



Anesthesia Management in Cesarean Section in Pregnant Patients with COVID-19 Diagnoses

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Abstract

Aim: The recommendation to avoid general anesthesia in pregnant women with coronavirus disease-2019 (COVID-19) and to use neuraxial blockade techniques, if possible, has not changed over time. On the other hand, general anesthesia also has to be applied to some patients in clinical practice. In this study, we evaluated anesthesia management, maternal outcomes, and clinical course in pregnant women with COVID-19 who delivered by cesarean section.

Methods: One hundred and seven pregnant women with COVID-19 who underwent cesarean sections between October 2020 and April 2021 were included in the study. Anesthesia methods, presenting symptoms, comorbidities, laboratory test results, and radiological data at admission, length of hospital stay, intensive care unit admissions, and mortality rates were retrospectively analyzed.

Results: Out of 107 pregnant women, 85 underwent cesarean surgery under spinal anesthesia and 22 under general anesthesia. Forty patients (37%) had at least one symptom, whereas sixty-seven (63%) had no symptoms at all. Fifty percent of symptomatic and only 6% of asymptomatic pregnant women were admitted to the intensive care unit, and there was a significant difference between them. Mortality was 30% in symptomatic patients and only 1% in asymptomatic patients, and the difference in mortality was significant ($p<0.05$).

Conclusion: Since the risk of intensive care and mortality is higher, particularly in symptomatic pregnant women with COVID-19, these patients should be evaluated, operated and followed up by experienced teams.

Keywords: COVID-19, anesthesia, obstetrical, spinal, intensive care units

Introduction

Severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), the cause of coronavirus disease-2019 (COVID-19), started in Wuhan, China, in December 2019, is a novel coronavirus that causes a spectrum of diseases ranging from asymptomatic to severe acute respiratory distress syndrome (ARDS), septic shock, cardiovascular symptoms, and death (1,2).

COVID-19 infection was discovered in 10% of pregnant women who presented to the hospital for any reason, according to a meta-analysis of 192 studies (3). However,

compared with non-pregnant women, pregnant women have a higher risk of having more severe symptoms and being admitted to an intensive care unit (ICU) or hospital (4). Since the lungs are the main target of the coronavirus disease, anesthesia management during cesarean surgery is essential (5,6).

The use of neuraxial blockade techniques has advantages over general anesthesia and causes less respiratory depression. It is also thought to reduce the spread of the virus to healthcare workers via aerosol. For all these reasons, the recommendation to avoid general

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anesthesia in pregnant women with COVID-19 and to use neuraxial blockade techniques, if possible, has not changed over time (4,7). On the other hand, general anesthesia also has to be applied to some patients in clinical practice.

We evaluated anesthesia management, maternal outcomes, and clinical course in pregnant women with COVID-19 who delivered by cesarean section.

Materials and Methods

Compliance with Ethical Standards

The study was carried out in accordance with the principles of the Helsinki Declaration, with the approval of the local Ethics Committees of University of Health Sciences Turkey, Basaksehir Cam and Sakura City Hospital (decision no: 2021.04.71, date: 28.04.2021). This article was not funded. Written informed consent was obtained from all patients in this study before participation.

Study Design

The study was conducted as a single-center and cross-sectional study. Pregnant women who underwent cesarean sections with COVID-19 between October 2020 and April 2021 were included in the study. Anesthesia methods (general or regional), patient characteristics (age, symptoms at admission, comorbidities), laboratory test results and radiological findings at admission, length of hospital stay, ICU needs, and mortality were analyzed. The patients' medical data were obtained from our hospital's digital automation system and anesthesia records. Patients were divided into two groups, symptomatic and asymptomatic, and the data were analyzed statistically.

Patient Management

Patients were taken to the negative pressure operating room by personnel wearing personal protective equipment, and routine monitoring was performed. Oxygen therapy was given only to those who needed it. For the spinal block, 0.5% hyperbaric bupivacaine was administered with a 25-gauge needle, and sedation was given to the patients after the baby was discharged if necessary. General anesthesia was administered when spinal anesthesia failed or was contraindicated, in cases of fetal distress with insufficient time for spinal anesthesia, and when the patient was orotracheally intubated from the ICU.

Statistical Analysis

The SPSS 24.0 (Statistical Package for the Social Sciences) program was used to evaluate and statistically analyze the data obtained in the study. Descriptive statistics were expressed as numbers and percentages (%) for discrete variables and median (minimum-maximum) for continuous variables. The Kolmogorov-Smirnov test was used to determine the normal distribution of quantitative

data, and since the assumption of normal distribution was not met, the analyses were performed using the Mann-Whitney U test. Chi-square test statistics were used to analyze the relationship between categorical variables. The statistical significance level was set at a p-value less than 0.05.

Results

In 85 of the 107 women who had cesarean surgery, spinal anesthesia was used, and general anesthesia was used in 22. Sixty-four patients had no comorbidity; fifty-seven had anemia, nine had hypothyroidism, and six had diabetes mellitus. A patient had diabetic ketoacidosis. Others had chronic bronchitis, allergic asthma, hypertension, cholestasis, preeclampsia, epilepsy, and lymphoma (Table 1).

Of the 107 pregnant women, 67 (63%) were asymptomatic. The symptoms of symptomatic women included dyspnea (30%), cough (20%), fever (4%), diarrhea (3%), and vomiting (3%). One patient had a headache, and another patient had chest pain (Table 2). All 107 patients were PCR-positive for SARS-CoV-2. There were signs of pneumonic infiltration in the chest radiograms of 25 patients (Table 3).

Table 1. Mean age and comorbidities of patients	
	Number of patients (n=107)
Average age, mean	30.7
Additional disease, No, n	64
Additional disease, Yes, n	43
Anemia, n	57
Chronic bronchitis, n	1
Allergic Asthma, n	4
Hypertension, n	4
Preeclampsia, n	2
Valvular heart disease, n	1
History of thrombus, n	1
Cholestasis of pregnancy, n	5
Fatty liver, n	1
Diabetes, n	6
Insulin resistance, n	1
Diabetic ketoacidosis, n	1
Hypothyroidism, n	9
Hepatitis, n	2
Scoliosis, n	1
Migraine, n	1
Epilepsy, n	2
Lymphoma, n	2
Thalassemia, n	1
*Unless otherwise stated, results are given as n (%)	

	Number of patients
Symptoms and findings	
No symptoms, n (%)	67 (63%)
Fever, n (%)	4 (4%)
Cough, n (%)	21 (20%)
Palpitations, n (%)	1 (1%)
Shortness of breath, n (%)	32 (30%)
Diarrhea, n (%)	3 (3%)
Chest pain, n (%)	1 (1%)
Headache, n (%)	1 (1%)
Vomiting, n (%)	3 (3%)
Itching, n (%)	1 (1%)
*Unless otherwise stated, results are given as n (%)	

Leucocytosis was present in 27 (25%) patients, and lymphopenia in 34 (32%) patients. Twenty-four patients without preeclampsia showed thrombocytopenia. The lowest thrombocyte counts were 63,000 and 65,000, and these patients were under general anesthesia. A patient with a thrombocyte count of 70,000 underwent spinal anesthesia without any neurological sequelae. Patients with thrombocyte counts of 91,000 and 99,000 were operated on under general anesthesia. Seventy-three patients had an elevated C-reactive protein level, 16 had an elevated PCT level, and 71 had an elevated LDH level (Table 3).

The mean length of hospitalization was 9 days for pregnant women who were operated on under spinal anesthesia and 15 days for those who were operated on under general anesthesia. Twenty-four pregnant women were admitted to the ICU. In 107 pregnant

	Number of patients, n
Laboratory results	
Leucocytosis, n	27
Lymphopenia, n	34
Thrombocytopenia, n	24
Elevated CRP concentrations, n	73
Elevated ALT concentrations, n	24
Elevated AST concentrations, n	47
Elevated PCT levels, n	16
Elevated LDH levels, n	71
Radiographic evidence of pneumonia, n	25
*Unless otherwise stated, results are given as n (%). (Leucocytosis >10.000, lymphopenia <1.000, thrombocytopenia <150.000, elevated CRP >10, elevated ALT >33, elevated AST >31, elevated LDH >214, elevated PCT >0.5) CRP: C-reactive protein, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, PCT: Procalcitonin, LDH: Lactate dehydrogenase	

women with COVID-19, the overall mortality rate was 12%. Among them, those who were operated on under spinal anesthesia had a mortality rate of 11%, and those who were operated on under general anesthesia had a mortality rate of 18 (Table 4).

Forty of 107 pregnant women had at least one symptom, and 67 had none. While at least one comorbidity in 43 of them, 64 had no comorbidity. Fifty percent of symptomatic and only 6% of asymptomatic pregnant women were admitted to the ICU, and there was a significant difference between them ($p < 0.05$). Mortality was 30% in symptomatic patients and only 1% in asymptomatic patients, and there was a significant difference in mortality ($p < 0.05$). ICU admission was 21% in patients with comorbidity and 23% in those without comorbidity, and the difference was insignificant. Mortality was 16% in patients with comorbidity and 9% in those without comorbidity. There was no significant difference in mortality between patients with comorbidity and those without comorbidity (Table 5).

Discussion

SARS-CoV-2 infection enters the respiratory tract through nasopharyngeal mucosal membranes. A mild form affecting the upper respiratory tract occurs in approximately 80% of the cases. In contrast, a very severe form of the disease occurs in 20% of cases, affecting pulmonary alveolar cells and causing a systemic inflammatory response due to the cytokine storm. It has been shown that disease severity is related to advanced age and the presence of comorbidities (2,7). Most COVID-19-positive pregnant women are asymptomatic, but it has been reported that pregnancy increases the risk of having severe COVID-19 (8-10). Many studies have shown that pregnant women admitted to the hospital with critical coronavirus disease are more likely than non-pregnant women of reproductive age to be admitted to an ICU, be mechanically ventilated, or have a higher morbidity burden. Pre-existing maternal comorbidities, in particular, increase the risk (6,11-13).

	Spinal anesthesia (n=85)	General anesthesia (n=22)
Length of hospitalization, days	9	15
Number of patients admitted to ICU, n	12	12
Length of stay in ICU, days	14	16
Mortality, n (%)	9 (11)	4 (18)
*Unless otherwise stated, results are given as n (%). ICU: Intensive care unit		

Table 5. The effect of patients' symptoms and comorbidities on ICU hospitalization and mortality

Number of patients		Admission to ICU				p-value	Mortality				p-value
		A		N/A			A		N/A		
Symptom	Yes	20	(50%)	20	(50%)	0.000	12	(30%)	28	(70%)	0.000
	No	4	(6%)	63	(94%)		1	(1%)	66	(99%)	
No	Yes	9	(21%)	34	(79%)	0.760	7	(16%)	36	(84%)	0.284
	No	15	(23%)	49	(77%)		6	(9%)	58	(91%)	

*Unless otherwise stated, results are given as n (%).
ICU: Intensive care unit

In a cohort study of 126 obstetric patients by Keita et al. (14), 17% of cases with COVID-19 were hospitalized in the ICU. It has been reported that symptomatic pregnant women are more likely to be admitted to the ICU and require mechanical ventilation (15). ICU hospitalization was 22.4% in our study. While the rate of ICU admission was 50% in pregnant women with symptoms, it was only 6% in those without symptoms, and there was a significant difference between them ($p < 0.05$). While 21% of patients with comorbidity were admitted to the ICU, 23% of those without comorbidity were admitted.

Fever, coughing, dyspnea, sore throat, myalgia, nasal discharge, smell or taste abnormalities, ARDS, arrhythmias, acute cardiac damage, and shock are all signs and symptoms of COVID-19 in pregnant women (2). Sutton et al. (16) evaluated 454 women who gave birth and found COVID-19 in 79 (17%). 27.9% of pregnant women were symptomatic, with symptoms including cough (13.9%), fever (10.1%), chest pain (5.1%), and myalgia (5.1%). In our study, all the patients had a positive SARS-CoV-2 polymerase chain reaction (PCR) test, and 63% were asymptomatic. Of those who were symptomatic, 30% had dyspnea, 20% were coughing, and 4% had a fever. Nine percent% complained of diarrhea, vomiting, palpitations, chest pain, headache, and itching.

Pregnant women may be more susceptible to respiratory tract pathogen infection due to elevated diaphragm muscles, airway oedema, increased oxygen demand, and immunological changes. Simultaneously, all these pregnancy-related changes make pregnant women more susceptible to hypoxemia (17). Pregnant women with COVID-19 are managed according to the disease's severity. Depending on the clinical course of the disease, arterial blood gas analysis, lactate, liver and kidney function tests, and cardiac enzymes should be serially measured. Monitoring vital signs and oxygen saturation are important. Maternal vital signs should be closely monitored.

Maintain maternal oxygen saturation (SpO_2) of 95%; if SpO_2 drops below 95%, an arterial blood gas analysis should be performed to evaluate PaO_2 . To maintain an adequate oxygen gradient between the mother and

the fetus, PaO_2 should be maintained above 70 mmHg. Depending on the severity of hypoxemia, inhaled oxygen can be administered. To achieve adequate oxygenation, high-flow oxygenation, intubation or mechanical ventilation, and extracorporeal membrane oxygenation (ECMO) can be used (18). COVID-19 by itself is not a reason to change the delivery method. If pregnancy is beyond 32 weeks and delivery would improve respiratory function in pregnant women, delivery is recommended (19). In this study, 20 (18%) pregnant women needed oxygen therapy, of whom 2 were intubated and mechanically ventilated before cesarean surgery.

When an anesthesia technique for cesarean surgery is selected for a COVID-19-positive pregnant woman, the urgency of the operation should be the primary consideration. COVID-19 is not a contraindication for neuraxial anesthesia. Evaluation of thrombocytopenia should be given priority when managing patients suspected of having confirmed COVID-19. It should be remembered that respiratory distress may be aggravated due to a further decline in functional residual capacity caused by neuraxial anesthesia (20). Regional anesthesia is recommended because the target organs of the SARS-CoV-2 infection are the lungs, and regional anesthesia will reduce intubation-related pulmonary complications and aerosol release (4,8). Binyamin et al. (21) found that the rate of neuraxial block in elective cesarean surgery was 44.8% before the SARS-CoV-2 pandemic, whereas it rose to 79.3% during the pandemic.

In our study, spinal anesthesia was the anesthesia technique of choice during cesarean surgery. In 79% of the 107 pregnant women, spinal anesthesia was used, while general anesthesia was used in 21%. General anesthesia was used when any maternal or fetal emergency condition existed (when there was no waiting time for regional anesthesia), when spinal anesthesia was contraindicated, when a patient was brought to the operating room from the ICU while intubated, or when intrathecal anesthesia failed. A study from the United Kingdom reported a significant drop in the rate of general anesthesia for cesarean surgery during the COVID-19 pandemic (22). Since our hospital was opened during the COVID-19 pandemic, we could

not compare the anesthesia management in cesarean deliveries during and before the pandemic.

Studies have reported thrombocytopenia in one-third of patients with COVID-19 infection (23). A thrombocyte count of 75,000 and above is recommended as an acceptable level for neuroanesthesia (20,23-25). Lee et al. (26) recommend that regional anesthesia be performed at lower thrombocyte counts (70,000 or lower) in pregnant women who may develop respiratory failure with general anesthesia. In this study, 24 pregnant women without preeclampsia developed thrombocytopenia. Patients with thrombocytopenia underwent cesarean surgery under general anesthesia. Only one patient with a thrombocyte count of 70,000 was operated on under spinal anesthesia without any neurological complications. Studies have recommended using neuraxial procedures for pregnant women with COVID-19 without contraindications (8). Sangroula et al. (27) also demonstrated that neuraxial anesthesia with standard-dose local anesthetic agent administration was safe and effective in COVID-19-positive pregnant women who were asymptomatic or mildly symptomatic.

According to Villar et al. (28), 11 out of 706 pregnant women diagnosed with COVID-19 died. COVID-19 symptoms were also linked to higher morbidity and mortality, with a 22-fold increase in the probability of death. In our study, on the other hand, 13 (12%) of 107 pregnant women with COVID-19 died. Of these, seven had comorbidities (hypothyroidism, diabetic ketoacidosis, hypertension, a history of intracerebral thrombus, epilepsy, asthma, and Hodgkin lymphoma), while six had none. Twelve patients died in the ICU, and a patient who refused treatment after cesarean surgery died after discharge. There was no significant difference in mortality between patients with and without comorbidities. Mortality was 30% in symptomatic pregnant women and 1% in asymptomatic women. In the study, mortality was significantly higher in the presence of symptoms in pregnant women with COVID-19.

According to the data provided by the Turkish Ministry of Health, maternal mortality increased after the COVID-19 pandemic compared with pre-pandemic figures. Increased morbidity and mortality have been observed in COVID-19-positive pregnant women with comorbidities. Despite a multidisciplinary approach, mortality rates are particularly high during peripartum care in advanced centers. Our hospital is also a leading referral center for pregnant patients with multiple comorbidities and clinical findings, as well as pregnant women from other hospitals. All available treatments, including ECMO, can be performed at our center. This explains the increased ICU admission and mortality rates among our pregnant patients. In our

study, patients with COVID-19 who underwent cesarean surgery had a mortality rate of 12%.

Study Limitations

The most important limitation of the study is that it is retrospective in nature. The lack of long-term results is another important limitation. Despite these limitations, the relatively high number of patients in the study and the fact that we are a center with many treatment possibilities make the study valuable.

Conclusion

In this study, the incidence of cesarean delivery under spinal anesthesia was higher than that under general anesthesia in pregnant women with COVID-19. Spinal anesthesia is safe for pregnant women with COVID-19. Symptoms and comorbidity increase the rate of intensive care hospitalization, mechanical ventilation, and morbidity, and in our study, we found that intensive care and mortality rates were higher in symptomatic COVID-19 pregnant women. These patients should be evaluated, operated and followed up by experienced teams.

Ethics

Ethics Committee Approval: The study was approved by the local ethics committees of University of Health Sciences Turkey, Basaksehir Cam and Sakura City Hospital (decision no. 2021.04.71, date: 28.04.2021).

Informed Consent: Written informed consent was obtained from all patients in this study before participation.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: N.A., Concept: N.A., D.A., Design: N.A., D.A., Data Collection or Processing: G.N.K.K., Analysis or Interpretation: N.A., D.A., G.N.K.K., M.C., F.G.O., Literature Search: N.A., D.A., M.C., F.G.O., Writing: N.A., D.A., G.N.K.K., M.C., F.G.O.

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