,13,14] In a study including 38 COVID-19-positive pregnant women, the rate of who were intubated or underwent mechanical ventilatory support was 26.3%.[15] Tezcan Keleş et al[16] reported the mean (SD) duration of mechanical ventilation was 3.8 (3.5) days, and Dirik et al[17] reported it as 4.9 days. In a 10-year cohort study in which obstetric patients were evaluated, the mean (SD) duration of mechanical ventilation was reported as 2.2 (2.9) days.[2] In our research, while mechanical ventilation was applied in 52.9% of all pregnant women, the median duration of mechanical ventilation was 3 days. In our study, although the mechanical ventilation requirement was higher in the COVID-19 group, no significant difference was found (*P*=.70). The duration of mechanical ventilation was significantly higher in the COVID-19 patients (*P*<.03). At the same time, the duration of mechanical ventilation was considerably higher in patients who died than in patients who were discharged (*P*<.001). Togal et al[18] reported that the average length of stay of obstetric patients in the ICU was 7 days, Demirkıran et al[19] reported 8 days. In a study evaluating COVID-19-positive obstetric patients, the mean (SD) duration of stay in the ICU was reported as 6.4 (7) days.[15] In our study, the median ICU stay was 2 days in the non-COVID-19 group and 6 days in the COVID-19 group (*P*<.001). This situation can be attributed to the multisystemic adverse effects of COVID-19 infection, especially in the pulmonary system of pregnant women.

It is reported that APACHE-2 scores can predict prognosis in obstetric patients followed in the ICU.[2,6,20] In another study, it was stated that scoring systems such as APACHE-2 and APACHE-3 would not help predict mortality due to the physiological effects of pregnancy.[6] While no significant difference was observed between the COVID-19 and non-COVID-19 groups in our study, the APACHE-2 scores in the first 24 hours of the deceased patients were significantly higher than in the discharged group (*P*=.007). However, GCS and arterial blood lactate levels at the time of admission to the ICU did not differ significantly in discharged and deceased obstetric patients (*P*=.07, *P*=.86). When admitted to the ICU, they had not been intubated and were conscious.

Bleeding is common in obstetric patients. It is also among the most common causes of maternal mortality.[21] Massive hemorrhage is usually seen in the intrapartum and early postpartum period and is often the result of uterine atony. Abnormalities of placental adhesion (placenta previa, placenta accreta, ablatio placenta) and peripartum hemorrhages are also responsible. In the literature, blood transfusions applied in obstetric patients in the ICU vary.[2,6,15] Ceray et al reported that blood transfusion was given to 33% of obstetric patients in the ICU in their studies before the pandemic, and vasopressor agents were administered to 12%.[6] Another study reported that 68% of patients were given a blood transfusion, while a vasopressor agent was administered in 27.7%.[2] In a study examining severe COVID-19-positive obstetric patients in the ICU, the blood transfusion rate was 3.5%.[15] In our study, postpartum bleeding and placental invasion anomalies constituted 23.5% of the indications of obstetric patients in the ICU. Blood transfusion was performed in 50% of all obstetric patients, and vasopressor agents were used in 14.7%. While blood transfusion was significantly less in the patients in the COVID-19 group (P=.001), the need for vasopressor agents was significantly higher (P<.001). We think that this is because COVID-19-positive obstetric patients are followed up primarily for pulmonary and systemic complications, and their mortality is higher than COVID-19-negative obstetric patients.

Acute renal failure, preeclampsia-eclampsia, postpartum bleeding, sepsis, and atypical hemolytic uremic syndrome are seen in obstetric patients due to secondary renal and systemic changes. Although the incidence is low, they can cause morbidity and mortality.[2,22] Ozcelik et al reported that 14.6% of postpartum obstetric patients were treated with RRT, and 43.8% received plasmapheresis.[23] Sevdi et al said that 14.5% of the patients were treated with RRT and 3.6% with plasmapheresis.[2] In our study, 8.8% of all patients were treated with RRT and 13.7% with plasmapheresis. Although the number of RRT administered in the COVID-19 group was higher than in the Non-COVID-19 group, no significant difference was observed (P=.12). However, the number of patients who underwent plasmapheresis in the COVID-19 group was significantly higher (P=.02). We think this is due to the renal and systemic effects of the COVID-19 pandemic.

The main limitation of this study is that it was retrospective and single-center. In conclusion, the most common indication for hospitalization of obstetric patients has been COVID-19 since the start of the pandemic. In the patients in the COVID-19 group, gestational week, duration of stay in ICU and mechanical ventilation, blood products, plasmapheresis, vasopressor agent requirements, and mortality were significantly higher. Before the pandemic, APACHE-2 scoring helped predict mortality. We think there is a need for multicenter studies with a larger sample size of COVID-19 patients since the disease can cause severe mortality and morbidity in critically ill obstetric patients and may also affect newborn outcomes by causing premature birth earlier in the gestation period.

Author contributions

KA wrote the original draft, reviewed and edited, KA, HÇA, ASŞ provided conceptualization, data collection, formal analysis, investigation, and methodology. KA, HÇA data collection.

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