ORIGINAL ARTICLE

Evaluation of 254 cesarean sections with COVID-19 in terms of anesthesia and clinical course: 1-year experience

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Abstract

Purpose The study aims to compare anesthesia methods, clinical course, and maternal and fetal outcomes of symptomatic and asymptomatic pregnant women undergoing cesarean operation with confirmed COVID-19.

Methods 254 pregnant women with COVID-19 who had a cesarean section in our hospital between March 2020 and March 2021 were included in the study. Demographic information, laboratory test results, radiological data, treatments, anesthesia methods, and prognoses of the patients were evaluated retrospectively.

Results On admission, 160 (63%) patients were asymptomatic (Group A), and 94 (37%) patients were symptomatic (Group S). The ratio of patients who needed oxygen therapy in the obstetric ward ($p < 0.001$) and intraoperative period ($p < 0.001$) and ICU admission ($p = 0.005$) was higher in Group S. Neutrophil-to-lymphocyte ratio (NLR), ferritin, procalcitonin, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels were higher in Group S. In both groups, spinal anesthesia was performed predominantly. The rate of general anesthesia was significantly higher in Group S (16.0% vs. 4.4%, $p = 0.003$). No difference was found in the amount of sedatives during the spinal anesthesia.

Conclusion Close follow-up of the laboratory values and comorbidities (especially asthma) of pregnant will provide information about the clinical course as in other patient groups. Spinal anesthesia is a safe and sufficient anesthesia method in both symptomatic and asymptomatic COVID-19 pregnant women when performed by experienced hands.

Keywords SARS-CoV-2 · COVID-19 · Pregnancy · Cesarean section · Anesthesia

Introduction

Coronavirus disease of 2019 (COVID-19)-positive pregnant women experience worse perinatal outcomes compared with pregnant women without COVID-19. Comorbidities increase pregnancy complications, incidence, and severity of the infection. In a meta-analysis, the mortality rate of non-pregnant COVID-19 hospitalized patients was 6.4%, while the mortality rate of all pregnant patients was 11.3% [1]. These patients have a high probability of maternal morbidity, ICU admission, mechanical ventilation, and perinatal death [2–4]. Compared with non-pregnant women aged 35–44 years with COVID-19, pregnant patients in the same age group were found approximately four times more likely to require invasive ventilation and twice as likely to die [5].

Although elective operations can be delayed, when the cesarean section (c-section) indication occurs, it is inevitable for patients to receive anesthesia. In our hospital, which is a pandemic center, pregnant women constituted the largest group of COVID-19-positive patients who needed an operation. Some of these COVID-19-positive patients present with symptoms mostly like fever, dry cough, dyspnea, and bilateral ground-glass opacities on chest computed tomography scan (CT). Despite this, some COVID-19-positive patients are completely asymptomatic. Those with severe illness may rapidly develop acute respiratory distress syndrome and require intensive care unit admission.

The aim of this study is to compare anesthesia methods, clinical course and maternal and fetal outcomes of symptomatic and asymptomatic pregnant women undergoing c-section with confirmed COVID-19.

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Materials and method

Ethical approval for this study (E1/1733/2021) was provided by the Ethical Committee of Ankara City Hospital, Ankara, Turkey, on 14 April 2021.

Patient selection

Parturients with confirmed COVID-19 positivity by real-time polymerase chain reaction (RT-PCR) test who underwent c-section in our hospital between March 2020 and March 2021 were included in this retrospective, observational, single center cohort study. Patients who were even assumed to have COVID-19 infection (clinical situation, travel, or contact history) yet were not confirmed with a real-time polymerase chain reaction (RT-PCR) test were not included in the study.

For the routine practice of our institution, all patients admitted for hospitalization were tested for COVID-19 by RT-PCR. Patients were distributed into two groups according to their symptom status. Group S consists of the patients with positive RT-PCR test with any of the COVID-19 symptoms (cough, headache, dyspnea, fever, anosmia-ageusia, myalgia, diarrhea, sore throat). Group A consists of the patients with positive RT-PCR tests without any symptoms. Asymptomatic patients were the pregnant women who were found positive as a routine PCR test result when they were admitted to our hospital for delivery due to their pregnancy follow-up or who were followed-up in an external center and found positive for COVID-19 during preoperative examinations and were referred to our hospital, which is a pandemic center, for delivery.

Data collection

The following parameters were recorded by examining the clinical records of all cases:

1. *Patient characteristics* Age, gestational week, symptoms at admission, comorbid diseases. 2. *Laboratory and radiographical examinations* Laboratory examinations before the operation, radiological findings. 3. *Surgical and anesthetic management* Cesarean indications, Apgar scores, type of anesthesia, used anesthesia drugs, duration of anesthesia and surgery, amount of fluids, ephedrine, methylergonovine, and oxytocin administered, number of patients needed tranexamic acid, blood transfusions, intraoperative and postoperative complications. 4. *COVID-19 treatment* Drugs administered for COVID-19 treatment, perioperative oxygen therapy and postoperative intensive care unit (ICU) needs, length of hospital stay, length of stay in ICU, the number of patients needed ventilation support (invasive or non-invasive).

Patient management

All the patients were operated on in two operating rooms with negative pressure prepared for COVID-19 patients. While PCR-positive patients were operated in one of the rooms and suspected patients with no proven COVID-19 positivity in the other, the same precautions were taken in both operating rooms. After the entire team was dressed and prepared with the equipment, including gloves, goggles, face shields, N95 respirators, and gowns, the patient was brought to the operating room. The surgery team consisted of two surgeons, one of whom was a senior, and a surgical nurse, and the anesthesia team consisted of an anesthesiologist and an anesthesia nurse.

Before the patients came to the room, controls of the patient's file information and consents, anesthesia tools, and medications were completed, and the patients were quickly monitored, vascular access was secured, and anesthesia interventions were initiated. The patients were administered 500 ml of crystalloid fluid to prevent hypotension in the ward.

All patients with oxygen saturation below 93% were started on 5 l/min oxygen therapy immediately. In cases where spinal anesthesia was performed, if the oxygen saturation were 93% and above, oxygen therapy was not initiated not to cause aerosol emission. For the spinal block, the most suitable L_{2-3} or L_{3-4} intervertebral space was selected, and 0.5% hyperbaric bupivacaine was administered with a 26 gauge atraumatic spinal needle passed through a 22 gauge guide needle. Sedation was administered to the patients who experienced pain or anxiety. Whereas propofol and ketamine were given whenever needed during the c-section, fentanyl and midazolam were only given after the delivery of the baby.

After spinal anesthesia, cases where the mean arterial pressure fell below 65 mmHg or systolic arterial pressure decreased to 30% compared to the baseline value were accepted as hypotension and 5 mg i.v. bolus ephedrine was administered and repeated every 2.5 min until normal values.

If general anesthesia was to be performed, the surgical team was taken out of the room until tracheal intubation. Preoxygenation was made with low flow and two-hand technique. General anesthesia was induced with propofol and rocuronium, and hand-bag ventilation was not performed after induction as much as possible. Sevoflurane was used for maintenance of anesthesia. If for some reason, the circuit had to be disconnected, the tube was clamped. For respiratory circuit and anesthesia machine, antiviral filters were used. Sugammadex was used for reversal of neuomuscular blockage in all patients. Aerosol distribution was prevented by covering the plastic sheet over the tracheal tube and patient's face during extubation. Extubation time was

carefully chosen to prevent the patient from coughing. Post-operative care of all patients was performed in the same operating room for approximately 30 min. In patients who received general anesthesia, intravenous tramadol sulphate and tenoxicam were administered for postoperative pain.

Statistical analyses

Statistical analyses were performed using SPSS Software (Version 21.0, SPSS Inc., IL). Categorical data were expressed as numbers and percentages (%) and continuous data as mean ± SD (range). Kolmogorov–Smirnov test was used for determining normal distribution for quantitative data; as normal distribution was not provided for any of the quantitative data, analyses were performed using Mann–Whitney U test. Chi-square test and The Fisher–Freeman–Halton exact test was used to examine the relationship between categorical variables. A p value of < 0.05 was considered statistically significant.

Results

A total of 308 cases were operated in two operating rooms with negative pressure prepared for COVID-19 patients between March 2020 and March 2021. Thirty of them were non-cesarean procedures. 24 of the remaining 278 cases (except 254 that have been proven to be COVID-19 by PCR) were considered as COVID-19 positive due to the presence of COVID-19-like symptoms or history of contact but the PCR result could not have been waited, or the cases with negative results. On admission, among 254 COVID-19-positive pregnants, 160 (63%) patients were asymptomatic, 94 (37%) of the patients were symptomatic. The most common symptom was cough (19.3%), while the least common was diarrhea (2%). Demographic features and comorbities, c-section indications and initial COVID-19 symptoms of the cases are given in Tables 1 and 2.

The mean gestational age was lower ($p < 0.001$) and preterm delivery rate was higher ($p < 0.001$) in Group S. The ratio of ASA 3 patients ($p = 0.001$) and existence of co-morbid diseases ($p = 0.02$) was also higher in Group S.

There was a significant difference between the two groups in terms of lymphopenia ($p = 0.012$) and normal and high platelet counts ($p = 0.017$). The mean hemoglobin level and leucocyte count were lower, Neutrophil-to-lymphocyte ratio (NLR), ferritin, procalsitonin, aspartate aminotransferase (AST), and alanine aminotransferase (ALT) levels were higher in Group S. There was a significant difference between the two groups in terms of mean hemoglobin level ($p = 0.024$), leucocyte count ($p = 0.001$), NLR ($p = 0.01$), ferritin ($p = 0.022$), procalcitonin ($p < 0.001$), AST ($p < 0.001$) and ALT ($p = 0.001$) levels (Table 3).

Anesthesia management of the cases is presented in Table 4. The rate of general anesthesia was significantly higher in Group S (16.0% vs. 4.4%, $p = 0.003$). When the oxygen requirement of the patients who underwent spinal anesthesia during the operation was evaluated, the oxygen requirement of Group S was significantly higher (2.6% vs 31.6%, $p < 0.001$). The amount of intravenous fluid used in Group A was higher ($p < 0.001$). No difference was found in the amount of midazolam, propofol, ketamine, and fentanyl used for sedation in patients who underwent spinal anesthesia. The time between the patient's entrance to the room and the onset of anesthesia was 6.4 ± 2.4 min in Group A and 6.0 ± 2.3 min in Group S. Anesthesia administration duration was 6.0 ± 2.0 min and 5.9 ± 3.4 min, surgery duration was 35.7 ± 12.3 min and 36.0 ± 13.4 min, respectively. There were no significant differences between the two groups in terms of timing (Table 4).

The ratio of newborns with an Apgar Score > 7 in Group S vs. Group A was 77.7% vs. 90.0% ($p = 0.025$) and also the ratio of newborns with an Apgar Score < 4 in Group S vs. Group A was 4.3% vs. 0.6% ($p = 0.025$) (Table 4).

Cesarean indication of the patients who underwent general anesthesia is presented in Fig. 1 (Ivf-twin intrauterine fetal demise and intrauterine fetal demise were evaluated as a single indication in Fig. 1). Fetal distress and previous cesarean delivery were the major indications of cesarean with general anesthesia in the Group S. The indications for the choice of general anesthesia in Group A were: history of epilepsy for 1 patient; history of the cerebrovascular event for 1 patient; cardiac disease necessitating general anesthesia for 1 patient and not appropriate timing of low-molecular weight heparin (LMWH) for regional anesthesia for 4 patients. The indications for the choice of general anesthesia in Group S were: cardiac disease necessitating general anesthesia for 2 patients, deterioration of the mother's health for 2 patients, fetal distress for 5 patients, and not appropriate timing of LMWH for regional anesthesia for 6 patients.

Complications occurred in the COVID process in 8 (3.1%) patients. Cavernous sinus thrombosis, toxic ischemic hepatitis, and splenic infarction occurred in patients in Group S. Post-COVID sarcopenia occurred in one patient in Group A. One patient in Group A was hospitalized again after dyspnea developed 2 days after discharge and was discharged after one week of treatment. Two patients—one for each group—underwent re-laparotomy within 24 h due to postoperative bleeding, and a blood transfusion was performed at the second operation. One patient from Group S needed a blood transfusion due to bleeding during the operation.

The mean duration of hospitalization was 7.2 ± 6.1 days in Group S and 4.4 ± 4.2 days in Group A ($p < 0.001$).

The ratio of patients who needed oxygen therapy in the obstetric ward ($p < 0.001$) and intraoperative period

Table 1 Demographic features and comorbities, cesarean section indications

	Asymptomatic	Symptomatic	p
Maternal age (years) (mean ± SD) (min–max)	29.5 ± 4.9 (19–42)	29.6 ± 5.5 (18–42)	0.779
Gestational age (weeks) (mean ± SD) (min–max)	37.7 ± 2.1 (27–40)	35.7 ± 3.5 (26–41)	< 0.001*
Preterm	Yes/No	Yes/No	< 0.001*
n	33/127	42/52	
%	20.6/79.4	44.7/55.3	
ASA, n (%)			
2	153 (95.6)	78 (83.0)	0.001*
3	7 (4.4)	16 (17.0)	
Existince of co-morbid disease	Yes/No	Yes/No	
n	29/131	29/65	0.02*
%	18.1/81.9	30.9/69.1	
Comorbid disease, n (%)			
Diabetes mellitus type 1	0 (0.0)	1 (3.4)	
Diabetes mellitus type 2	1 (3.4)	3 (10.3)	
Gestational diabetes mellitus type 2	2 (6.9)	2 (6.9)	
Hypotyroidism	15 (51.7)	7 (24.1)	
Talassemia	1 (3.4)	3 (10.3)	
Hypertension	3 (10.3)	1 (3.4)	
Hypertension + Diabetes mellitus2	0 (0.0)	2 (6.9)	
Cardiac disease	1 (3.4)	2 (6.9)	0.260
Asthma + cardiac	0 (0.0)	2 (6.9)	
Asthma	1 (3.4)	2 (6.9)	
Cerebro vascular disease	1 (3.4)	0 (0.0)	
Macular congenital cataract	0 (0.0)	1 (3.4)	
Multiple sclerosis	0 (0.0)	1 (3.4)	
Wegener granulomatosis	1 (3.4)	0 (0.0)	
Leukemia	0 (0.0)	1 (3.4)	
Familial mediterranean fever	1 (3.4)	0 (0.0)	
Epilepsy	1 (3.4)	0 (0.0)	
Depression	1 (3.4)	0 (0.0)	
Cholestasis of pregnancy	0 (0.0)	1 (3.4)	
Cesarean indication, n (%)			
Previous cesarean delivery	75 (46.9)	36 (38.3)	
Fetal distress	29 (18.1)	19 (20.2)	
Breech presentation	7 (4.4)	7 (7.4)	
Cephalopelvic disproportion	21 (13.1)	7 (7.4)	
Multiple pregnancy	4 (2.5)	3 (3.2)	
Placenta previa	0 (0)	1 (1.1)	0.053
Pre-eclampsia	3 (1.9)	4 (4.3)	
Macrosomia, hydrocephaly	7 (4.4)	2 (2.1)	
Cholestasis of pregnancy	3 (1.8)	2 (2.1)	
Deterioration of the mother's health	0 (0.0)	5 (5.3)	
Preterm labor	1 (0.6)	2 (2.1)	
Ivf-twin intrauterine fetal demise	1 (0.6)	1 (1.1)	
Intrauterine fetal demise	0 (0.0)	1 (1.1)	

* $p < 0.01$

($p < 0.001$) and ICU admission ($p = 0.005$) was higher in Group S. The ratio of patients who needed favipiravir, lopinavir, corticosteroids, antibiotics, tocilizumab, convalescent plasma was higher in Group S (Table 5). Although the ratio of patients who had chest CT was

Table 2 Initial COVID-19 symptoms

	Yes n (%)	No n (%)
Symptoms	94 (37)	160 (63)
Headache	13 (5,1)	241 (94,9)
Anosmia-ageusia	7 (2,8)	247 (97,2)
Fever	41 (16,1)	213 (83,9)
Myalgia	38 (15)	216 (85)
Cough	49 (19,3)	205 (80,7)
Dyspnea	27 (10,6)	227 (89,4)
Sore throat	12 (4,7)	242 (95,3)
Diarrhea	5 (2)	249 (98)

higher in Group S ($p < 0.001$), infiltration in chest CT did not differ among groups (Table 5).

Of the 8 patients admitted to ICU (patients 1–8), 2 had no comorbid disease, while the other 6 had Wegener granulomatosis, hypothyroidism, multiple sclerosis, mitral stenosis, asthma, and asthma with mitral stenosis. The last 2 patients died in the ICU due to respiratory failure 36 and 10 days

after surgery, respectively. Our 2 patients who died were asthmatic, and both were in Group S.

The 28-week pregnant patient (patient 1) presented with dyspnea, and the 34-week pregnant patient (patient 2) with complaints of dyspnea, fever, and cough. 34-week pregnant patient had mitral stenosis together with asthma. Both patients did not apply to regular follow-ups for asthma and obstetrical management during pregnancy and not use their asthma medications regularly. Bilateral severe infiltration was detected on chest CT during ICU follow-up of these 2 patients. On the fourth day of hospitalization, the 28-week pregnant patient, who had a c-section due to poor general condition, was admitted to the ICU postoperatively. She was intubated on the second day in the ICU. The patient, who was connected to ECMO for the last 5 days, died on the 36th day in the ICU. The 34-week pregnant patient had a c-section due to preterm labor on the first day of admission. Then she was transferred to ICU and intubated. The patient died on the 11th day of hospitalization. Both patients were operated on under spinal anesthesia.

In Group A, only 1 patient needed ICU. This 33-year-old patient, at 39 weeks of gestational age, diagnosed with

Table 3 Laboratory test results

		Asymptomatic		Symptomatic	p
Lymphopenia		Yes/No		Yes/No	0.012*
n		93/66		69/24	
%		58.5/41.5		74.2/25.8	
Platelet count, n (%)					
Normal		151 (95.0)*		79 (84.9)*	0.017*
High		5 (3.1)*		10 (10.8)*	
$100–150 \times 10^3$		2 (1.3)		1 (1.1)	
$50–100 \times 10^3$		1 (0.6)		3 (3.2)	
Total		159 (100.0)		93 (100.0)	
	n	Mean ± SD (min–max)	n	Mean ± SD (min–max)	
Hemoglobin (g/dL)	159	11.6 ± 1.4 (8–15.6)	93	11.2 ± 1.5 (7.6–15.1)	0.024*
Leucocyte (10^3/mL)	159	9.2 ± 3.3 (3.5–22.4)	93	7.9 ± 2.8 (2.7–17)	0.001*
NLR	159	4.7 ± 2.4 (0.01–15)	89	6,7 ± 4,7 (1.5–26)	0.01*
IL-6 (pg/ml)	81	21.5 ± 21.6 (1.9–113)	55	28.1 ± 93.5 (2.5–701)	0.282
D-Dimer (mg/L)	159	2.58 ± 2.17 (0.3–14)	92	3.74 ± 5.04 (0.2–32.6)	0.144
CRP (g/L)	152	0.0398 ± 0.0406 (0–0.18)	89	0.0475 ± 0.0437 (0–0.2)	0.103
Procalsitonin	137	0.04 ± 0.05 (0–0.56)	88	0.31 ± 1.95 (0.02–18.34)	<0.001*
Ferritin	136	28.9 ± 45.2 (2–317)	86	199.1 ± 1021.1 (3–9130)	0.022*
Fibrinogen	74	4.8 ± 0.8 (2.4–6.7)	43	7.0 ± 14.2 (3.3–98)	0.366
AST	135	23.6 ± 18.9 (4–162)	75	34.5 ± 37.7 (6–312)	<0.001*
ALT	135	18.4 ± 16.1 (2–128)	75	26.8 ± 29.7 (2–241)	0.001*
BUN	122	16.5 ± 5.2 (0.6–39)	65	17.1 ± 7.2 (9–43)	0.504
Creatinine	132	0.5 ± 0.1 (0.3–0.92)	68	0.5 ± 0.1 (0.3–0.74)	0.399

NLR neutrophil-to-lymphocyte ratio, *IL-6* Interleukin-6, *CRP* C-reactive protein, *AST* aspartate aminotransferase, *ALT* alanine aminotransferase, *BUN* blood-urea nitrogen

*$p < 0.01$

Table 4 Anesthesia management

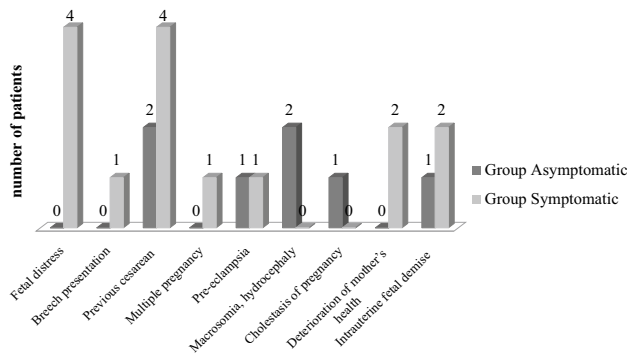|	Asymptomatic	Symptomatic	p
Anesthesia type, n (%)			
Spinal anesthesia	152 (95.0)*	79 (84.0)*	0.003*
General anesthesia	7 (4.4)*	15 (16.0)*	
Spinal + general anesthesia	1 (0.6)	0 (0.0)	
Patient's entrance to the room-the onset of anesthesia (min), mean ± SD (min–max)	6.4 ± 2.4 (4–15)	6.0 ± 2.3 (5–19)	0.207
Anesthesia administration duration (min), mean ± SD (min–max)	6.0 ± 2.0 (3–10)	5.9 ± 3.4 (3–25)	0.081
Surgery duration (min), mean ± SD (min–max)	35.7 ± 12.3 (15–80)	36.0 ± 13.4 (12–100)	0.949
O_2 need	Yes/No	Yes/No	
n	4/148	25/54	< 0.001*
%	2.6/97.4	31.6/68.4	
Bupivacaine (mg), mean ± SD (min–max)	12.5 ± 1.0 (10–15)	12.4 ± 1.1 (10–15)	0.396
Intravenous fluid (ml), mean ± SD (min–max)	1375 ± 350 (500–2500)	1249 ± 312 (750–2500)	< 0.001*
Oxytocin (U), mean ± SD (min–max)	22.5 ± 5.9 (20–60)	21.1 ± 4.0 (15–40)	0.100
Midazolam need	Yes/No	Yes/No	0.669
n	93/59	51/28	
%	61.2/38.8	61.2/38.8	
Midazolam (mg), mean ± SD (min–max)	1.94 ± 0.2 (1–3)	1.90 ± 0.4 (1–3)	0.536
Propofol need	Yes/No	Yes/No	0.464
n	15/137	5/74	
%	9.9/90.1	6.3/93.7	
Propofol (mg), mean ± SD (min–max)	100 ± 80 (20–300)	116 ± 72 (50–240)	0.445
Ketamine need	Yes/No	Yes/No	0.417
n	33/119	21/58	
%	21.7/78.3	26.6/73.4	
Ketamine (mg), mean ± SD (min–max)	46 ± 11 (25–75)	50 ± 17 (25–100)	0.495
Fentanyl need	Yes/No	Yes/No	0.228
n	10/142	2/77	
%	6.6/93.4	2.5/97.5	
Fentanyl (μg), mean ± SD (min–max)	65 ± 21 (50–100)	62.5 ± 17 (50–75)	1.000
Ephedrine need	Yes/No	Yes/No	0.869
n	35/117	17/62	
%	23.0/77.0	21.5/78.5	
Ephedrine, mg mean ± SD (min–max)	12.1 ± 5.5 (5–25)	13.2 ± 6.3 (5–25)	0.574
Tranexamic acid need	Yes/No	Yes/No	0.362
n	2/158	3/91	
%	1.3/98.7	3.2/96.8	
Packed red blood cell need	Yes/No	Yes/No	0.532
n	2/158	0/94	
%	1.3/98.7	0.0/100	
Methylergonovine need	Yes/No	Yes/No	0.375
n	28/132	12/82	
%	17.5/82.5	12.8/87.2	
Apgar Score, 1st min, n (%)			
>7	144 (90.0)*	73 (77.7)*	0.025*
5–6	13 (8.1)	15 (16.0)	
<4	1 (0.6)*	4 (4.3)*	
0	2 (1.3)	2 (2.1)	

*$p < 0.01$

Fig. 1 Cesarean section indications in patients who underwent general anesthesia

Wegener granulomatosis (patient 3) was found positive as a routine PCR test result when she was admitted to our hospital because of premature rupture of the fetal membranes. Severe respiratory distress, tachycardia, and tachypnea were observed on the third day after the c-section under spinal anesthesia, and the patient was admitted to the ICU and intubated. After pulmonary CT angiography, massive pulmonary thromboembolism was detected. She was followed-up in the ICU for 33 days, 10 days of which were in intubated condition. The patient, who was followed-up on the ward for 12 days after the ICU, was discharged 48 days later.

In the ICU, 3 patients were followed-up without intubation. A 33-year-old, 28-week-pregnant woman without any comorbid disease (patient 4) presented with cough, dyspnea, and sore throat, had a c-section with multiple pregnancy

indication on the second day of her admission. Because of the inappropriate timing of LMWH for regional anesthesia, general anesthesia was applied. After 6 days in the ICU and 3 days on the ward, the patient was discharged. The second patient, a 38-year-old, 32-week-pregnant with multiple sclerosis (patient 5), presented with fever, myalgia, cough, and dyspnea. Due to the deterioration of the patient's health, she was quickly delivered by c-section under general anesthesia. The patient was admitted to the ICU postoperatively for 7 days and was discharged on the 10th day of her hospitalization. The third patient was a 32-year-old, 36-week pregnant woman with hypothyroidism (patient 6). She presented with headache, dyspnea, and cough. On the 2nd day of hospitalization, she underwent c-section under general anesthesia due to fetal distress. Because of the increase of dyspnea on the third day, the patient was followed-up in the ICU for 2 days and was discharged on the 5th day of the hospitalization.

Another patient followed-up in the ICU was a 29-year-old, 37-week pregnant woman with mitral stenosis (patient 7) who presented with myalgia. The patient was delivered by c-section under general anesthesia because of fetal distress on the day of hospitalization. She was admitted to ICU due to postoperative dyspnea and was intubated. The patient, who was extubated after 5 days, was discharged on the 20th day of admission after 18 days of ICU follow-up.

The last patient followed-up in the ICU was an 18-year-old, 28-week pregnant woman without comorbidity (patient 8). The patient, who had dyspnea and cough, was delivered quickly by c-section under general anesthesia on the day of

Table 5 COVID-19 course and treatment

	Asymptomatic		Symptomatic		p
	Yes n (%)	No n (%)	Yes n (%)	No n (%)	
O_2 need intraoperatively	4 (2.6)	148 (97.4)	25 (31.6)	54 (68.4)	< 0.001*
O_2 need in obstetric ward	4 (2.5)	156 (97.5)	32 (34.0)	62 (66.0)	< 0.001*
ICU admission	1 (0.6)	159 (99.4)	7 (7.4)	87 (92.6)	0.005*
Intubation	1 (0.6)	159 (99.4)	4 (4.3)	90 (95.7)	0.064
Maternal mortality	0 (0.0)	160 (100.0)	2 (2.1)	92 (97.9)	0.136
Favipiravir	13 (8.1)	147 (91.9)	24 (25.5)	70 (74.5)	< 0.001*
Remdesivir	0 (0.0)	160 (100.0)	2 (2.1)	92 (97.9)	0.136
Lopinavir	0 (0.0)	160 (100.0)	7 (7.4)	87 (92.6)	0.001*
Corticosteroids	4 (2.5)	156 (97.5)	31 (33.0)	63 (67.0)	< 0.001*
Colchicine	0 (0.0)	160 (100.0)	2 (2.1)	92 (97.9)	0.136
Hydroxychloroquine	38 (23.8)	122 (76.3)	45 (47.9)	49 (52.1)	< 0.001*
Antibiotics	8 (5.0)	152 (95.0)	39 (41.5)	55 (58.5)	< 0.001*
Anakinra	0 (0.0)	160 (100)	2 (2.1)	92 (97.9)	0.136
Tocilizumab	0 (0.0)	160 (100)	4 (4.3)	90 (95.7)	0.018*
Convalescent plasma	0 (0.0)	160 (100)	8 (8.5)	86 (91.5)	< 0.001*
Chest CT	11 (6.9)	149 (93.1)	39 (41.5)	55 (58.5)	< 0.001*
Infiltration in chestCT	10 (90.9)	1 (9.1)	36 (92.3)	3 (7.7)	1.00

*$p < 0.01$

admission due to deterioration of the mother's health. The patient, admitted to the ICU as intubated, was extubated two days later. She stayed in the ICU for a total of 7 days and was discharged after 3 days of ward follow-up.

Three of the patients admitted to ICU were at 28 weeks of gestational age, and all in Group S, and the others (5 patients) were at higher gestational weeks. The patients who died were at the 28th and 34th gestational weeks, both were 31 years old and both were in Group S. The only patient in Group A was at the pregnant age of 39th weeks.

Discussion

We found that 63% of pregnant women with COVID-19 presenting for delivery are asymptomatic, suggesting a protocol of universal testing for pregnant women admitted to the labor unit. Our findings are similar to the results of the study of Karasu et al., in which 67.2% of 61 patients who tested positive for COVID-19 were asymptomatic [6]. Breslin et al., was found this ratio as 32.6% [7].

Another important finding of our study is that the mean gestational age was lower, and the preterm delivery rate was higher in Group S. Our results are consistent with a study showing that symptomatic COVID-19-positive parturients have a higher rate of preterm labor than asymptomatic COVID-19-positive pregnant women [8]. The ratio of newborns with an Apgar Score > 7 in Group S was lower, and also the ratio of newborns with an Apgar Score < 4 in Group S was higher. These results may indicate that pediatric team taking care of the neonates should be more alerted in delivery or c-section of symptomatic COVID-19 parturients.

The percentage of patients with a co-existing disease was higher in Group S. Also, 5 of 6 patients admitted to ICU who had co-existing diseases were symptomatic. This situation may indicate that the results that comorbidities especially, asthma affect the course of COVID-19 are also valid for pregnant women, particularly those presenting with symptoms [8, 9].

In our patients, NLR values were significantly higher in symptomatic patients than in asymptomatic patients. This observation is in accordance with other studies that evaluate non-pregnants. Güner et al. found the median value of NLR as 5.6 in the critically ill due to the COVID-19 group in the general population and 2.5 in the other patients [10]. Another retrospective study indicated that lymphocyte count was higher in patients with good prognoses than in those with poor prognoses. In patients who died, D-Dimer, ferritin, and IL-6 values continued to increase throughout the clinical course and were higher than in recovered patients [11]. Based on these results, the laboratory parameters used for clinical evaluation in the non-pregnant COVID-19 patient group may also be used in pregnant.

There was a significant difference between the groups in terms of the number of patients who received Favipiravir ($p < 0.001$) and Lopinavir ($p = 0.001$), their effects on anesthesia could not be evaluated as antiviral treatments were used after c-section.

Another finding of our study is that although the need for a chest CT was higher in symptomatic patients, the ratio of infiltration did not differ among groups. This unexpected finding is consistent with the results of Chao et al., who reported the radiographic abnormalities of the asymptomatic patients to be almost similar to those of the symptomatic patients [12]. In addition, pregnants who are initially asymptomatic may experience serious symptoms suggesting pulmonary infiltrate, which may necessitate CT during follow-up. For this reason, all COVID-19-positive pregnants must be informed in detail about when they should consult a clinician, even if they are asymptomatic.

Spinal anesthesia was performed on all patients whose time to perform LMWH was appropriate and whose anamnesis, laboratory tests and general condition were appropriate for regional anesthesia. Although low platelets have been reported in both severe and mild cases [13–15], in our patients, it was found in only 4 (1.6%) patients in the range of $50–100 \times 10^3$ initially. None of the patients had a platelet count of less than 50×10^3. The rate of general anesthesia was significantly higher in Group S. Fetal distress, deterioration of the mother's health, and not appropriate timing of LMWH for regional anesthesia were the major reasons for choosing general anesthesia in symptomatic patients.

All the spinal anesthesia procedures were successfully performed, but when no block occurred in 2 patients, one was converted to general anesthesia. The other patient was re-applied spinal anesthesia 15 min later, and no problem was experienced.

The duration of anesthesia administration did not differ between Group S and Group A. The anesthesia procedures took an average of 5.9–6 min in both groups, so in Group S, symptoms did not complicate anesthesia intervention.

While using personal protective equipment, involves difficulties such as performing regional anesthesia, fogging of glasses, inability to see, narrowing the field of vision, not feeling the anatomy well enough due to double gloves, the overalls obstructing the arm movements, also making it difficult to adjust the position, because the patient cannot hear what is being said. The anesthesiologist must be able to cope with the complications that may occur during the operation, because in cases of COVID-19, the support team takes longer to arrive when help is requested due to the preparation phase. Therefore, all anesthesia procedures for COVID-19 pregnant women in our clinic were performed by anesthesiologists with many years of experience in obstetric

anesthesia. Similarly, the surgical team's experience will reduce the duration of the operation, cope with possible surgical complications, and reduce the patient's stay in the operating room and the risk of contamination.

To reduce contamination that may occur by taking the patient to different units and to keep the number of personnel required to a minimum, the postoperative care of all patients was performed in the operating room.

We think that spinal anesthesia is a safe and sufficient form of anesthesia for c-section in pregnant women who are positive for COVID-19. The sedation we applied in long-lasting cases where the patient started to feel pain was adequate for all patients, and none of the patients had to be converted to general anesthesia. However, we think that general anesthesia may be safer in pregnant women with low saturation and impaired general condition, as respiratory muscle weakness and associated hypercapnia, which can be seen with the increase in spinal anesthesia level, may worsen the patient's clinical presentation.

Communication between the surgery team and anesthesiologists should be well established to prevent LMWH timing from interfering with regional anesthesia. It will be appropriate to arrange the birth plan of COVID-19 pregnant women meticulously and perform the c-section, as much as possible, without the need for emergencies, without jeopardizing the safety of the whole team, patient and baby, by allowing time for the preparation of the team. Even if general anesthesia does not pose any problem for the patient, since it will increase the risk of transmission with aerosol generation procedures such as tracheal intubation and extubation, regional anesthesia techniques should be applied in every possible patient, and patient management should be arranged accordingly [16, 17].

The COVID-19 pandemic affected pregnant patients not only physically but also psychologically. The prevailing emotion in pregnant women, including asymptomatic ones, was anxiety. Most of them were worried about their babies, apart from their health conditions. Besides, the fact that the team's appearance in the personal protective equipment was frightening and the difficulty in verbal communication with the patient increased the anxiety of the pregnant women. For this reason, we think that during the surgery, pregnant women should be touched as sincerely as possible, they should be talked comfortably as they can hear, and sedation should be done in cases of insufficiency.

In conclusion, anesthesiologists should evaluate pregnant women well, provide the most accurate anesthesia management they deserve without neglecting them and ensure the safety of all healthcare professionals during the operation.

Presence of symptoms may affect anesthesia method choice in favor of general anesthesia but when regional anesthesia is administrated neither the drug doses nor the sedation needs differ between symptomatic and asymptomatic patients except the need of intraoperative oxygen. Symptomatic patients with asthma may have a higher risk of requiring ICU and death. In our view, close follow-up of laboratory results and being aware of additional morbidities in pregnant women with COVID-19 can give an idea about the clinical course. Experienced teams should be involved in the interventions of these patients, and spinal anesthesia is a safe method of anesthesia for them.

Declarations

Conflict of interest The authors report no conflict of interest.

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