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Original Article

Mechanical ventilation and prone positioning in pregnant patients with severe COVID-19 pneumonia: experience at a quaternary referral center

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ABSTRACT

Background: We present the care of 17 consecutive pregnant patients who required mechanical ventilation for Coronavirus Disease 2019 (COVID-19) pneumonia at a quaternary referral center in the United States. We retrospectively describe the management of these patients, maternal and fetal outcomes, as well as the feasibility of prone positioning and delivery.

Methods: Between March 2020 and June 2021, all pregnant and postpartum patients who were mechanically ventilated for COVID-19 pneumonia were identified. Details of their management including prone positioning, maternal and neonatal outcomes, and complications were noted.

Results: Seventeen pregnant patients required mechanical ventilation for COVID-19. Thirteen patients received prone positioning, with a total of 49 prone sessions. One patient required extracorporeal membrane oxygenation. All patients in this series survived until at least discharge. Nine patients delivered while mechanically ventilated, and all neonates survived, subsequently testing negative for SARS-CoV-2. There was one spontaneous abortion. Four emergent cesarean deliveries were prompted by refractory maternal hypoxemia or non-reassuring fetal heart rate after maternal intubation.

Conclusions: Overall, maternal and neonatal survival were favorable even in the setting of severe COVID-19 pneumonia requiring mechanical ventilation. Prone positioning was well tolerated although the impact of prone positioning or fetal delivery on maternal oxygenation and ventilation are unclear.

Introduction

Coronavirus Disease 2019 (COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), may lead to respiratory failure, multi-organ dysfunction, and death.[1] As with other recent coronavirus epidemics, pregnant patients are at risk for severe COVID-19.[2] Such vulnerability is potentially related to physiologic changes of pregnancy such as altered respiratory mechanics, increased oxygen consumption, hypercoagulability, and altered cellular and innate immunity.[3–4]

With few randomized controlled trials to guide treatment during pregnancy, COVID-19 management in this population is informed by a heterogeneous body of case reports, case series, and observational studies. Many case series and cohort studies have been broad in scope, with patient acuity ranging from asymptomatic to critically ill. There are still few data focused on managing pregnant patients with severe COVID-19, especially those needing mechanical ventilation,[5–10] so questions remain about their optimal management.

There is growing interest in prone positioning. This intervention is common in the general population as a rescue therapy for moderate or severe acute respiratory distress syndrome (ARDS),[11] as well as severe COVID-19 pneumonia requiring mechanical ventilation.[12] However, prone positioning has been infrequently applied during pregnancy historically, so experience with this during pregnancy is limited. Recent investigations indicate that self-proning in the third trimester appears to be well tolerated by healthy volunteers, without a substantial effect on maternal hemodynamics or the fetal heart rate tracing.[13] However, the safety and effectiveness are unclear in the context of prolonged prone positioning of pregnant women with ARDS and the multisystem physiologic derangements seen during critical illness.

Additionally, the impact of fetal delivery on patients with ARDS continues to be controversial.[14–16] This is an area of uncertainty that

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has not been subject to rigorous evaluation, particularly in the context of COVID-19. Recent evidence in patients with ARDS is that delivery affords only modest maternal benefit, although data are limited.[14,17]

This retrospective case series describes the clinical features, management, and outcomes of pregnant patients with severe COVID-19 requiring mechanical ventilation at our quaternary referral center. This study also characterizes the feasibility and effect of prone positioning and fetal delivery on arterial blood gas and ventilation parameters in these patients.

Methods

Study design

This study had Institutional Review Board approval and was exempted from the requirement for written informed consent. It was prepared in accordance with the STROBE/CARE guideline.[18] Patients had been admitted to an urban quaternary care hospital and Level IV maternal care center in the United States, which accepted high-risk obstetric referrals statewide and from the surrounding region.

We included all consecutive pregnant patients between March 2020 and June 2021 who required mechanical ventilation for COVID-19 pneumonia. The diagnosis of COVID-19 was confirmed by positive reverse transcriptase polymerase chain reaction (RT-PCR) for SARS-CoV-2 from a nasopharyngeal swab, sputum sample, or broncho-alveolar lavage specimen. All patients with symptoms indicative of COVID-19 infection were tested and, beginning in April 2020, a universal on-site SARS-CoV-2 testing protocol was implemented on our Labor and Delivery unit for all patients admitted for delivery, antepartum care, or postpartum complications. Neonatal testing was routinely conducted at 24 and 48 h of life, via RT-PCR nasopharyngeal swab. Patients were excluded if they were only briefly intubated for reasons unrelated to COVID-19, such as for non-obstetric surgery.

From the electronic medical record, we collected data on patient demographics, comorbidities, as well as maternal and umbilical blood gas measurements. We documented the use of prone positioning, as well as the number and duration of each proning session. We recorded use of other therapies, including supplemental oxygen, antiviral drug, inhaled pulmonary vasodilator and corticosteroid administration, non-invasive and invasive positive pressure ventilation, the duration of respiratory support, neuromuscular blockade, and extracorporeal membrane oxygenation (ECMO) therapy. We noted delivery indications, mode of delivery, and estimated delivery blood loss. Other abstracted data included hospital length of stay, maternal and fetal survival, and complications such as thrombosis, hemorrhage, and ventilator-associated pneumonia.

Institutional practices

Pregnant patients with stable and non-critical respiratory status were managed on the Labor and Delivery unit in dedicated negative pressure isolation rooms, with high-flow supplemental oxygen provided if necessary (Optiflow, Fisher 7 Paykel Healthcare, Auckland, New Zealand). Severe COVID-19 infection with respiratory failure requiring non-invasive positive pressure ventilation, tracheal intubation, or ECMO, was managed in one of two dedicated negative-pressure critical care isolation wards. Management of severe COVID-19 infection was conducted according to institutional protocols and guidance from the US National Institutes of Health. Institutional practices were modified throughout the study period as emerging data were incorporated into clinical use.

At our institution, the recommended practice for out-of-operating-room intubation of pregnant patients is to notify the obstetric anesthesiology, high-risk obstetrics, and neonatal teams. If an obstetric anesthesiologist was unavailable due to Labor and Delivery commitments, intubations were performed either by an on-call anesthesiologist managing the main operating rooms or an intensivist. The mode of ventilation (i.e. pressure control, volume control, pressure-regulated volume control) was chosen at the discretion of the intensivist. In general, patients received intravenous sedation infusions (e.g. propofol, hydromorphone) titrated to a Richmond Agitation and Sedation Scale (RASS) score of -1 to -4, to minimize harmful ventilator dyssynchrony.

Non-critically-ill patients receiving supplemental oxygen were encouraged to try awake self-proning intermittently, or the lateral decubitus position if better tolerated (Supplemental Video 1). Prone positioning was also employed for mechanically ventilated pregnant patients in the intensive care unit (ICU) (Supplemental Video 2), including those on ECMO support. During each session, patients were placed in the prone position for a goal period of 16 to 20 h. The duration of proning sessions was influenced by maternal hemodynamics, fetal heart rate tracings, the ability to maintain fetal monitoring, and the availability of ICU personnel for repositioning. The number of subsequent proning sessions was informed by maternal and fetal tolerance, as well as improvement in maternal blood gas measurements, chest radiography signs, and lung compliance. Ventilator settings were typically continued without alteration during prone positioning. Pregnant patients undergoing voluntary self-proning or admitted to ICU were assigned a dedicated obstetric nurse. For patients at a viable gestational age, continuous fetal monitoring and tocodynamometry were maintained during proning.

Diagnostic imaging of critically-ill COVID-19 patients was performed at the intensivists' discretion. In general, bedside chest x-rays were performed on a near-daily basis to monitor for disease progression and complications such as pneumothorax, and were also performed prior to prone positioning. At our institution, many patients with COVID-19 infection have computed tomography (CT) angiography early in their disease course to rule out pulmonary embolus; however, this was rarely performed for pregnant patients with COVID-19. Later during admission, CT scans were considered only in the event of an acute change in clinical status or if there was difficulty weaning ventilatory support.

The COVID-19 infection itself did not prompt cesarean delivery, which was reserved for obstetric indications. To avoid morbidity due to prematurity, pregnancies were continued in mechanically ventilated patients, with a goal of achieving at least 32 weeks' gestation prior to scheduled cesarean delivery. Urgent delivery was considered for fetal heart tracing abnormalities or deteriorating fetal biophysical profile despite optimization of maternal respiratory and hemodynamic parameters. Non-critical patients delivered vaginally in their Labor and Delivery isolation room, or via cesarean in an adjacent negative-pressure operating room. For ICU patients, cesarean deliveries were conducted in a negative-pressure operating room or, in emergent cases, within the patient's ICU room.

Statistical analysis

Statistical analysis was conducted with R version 4.03 (R Core Team, Vienna, Austria). Categorical variables were summarized using number and percentage, while continuous variables were described using mean and standard deviation (SD). For non-normally distributed continuous variables, as indicated by Shapiro-Wilk test and visual inspection, median and interquartile range (IQR) were used. Missing data were not imputed or replaced. Detailed statistical analysis was not attempted due to the small number of patients.

Results

Patients

During the study period, a total of 108 pregnant patients were admitted to our Labor and Delivery unit for management of laboratory-confirmed COVID-19 infection. Among these patients, 17 patients required ICU admission with mechanical ventilation. Characteristics of these mechanically ventilated patients are summarized in Table 1 and their clinical course is summarized in Fig. 1 (see Supplemental Data for further details). Only one of the mechanically ventilated patients had no pre-existing comorbidities at the time of admission.

Management: tracheal intubation

Three patients were intubated at outside hospitals before admission (Patients 1, 13, 14). For the remaining patients, videolaryngoscopy was used during all intubations (six by an obstetric anesthesiologist, four by a non-obstetric anesthesiologist, and four by an intensivist). Cricoid pressure was applied in 64% and all intubations were successful at the first attempt. Two patients required re-intubation, one after self-extubation (Patient 6) and another due to aspiration several days after delivery and initial extubation (Patient 4).

Maternal hypotension or desaturation was occasionally observed, though typically transient. However, in three instances there was persistent fetal bradycardia after intubation, despite management of maternal hemodynamics and ventilation; these cases required emergent bedside cesarean delivery (Patients 2, 6, 12).

The median duration of mechanical ventilation was 10 days (interquartile range [IQR] 18, range 2–85 days). No patient received airway pressure release ventilation.

Management: prone positioning

Thirteen patients had prone positioning during their admission, with 49 proning sessions of median duration 16 h (IQR 2.8, range 1–18) conducted in total. No proning sessions were terminated urgently due to maternal hemodynamic instability, worsening oxygenation or ventilation, or fetal intolerance. On one occasion (Patient 3), uterine contractions while prone led to repositioning supine, after which the contractions resolved. The patient was maintained prone subsequently without issue. On some occasions, difficulty maintaining continuous fetal monitoring while in the prone position required an early return to the supine position.

Table 2 summarizes arterial blood gas and ventilation parameters prior to and after proning sessions. Blood gas measurements were typically drawn within an hour prior to prone positioning, and 1–4 h after cessation of proning.

Table 1
Baseline characteristics and outcomes of mechanically ventilated pregnant patients

Characteristic	Total patients (n = 17)
Age (y)	31.6 ± 6.1 (22–42)
Race	
White	9 (53)
Black	6 (35)
Other	2 (2)
Hispanic ethnicity	8 (47)
Body mass index (kg/m^2)	35.1 ± 6.9 (23–47)
Pre-existing comorbidity	
Advanced maternal age	6 (35)
Obesity	11 (65)
Diabetes	3 (18)
Chronic hypertension	1 (6)
Gestational hypertension	1 (6)
Tobacco use during pregnancy	0 (0)
Asthma	6 (35)
Renal insufficiency	2 (12)
Autoimmune disorders	0 (0)
Extracorporeal membrane oxygenation	1 (6)
Delivery while mechanically ventilated	9 (53)
Complications	
Deep vein thrombosis	3 (18)
Pulmonary embolus	1 (6)
Ventilator-associated pneumonia	8 (47)
Postpartum hemorrhage	5 (29)
Acute kidney injury	2 (12)
Death	
Maternal	0 (0)
Fetal	1 (6)
Neonatal	0 (0)

Data are mean ± SD (range) or n (%).

Management: delivery during mechanical ventilation

Nine patients delivered while mechanically ventilated, at a mean gestational age of 32 weeks (Table 3). Among these nine patients, there was one vaginal delivery due to preterm labor (Patient 4) and eight cesarean deliveries. Three cesarean deliveries were prompted by an abnormal fetal heart rate tracing (Patients 2, 6, 12), one by preterm labor in the setting of breech presentation (Patient 15), one by a deteriorating biophysical profile (Patient 5), and one by worsening maternal hypoxemia and acidosis with anticipated fetal decompensation (Patient 9). Two cesarean deliveries were electively planned during mechanical ventilation at 33 weeks (Patient 3) and during venovenous (VV) ECMO therapy at 32 weeks' gestation (Patient 1). Four patients underwent bedside emergent cesarean delivery in the ICU (Patients 2, 6, 9, 12).

Mean estimated blood loss during these deliveries was 685 mL (SD 368, range 150–1206 mL). Peripartum arterial blood gas parameters are summarized in Table 4.

All the neonates of mechanically ventilated patients delivered were admitted to the neonatal ICU, and all survived to discharge home. All neonates tested negative for SARS-CoV-2 at 24- and 48-h screening after delivery. At our institution, there has yet to be a case of SARS-CoV-2 positivity on initial newborn screening among neonates born to patients with active COVID-19 infection.

Pregnancy outcome in remaining patients

One patient (Patient 11) had induction of labor for preterm premature rupture of membranes within one week of tracheal extubation. One pre-viable, hemodialysis-dependent patient (Patient 16) with COVID-19 and superimposed volume overload from missing scheduled dialysis had a spontaneous abortion shortly after admission but prior to intubation. The other patients (Patients 7, 10, 13, 14, 17) continued their pregnancies through to discharge and later delivered at term uneventfully or are currently still pregnant (Patient 8).

Management: ECMO support

One patient (Patient 1) at 28 weeks' gestation was transferred from an outside hospital for initiation of VV-ECMO after seven days of mechanical ventilation. Due to refractory epistaxis, systemic anticoagulation was discontinued at 31 weeks' gestation until cessation of ECMO support, using only a heparin-bonded circuit. Elective cesarean delivery at 32 weeks was planned to balance maternal and fetal risk, and she delivered a healthy neonate. Her postoperative course was complicated by intra-abdominal hemorrhage requiring massive transfusion and several operations. Without systemic anticoagulation, she required six oxygenator changes while receiving ECMO support but had no significant circuit thrombosis. Mother and infant survived to discharge and are currently well.

Diagnostic imaging

Portable chest X-rays were performed in the ICU every 1–4 days to monitor disease progression in the 17 patients. Three patients had

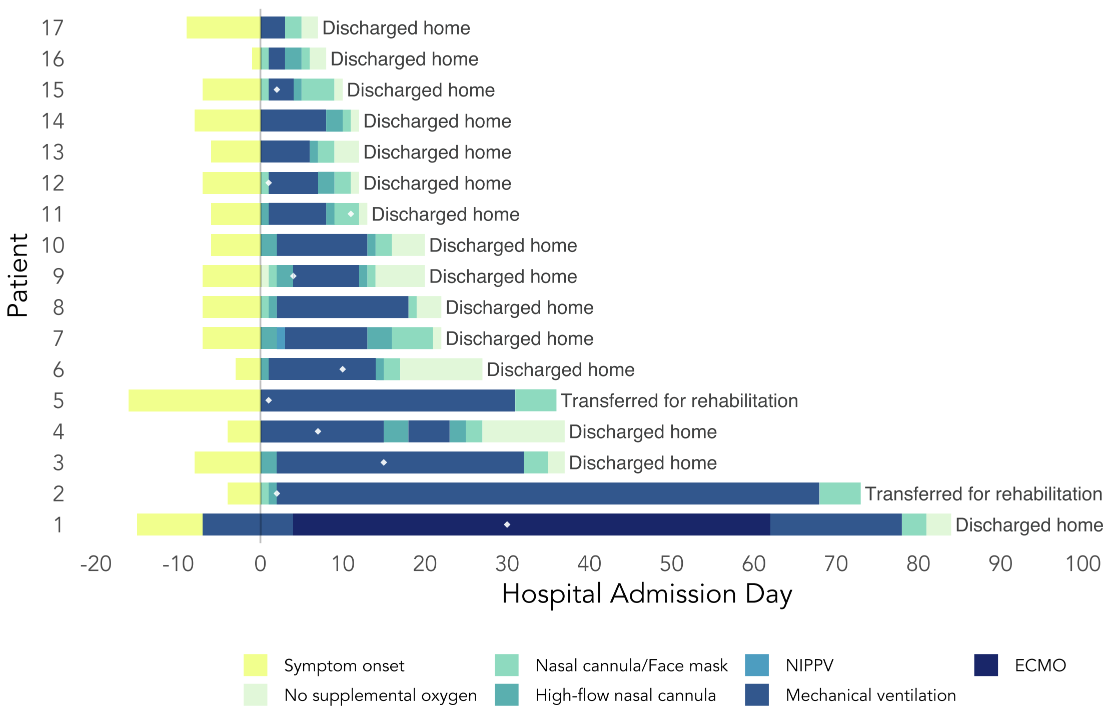

Fig. 1. Clinical course of mechanically ventilated patients with COVID-19 pneumonia. For patients who delivered during their hospitalization for COVID-19, the time of delivery is represented by the white diamonds. Nine patients delivered while mechanically ventilated, while another patient delivered several days after tracheal extubation. ECMO: extracorporeal membrane oxygenation. NIPPV: non-invasive positive pressure ventilation

Table 2
Maternal ventilation and oxygenation in relation to a prone positioning session

Parameter	Before proning session	After proning session
pH	7.35 [0.10] (7.13–7.50)	7.37 [0.12] (7.12–7.52)
PaO_2 (mmHg)	121 [65] (44–228)	111 [48] (60–233)
$PaCO_2$ (mmHg)	47 [12] (33–102)	45 [13] (34–88)
HCO_3 (mmol/L)	25 [5] (17–34)	25 [4] (19–32)
FiO2 (%)	65 [30] (40–100)	60 [25] (40–100)
PEEP (cmH_2O)	12 [2] (10–18)	12 [2] (5–18)
PIP (cmH_2O)	33 [7] (15–43)	32 [7] (16–40)
PaO_2/FiO_2 ratio	177 [120] (55–538)	187 [125] (100–430)

Data presented as median [IQR] (range). PEEP: positive end-expiratory pressure; PIP: peak inspiratory pressure.

chest CT performed before ICU admission (Patients 3, 10, 12). One patient receiving ECMO support had head and neck CT angiography to rule out abnormal vasculature as a cause of epistaxis (Patient 1). Other CT scans were performed following delivery for indications including persistent hypoxemia (Patient 15), undifferentiated sepsis (Patient 9), pneumomediastinum (Patient 5), and tracheal bleeding (Patient 2).

Discussion

Prone positioning may improve ventilation-perfusion matching in ARDS by reducing lung compression by mediastinal structures and enhancing dorsal lung aeration.[19] Our study attests to the feasibility and tolerability of proning during pregnancy. Seventeen patients received mechanical ventilation for severe COVID-19, among whom 13 patients underwent 49 sessions of prone positioning for up to 18 h per session. No patient was urgently repositioned supine for worsening ventilation, gas exchange, hemodynamic instability, or fetal intolerance. Continuous fetal monitoring was generally possible in the prone position without prolonged or concerning interruption. Due to logistic difficulties in transporting COVID-positive, mechanically ventilated pregnant patients for diagnostic imaging, the use of CT imaging was infrequent. The potential utility of such testing was weighed against the risk of complications during transportation.

In reviewing our data there was not an obvious impact of prone positioning on maternal arterial blood gas or ventilation parameters, however this study was not powered for formal hypothesis testing. There are several possible explanations for our observations. In many instances, prone positioning was initiated proactively rather than reactively (e.g. for arterial oxygen tension to inspired oxygen fraction ratios greater than 150–200) such that there may have been less potential for improvement. A proactive approach to ventilatory management may be particularly important during pregnancy when hypercapnia potentially exacerbates fetal acidosis. Decisions around proning and ventilator management were also based on clinician judgment and were not standardized. Although proning was well tolerated, some sessions were terminated prematurely for logistic reasons; however, the average duration of proning of 16 h was consistent with contemporary practice.[20] Finally, the timing of arterial blood gas measurements after proning sessions was variable and it is possible that benefits from a proning session were attenuated after returning to the supine position for several hours.

Respiratory mechanics and compliance are altered during pregnancy and these changes may interact with prone positioning. In pregnancy, alveolar dead space is reduced while chest wall antero-posterior diameter increases, promoting efficient gas mixing and distribution in the lungs.[21–22] Increased cardiac output also improves alveolar perfusion in superior lung regions, further improving ventilation-perfusion matching and gas exchange.[21,23,24] Therefore, proactive proning may help optimize gas exchange, although this effect may be offset by better baseline ventilation-perfusion matching during pregnancy. Additionally, sustained improvement in ventilation and oxygenation after repeated prone positioning may be more appropri-

Table 3
Characteristics of deliveries during mechanical ventilation

Patient	1	2	3	4	5	6	9	12	15
Delivery									
Gestational age at delivery (weeks + days)	32 + 2	30 + 1	33 + 0	32 + 5	32 + 5	29 + 2	37 + 0	26 + 3	31 + 3
Mode of delivery	Cesarean	Cesarean	Cesarean	Vaginal	Cesarean	Cesarean	Cesarean	Cesarean	Cesarean
Bedside delivery in ICU	No	Yes	No	Yes	No	Yes	Yes	Yes	No
Delivery indication	Planned repeat cesarean, preterm	Non-reassuring fetal heart rate	Planned repeat cesarean, preterm	Preterm labor	Poor biophysical profile	Non-reassuring fetal heart rate	Refractory hypoxemia	Non-reassuring fetal heart rate	Preterm labor, breech
Estimated blood loss at delivery (mL)	380	400	1206	150	1000	400	1200	630	800
Neonatal outcomes									
Birth weight (g)	2330	1310	1880	1960	2020	1785	3440	1200	2285
Apgar scores (1/5/10 min)	5/7/9	4/7/9	4/6/8	1/7/8	2/3/4	4/5/8	6/4/–	4/4/–	2/8/–
Umbilical artery blood gas – pH	7.28	–	7.19	–	7.18	–	7.20	–	7.20
Umbilical artery blood gas – $PaCO_2$	64	–	71	–	77	–	57	–	65
Umbilical artery blood gas – PaO_2	32	–	12	–	20	–	28	–	22
Umbilical artery blood gas – HCO_3	29	–	26	–	28	–	22	–	24

ICU: intensive care unit.

Table 4
Maternal ventilatory and acid-base status, for patients delivering while mechanically ventilated (n = 9)

Parameter	Before delivery	Postpartum	
		12 h	24 h
pH	7.40 ± 0.07 (7.27–7.45)	7.39 ± 0.08 (7.27–7.44)	7.42 ± 0.4 (7.39–7.46)
PaO_2 (mmHg)	126 ± 25 (88–156)	118 ± 26 (90–150)	155 ± 26 (131–182)
$PaCO_2$ (mmHg)	38 ± 6.4 (30–46)	40 ± 8 (31–48)	40 ± 7 (34–47)
HCO_3 (mmol/L)	23 ± 5.2 (16–29)	24 ± 5 (20–31)	25 ± 4 (22–30)
FiO_2 (%)	58 ± 20 (40–90)	53 ± 15 (40–70)	47 ± 21 (30–70)
PEEP	13 ± 2 (10–16)	13 ± 3 (10–16)	14 ± 2 (12–16)
PIP	29 ± 4 (24–34)	30 ± 6 (22–34)	28 ± 4 (25–33)
PaO_2/FiO_2 ratio	244 ± 97 (98–390)	249 ± 115 (150–375)	383 ± 172 (187–507)

Data presented as mean ± SD (range). PEEP: positive end-expiratory pressure; PIP: peak inspiratory pressure.

ately measured longitudinally throughout a patient's hospitalization rather than immediately before or after individual proning sessions.

Among critically-ill pregnant patients, the effect of delivery on maternal respiratory status has been subject to debate, with recent investigations suggesting only a modest maternal benefit.[14–17] Our sample size was too small to formally evaluate this question. Nonetheless, in the absence of robust evidence supporting maternal benefit of fetal delivery in pregnancies complicated by COVID-19 infection, delivery should generally be reserved for obstetrical indications, or as rescue therapy in the event of severe, refractory hypoxemia. This is important given the maternal inflammatory burden of cesarean delivery and the risk of neonatal complications with prematurity.

Although early case series during the COVID-19 pandemic reported high rates of cesarean delivery,[25] recent experience has been reassuring for safely continuing pregnancy. Concerningly, we had three emergency cesarean deliveries in the ICU due to non-reassuring fetal heart rate tracings after tracheal intubation or airway management, and one patient required delivery due to refractory maternal hypoxemia with the potential for imminent fetal deterioration. In addition to hypoxemia, the fetus may be exquisitely sensitive to any maternal hypotension during anesthetic induction. Obstetricians must be notified when airway management is anticipated, in the event of associated fetal bradycardia. The involvement of obstetric anesthesiologists can also be invaluable. These events highlight the importance of equipment, space, and personnel in ICU resource management planning to allow emergent delivery when indicated.

Pregnant patients are at greater risk for complications of COVID-19 infection.[26–29] All patients in this case series survived, which suggests an advantage of referring pregnant patients with severe COVID-19 infection to specialized centers. Pre-existing comorbidities such as obesity, hypertension, diabetes, hypertensive disorders of pregnancy, and advanced maternal age are associated with adverse outcomes such as ICU admission, mechanical ventilation, or death in patients with COVID-19 infection.[10,30,31] Almost all of our patients had such comorbidities.

We also had a large proportion of Black (35%) and Hispanic (47%) patients, possibly reflecting the racial and ethnic disparities of the COVID-19 pandemic in the United States.[32] Further efforts are necessary to identify solutions to these and other racial and ethnic disparities in maternal morbidity and mortality.

This study has several limitations, including lack of a comparison group and inherent constraints with retrospective observational research. Additionally, we were underpowered to perform detailed statistical analysis. Because our institution is a referral center for high-risk obstetric patients[33], the generalizability of our experience may be limited.

In summary, we observed favorable maternal and fetal survival among obstetric patients with severe COVID-19 requiring mechanical ventilation. We demonstrated the feasibility of prone positioning during pregnancy but were unable to assess the impact of proning or fetal delivery on maternal oxygenation and ventilation. Tracheal intubation represents a precarious event that may lead to emergent cesarean delivery, so obstetricians should be notified about plans for changes to airway management. Further study is required to better understand the long-term implications of COVID-19 infection on maternal and fetal outcomes. Inclusion of pregnant patients in preventative or interventional trials is important for improving COVID-19 management.

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Declaration of interests

The authors have no conflicts of interest to disclose.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijoa.2021.103236.

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