



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

# COVID-19 in the Critically Ill Pregnant Patient



Matthew Levitus, MD<sup>a,\*</sup>, Scott A. Shinker, DO, MS<sup>b</sup>, Mai Colvin, MD<sup>a</sup>

## KEYWORDS

• COVID-19 • Pregnancy • Critically ill • ARDS • ECMO • Fetal monitoring

## KEY POINTS

- Critically ill pregnant patients with coronavirus disease 2019 (COVID-19) are at increased risk for adverse outcomes.
- Management should focus on the early identification of life-threatening symptoms and initiation of a multi-modal therapy to treat the spectrum of severe disease ranging from hypoxia requiring noninvasive oxygen delivery to acute respiratory distress syndrome requiring extracorporeal membrane oxygenation.
- Fetal monitoring in the ICU is critical to ensure adequate placental perfusion and fetal acid/base status.
- The timing of delivery must be balanced by the potential benefit toward maternal status with the risk of prematurity.

## INTRODUCTION

Information related to coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in pregnant patients is limited and continues to emerge. Even less is known about critically ill pregnant patient requiring advanced respiratory support or those that progress to the development of acute respiratory distress syndrome (ARDS). Pregnant patients are more likely to have severe COVID-19 illnesses compared with nonpregnant patients. A large study from the Centers of Disease Control and Prevention (CDC) which reviewed reports of more than 1.3 million women of reproductive age with a laboratory-confirmed SARS-CoV-2 infection showed that among women with COVID-19, pregnant patients were at significantly increased risk for intensive care unit (ICU) admission, mechanical ventilation, receipt of extracorporeal membrane oxygenation (ECMO), and death.<sup>1</sup> Furthermore, they are at greater risk for adverse pregnancy-related outcomes, driven by an increased risk of iatrogenic prematurity.<sup>2-4</sup> Factors such as age above 25 years,

---

<sup>a</sup> Division of Critical Care Medicine, Montefiore Medical Center, Albert Einstein College of Medicine, 111 East 210th Street, Bronx, NY 10467, USA; <sup>b</sup> Department of Obstetrics and Gynecology, Beth Israel Deaconess Medical Center, Harvard Medical School, 330 Brookline Avenue, Boston MA 02215, USA

\* Corresponding author.

E-mail address: [mlevitus@montefiore.org](mailto:mlevitus@montefiore.org)

obesity, chronic hypertension, chronic lung disease, gestational diabetes, and pre-eclampsia further increase risks of serious complications.<sup>1,5-7</sup>

The physiologic changes in pregnancy necessitate special considerations when attempting to optimize management. Pregnancy results in hyperemia of the upper airway, increased oxygen consumption, reduction in chest wall compliance, and decreased functional residual capacity, all of which can exacerbate respiratory distress.<sup>8-10</sup> Moreover, pregnancy is a hypercoagulable state, leads to modifications of the immune system, and produces a state of increased cardiac output.<sup>9</sup> Standard COVID-19 management is also affected by the presence of the fetus, as maternal hypoxemia and hypercapnia can be harmful. The utility of treatments and interventions must, therefore, be weighed against their safety and risks to the developing fetus.

Given their increased risk of severe COVID-19, unique physiology, and fetal considerations, the clinician requires a detailed understanding of the management of critically ill pregnant patients. This article will provide a detailed review of the management and care for critically ill pregnant patient with severe COVID-19 pneumonia.

### ***Indications for Intensive Care Unit Admission in Pregnancy***

---

If pregnant women are suspected or proven to be infected with COVID-19, especially in the presence of high-risk factors, prompt clinical evaluation, early identification of severe symptoms, and appropriate triage are necessary to improve their outcomes. The International Society of Infectious Disease in Obstetrics and Gynecology (ISIDOG) guidelines suggest that ICU admission should be considered for the following patients:

- (A) "Pregnant patients with severe disease: respiratory rate  $\geq 30$ /min, resting oxygen saturation  $\text{SaO}_2 < 94\%$ , arterial blood oxygen partial pressure ( $\text{PaO}_2$ )/oxygen concentration ( $\text{FiO}_2$ ) (P/F)  $\leq 300$  mm Hg."
- (B) "Pregnant patients with oxygen requirement and comorbidities."
- (C) "Pregnant patients with critical disease: shock with organ failure, respiratory failure requiring mechanical ventilation or refractory hypoxemia requiring ECMO."<sup>11</sup>

In severe/critical cases or in cases whereby specialized treatment is required, pregnant patients should be referred to a tertiary center immediately.

### **MANAGEMENT**

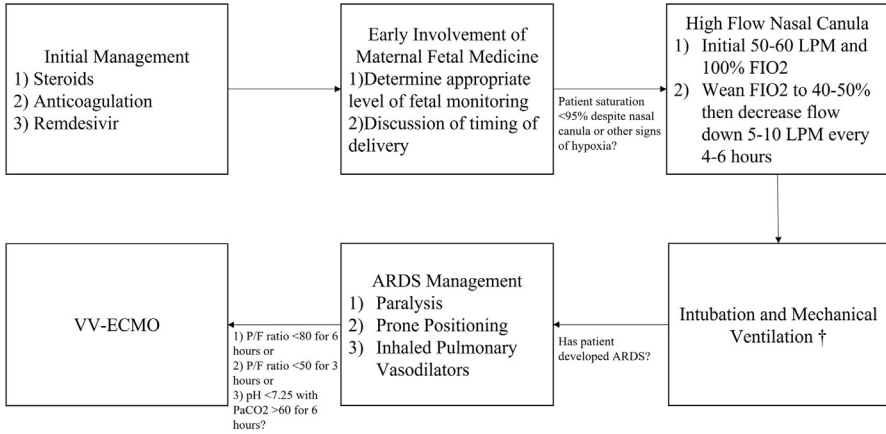
Overall, there are limited data regarding the management of critically ill pregnant patient with COVID-19 as many studies excluded pregnant patients or had limited participants. After the identification of critical illness, care should focus on specific treatments for the range of the disease caused by COVID-19 including those with acute respiratory failure to those who develop severe ARDS. Furthermore, there should be a focus on the monitoring of the fetus and discussion of treatment decisions regarding a viable versus nonviable fetus (**Fig. 1**).

#### ***Steroids***

---

It is well established that antenatal glucocorticoids in patients at high risk of preterm delivery within 7 days improves neonatal outcomes.<sup>12</sup> Treatment typically consists of either two 12 mg doses of betamethasone given intramuscularly (IM) 24 hours apart or four 6 mg doses of dexamethasone administered IM every 12 hours.<sup>12,13</sup> Prolonged use or multiple courses of steroids that readily cross the placenta is controversial as prior studies have shown potential adverse fetal effects such as unfavorable

Practical Approach Algorithm for the Critically Ill Pregnant Covid-19 Patient<sup>a</sup>



**Fig. 1.** Practical approach algorithm for the critically ill pregnant COVID-19 patient. <sup>a</sup> All management decisions should be individualized. <sup>b</sup> Similar strategy to nonpregnant patients but with goal SPO<sub>2</sub> > 95% with PaO<sub>2</sub> > 70 mmHg, avoidance of severe respiratory alkalosis or acidosis, and a plateau pressure greater than 30 mmHg may also be appropriate.

neurologic outcomes, small head circumferences, fetal growth restriction, and increased risk of neonatal hypoglycemia.<sup>12,14,15</sup>

The RECOVERY trial showed that oral or intravenous (IV) dexamethasone at a dose of 6 mg once daily for up to 10 days reduces mortality associated with COVID-19 among patients who required supplemental oxygen or mechanical ventilation compared with those who received standard of care.<sup>16</sup> Pregnant patients were not excluded from the trial, but the trial included only 6 pregnant patients and the protocol was modified to treatment with oral prednisolone 40 mg daily or IV hydrocortisone 80 mg twice daily.

Evidence on the choice and duration of corticosteroid treatment among pregnant patients with COVID-19 is limited and a definitive consensus is lacking. (Table 1) Based on the RECOVERY trial results, for patients that do not yet meet criteria for fetal lung maturity the Royal College of Obstetricians and Gynecologists (RCOG) suggests pregnant women who require supplemental oxygen or mechanical ventilators receive oral prednisolone 40 mg once daily or IV hydrocortisone 80 mg twice daily for 10 days or up to discharge.<sup>17</sup> However, Saad and colleagues recommend a total of 32 mg of methylprednisolone orally or IV (which is equivalent to 6 mg dexamethasone) once a day or in divided doses.<sup>15</sup> This is suggested due to the potential harm from additional dexamethasone exposure to the fetus.<sup>15</sup> In contrast, the Society of Maternal-Fetal Medicine (SMFM) recommends the use of dexamethasone in a similar manner to that studied in the RECOVERY trial.<sup>18</sup> The above recommendations are modified for patients that meet criteria for steroids for fetal lung maturity by treatment with dexamethasone 6 mg IM every 12 hours for 4 doses followed by each society’s recommended regimen to complete a total of 10 days.

**Anticoagulation Strategies**

Pregnancy is a hypercoagulable state and pregnant patients have up to a fivefold increased risk of thromboembolism compared with nonpregnant patients.<sup>19,20</sup> Studies have suggested there may be a confounding increased risk of coagulopathy

<b>Table 1</b> <b>Steroid regimens recommended for the critically ill pregnant Covid-19 patient</b>		
<b>Source</b>	<b>If Not Indicated for Fetal Lung Maturity</b>	<b>If Indicated for Fetal Lung Maturity</b>
Royal College of Obstetricians and Gynecologists <sup>17</sup>	Oral prednisolone 40 mg once a day or intravenous hydrocortisone 80 mg twice a day for 10 d or up to discharge, whichever is sooner	Intramuscular dexamethasone 6 mg every 12 h for 4 doses than oral prednisolone 40 mg once a day or intravenous hydrocortisone 80 mg twice a day to complete a total of 10 d or up to discharge, whichever is sooner
Society of Maternal-Fetal Medicine <sup>18</sup>	Oral or intravenous dexamethasone 6 mg daily for up to 10 d	Intramuscular dexamethasone 6 mg every 12 h for 4 doses followed by oral or IV Dexamethasone 6 mg daily up to a total of 10 d
Saad et al. <sup>15</sup>	Oral or intravenous methylprednisolone 32 mg once a day or in divided doses, for 10 d or up to discharge, whichever is sooner	Intramuscular dexamethasone 6 mg every 12 h for 4 doses followed by switching to oral or intravenous methylprednisolone 32 mg once a day to complete a total of 10 d or up to discharge, whichever is sooner

associated with COVID-19.<sup>21–23</sup> However, in critically ill patients, therapeutic heparin was not shown to increase survival to hospital discharge or affect the number of days for respiratory organ support.<sup>24</sup> Based on the current data, multiple professional societies and guidelines recommend prophylactic doses of anticoagulation unless contraindicated. The National Institutes of Health (NIH) COVID-19 Treatment Guidelines recommend that pregnant patients hospitalized for severe COVID-19 receive prophylactic dose anticoagulation.<sup>25</sup> SMFM recommends prophylactic unfractionated heparin or low-molecular-weight heparin (LMWH) in critically ill or mechanically ventilated pregnant women.<sup>18</sup> RCOG recommends all pregnant and recently pregnant women to be assessed for risk of venous thromboembolism (VTE) and receive thromboprophylaxis with LMWH.<sup>17</sup> The risk of bleeding and benefits of VTE prophylaxis must be carefully weighed in each case. Currently, there is not enough evidence to recommend therapeutic anticoagulation in the absence of proven VTE.

### **Remdesivir**

Remdesivir is an inhibitor of the viral RNA-dependent RNA polymerase and it inhibits SARS-CoV-2 replication in vitro.<sup>26</sup> In an international, multicenter, double-blind, randomized, placebo-controlled trial of 1062 nonpregnant patients hospitalized with COVID-19 with evidence of lower respiratory tract infection, IV remdesivir (for 10 days or until hospital discharge or death) was superior to placebo in shortening the time to recovery.<sup>27</sup> Remdesivir was approved by the Food and Drug Administration

(FDA) for use in adults and children (aged  $\geq 12$  years and weighing  $\geq 40$  kg) hospitalized with COVID-19. Safety data from the manufacture label of remdesivir states that there are insufficient data to evaluate for a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes when used in pregnant patients.<sup>28</sup> Data for the use of Remdesivir in pregnant women with COVID-19 are extremely limited. In a study by Burwick and colleagues, 67 hospitalized pregnant patients (82% were  $\geq 24$ -week gestation) with COVID-19 were treated on a compassionate use basis with remdesivir.<sup>29</sup> Among pregnant women, 93% of those on mechanical ventilation were extubated, 93% recovered, and 90% were discharged, and remdesivir was generally well tolerated.<sup>29</sup> Aside from this study, published data on outcomes and adverse events for remdesivir use in pregnant women with COVID-19 mostly come from smaller case series and case reports and are overall limited.

### ***Tocilizumab***

---

Tocilizumab is a monoclonal antibody against the interleukin-6 receptor, and it has been shown to improve outcomes in patients with severe COVID-19 pneumonia in some studies.<sup>30–33</sup> Tocilizumab is currently available under FDA emergency use authorization for the treatment of COVID-19. Tocilizumab crosses the placenta and data describing tocilizumab for use in pregnant patients with COVID-19 are scarce. The use for the treatment of COVID-19 in pregnancy is not currently recommended given limited data. Further study is necessary to confirm the benefit-risk profile of tocilizumab use among pregnant women.

### ***Noninvasive Ventilation***

---

The goal oxygen saturation for nonpregnant patients with COVID-19 is 92%. For pregnant patients, SMFM recommends a target of 95%.<sup>18</sup> Patients that do not require immediate intubation, high flow nasal cannula is an appealing alternative. Pacheco colleagues recommend the initiation of 50 to 60 L per minute (LPM) with 100%  $\text{FiO}_2$  and then subsequent weaning of  $\text{FiO}_2$  down to 40% to 50% followed by a decrease in flow by 5 to 10 LPM every 4 to 6 hours.<sup>34</sup> Noninvasive ventilation such as bilevel positive airway pressure (BIPAP) tends to be avoided in pregnancy because of an increased risk of aspiration due to decreased esophageal sphincter tone and increased abdominal pressure.<sup>35</sup>

### ***Mechanical Ventilation***

---

There are limited data regarding the management of mechanical ventilation for pregnant patients. In general, ventilatory strategies in pregnant patient are similar to nonpregnant patients but with some key differences, especially in ARDS. In general, the  $\text{Paco}_2$  should be aimed at a pregnancy-specific hypocapnia.<sup>36</sup> However, a severe respiratory alkalosis should be avoided as it leads to uterine vasoconstriction.<sup>37</sup> Hyperoxia in ARDS is avoided, but for the pregnant patient, the goal is an oxygen saturation of at least 95% and  $\text{PaO}_2$  of at least 70 mm Hg to allow for adequate fetal oxygenation.<sup>35</sup> In the nonpregnant patient, standard ARDS therapy also involves low tidal volume ventilation. If lung pathology constrains the use of low tidal volume ventilation, then permissive hypercapnia may be tolerated as it is not contraindicated in pregnancy; mild hypercapnia 50 to 60 mm Hg is general acceptable.<sup>36</sup> However, if hypercapnia is greater than 60 mm Hg there is a potential of fetal acidemia shifting the fetal oxyhemoglobin dissociation curve to the right.<sup>36,38</sup> ARDSnet protocol recommends a goal plateau pressure of less than 30 cmH<sub>2</sub>O but given the reduction in chest wall compliance a higher plateau

pressure greater than 30 cmH<sub>2</sub>O may be appropriate; especially because transpulmonary pressures may not be elevated.<sup>39</sup> Therefore, esophageal pressure monitoring may be helpful.<sup>36</sup>

### **Sedation**

---

Critically ill patients on a ventilator need some form of analgesia and/or sedation. The 2018 Clinical Practice Guidelines for the Management of Pain, Agitation/Sedation, Delirium, Immobility, and Sleep Disruption in Adult Patients in the ICU (PADIS) suggest using the analgesia-first approach to spare and/or minimize the use of both opioids and sedatives.<sup>40</sup> When sedation is needed, the guideline recommends using light sedation (vs deep sedation) in critically ill, mechanically ventilated patients using established assessment tools such as the Richmond Agitation and Sedation Scale.<sup>40</sup> There are some situations in which deeper sedation is targeted, such as patients with severe hypoxemia, severe ARDS, and patients who are receiving neuromuscular blocking agents.

There is limited evidence to guide decisions regarding sedation and analgesia in critically ill pregnant patient. In general, commonly used agents for sedation and paralysis are safe in pregnancy.<sup>41</sup> Analgesic medications such as fentanyl, hydromorphone, and morphine are considered safe in pregnancy.<sup>42</sup> However, if used in pregnant patients close to the delivery time, neonatologists should be alerted as the neonate may develop signs of neonatal abstinence syndrome.<sup>42</sup> For sedation, the PADIS guideline suggests using either propofol or dexmedetomidine over benzodiazepines for sedation in critically ill mechanically ventilated adults.<sup>40</sup> There is no clear evidence that propofol causes congenital anomalies or adverse pregnancy outcomes.<sup>42</sup> Moreover, although Dexmedetomidine crosses the placenta there is no evidence that it is teratogenic.<sup>42</sup> If benzodiazepines are used the association between in utero benzodiazepine exposure and congenital malformations are conflicting. Similar to opiates, if used close to the delivery time, neonatologists should be alerted as the neonate may require additional support.<sup>42</sup>

### **Paralysis**

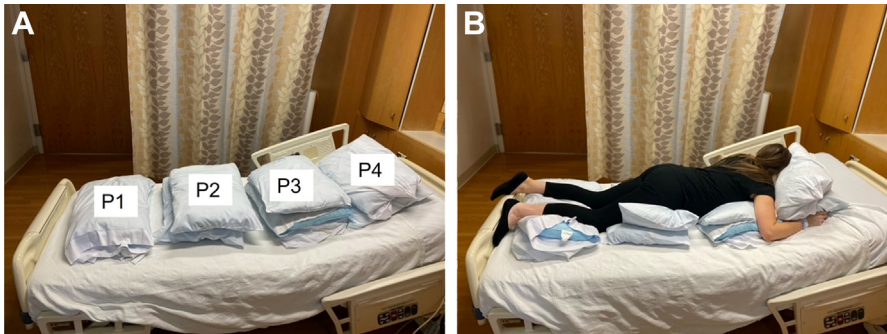
---

Paralytics are recommended for ventilated patients with moderate to severe ARDS to facilitate lung-protective ventilation.<sup>43</sup> They can be used for persistent ventilator dyssynchrony, to enable proning, and to limit high plateau pressures.<sup>43</sup> When indicated cisatracurium is the preferred neuromuscular blocker and may be used during pregnancy.<sup>42</sup>

### **Prone Positioning**

---

The prone positioning in severe acute respiratory distress syndrome (PROSEVA) trial has shown that in mechanically ventilated patients with ARDS, early application of prolonged prone-positioning sessions increases the rate of successful extubation and decreases mortality.<sup>44</sup> With regards to the management of ARDS due to COVID-19, international treatment guidelines of critically ill adults with COVID-19 by the Surviving Sepsis Campaign panel suggest prone ventilation in moderate to severe ARDS for 12 to 16 hours.<sup>43</sup> However, data on pregnant patients are lacking as they were excluded from the PROSEVA trial. There are several case reports reporting successful prone ventilation in both nonventilated and ventilated pregnant patients with severe ARDS.<sup>45–49</sup> Proning pregnant patients is more challenging owing to the large gravid uterus but is feasible with padding using pillows and blankets above and below the gravid uterus (**Fig. 2**). This method offloads the uterus and avoids aortocaval compression.<sup>36</sup>



**Fig. 2.** (A) Suggested support pillow location for prone positioning during pregnancy. P1: pillows supporting shins/knees, P2: pillows supporting maternal pelvis, P3: pillows supporting maternal chest, P4: pillows supporting maternal head. (Note: head of bed elevated 10–20°). (B) 33-week pregnant patient in the prone position with gravid abdomen supported between P2 and P3

### ***Inhaled Pulmonary Vasodilators***

Inhaled nitric oxide (iNO) is a selective pulmonary vasodilator that reduces the pulmonary artery pressure and increases arterial oxygenation in patients with severe ARDS.<sup>50</sup> While the antiviral property of iNO has been well described,<sup>51–55</sup> the role of iNO in the management of hypoxia due to COVID-19 remains unclear. The Surviving Sepsis Campaign panel recommends against the routine use of iNO in mechanically ventilated patients with COVID-19 ARDS but suggests a trial of iNO as a rescue strategy in mechanically ventilated adults with COVID-19, severe ARDS, and hypoxemia despite optimizing ventilation and other rescue strategies.<sup>43</sup> Data on iNO use in pregnant patients with COVID-19 are scarce. Safaei Fakhr and colleagues treated 6 pregnant patients meeting criteria for severe or critical COVID-19 with twice daily high-dose (160–200 ppm) nitric oxide via mask. They reported an increase in systemic oxygenation with each administration session and it was well-tolerated without acute adverse events.<sup>56</sup> Further studies and trials are needed to elucidate the potential benefits of iNO therapy in patients with COVID-19.

### ***Venous-Venous Extracorporeal Membrane Oxygenation***

Information on venous-venous extracorporeal membrane oxygenation (VV-ECMO) in pregnancy is limited. Nonetheless, pregnancy is not a contraindication.<sup>18</sup> A systematic review by Naoum and colleagues of critically ill pregnant patients that underwent VV-ECMO showed 80.2% survived with the most common complication being maternal bleeding.<sup>57</sup> Since the pandemic there have been many case reports of pregnant patients with COVID-19 ARDS and the use of VV-ECMO.<sup>58–60</sup> The decision to place patients on VV-ECMO should be undertaken with a multidisciplinary team approach with members from critical care, cardiothoracic surgery, obstetrics/maternal-fetal medicine (MFM), and neonatology. Indications for VV-ECMO in the hypoxic pregnant patient should follow as per Extracorporeal Life Support Organization (ELSO) guidelines.<sup>18</sup> If patients worsen despite standard ARDS management, VV-ECMO should be considered in patients with severe ARDS with  $\text{PaO}_2/\text{FiO}_2$  (P/F) ratios less than 80 for more than 6 hours, less than 50 for more than 3 hours, or a pH less than 7.25 with  $\text{Paco}_2$  greater than 60 for more than 6 hours.<sup>61</sup> Cannulation site is affected by the stage of pregnancy. If the uterus fundus is at the level of the umbilicus femoral



cannulation may be difficult.<sup>41</sup> Therefore, the preferred cannulation method is a single dual lumen catheter in the right internal jugal vein; however, their smaller size may not match adequate flow needs due to the increased cardiac output of pregnancy. Once initiated, the management of the ECMO circuit and weaning should follow ELSO protocols.<sup>61</sup> However, if the patient were to give birth on ECMO there is an increased risk of hemorrhage. Therefore, an ECMO strategy without anticoagulation could be considered as some reports have shown it to be safe.<sup>62,63</sup>

### ***Fetal Monitoring***

---

Fetal monitoring should be viewed as yet another measure of maternal hemodynamics. Fetal monitoring provides a noninvasive means of ensuring placental perfusion, as well as serving as a proxy for fetal oxygenation and acid–base status.<sup>64</sup> The key drivers to ensuring adequate placental perfusion are maternal hemodynamic stability, maternal oxygenation, volume status, and acid–base status.<sup>41,65,66</sup> There are little data to guide on the use of fetal monitoring in the critically ill pregnant patient; as such, a multidisciplinary team including MFM/high-risk obstetrics, critical care, neonatology, and nursing should be used to determine the frequency, duration, and location of monitoring. Many variables are considered in making the decision to perform fetal monitoring; however, gestational age and maternal acuity should be atop the list.<sup>67</sup>

The term “fetal viability” is often used when considering initiating fetal monitoring. At most centers, 22 weeks is the lowest threshold to consider a fetus viable, with most centers not recommending neonatal intervention until 24 weeks. The decision to initiate fetal monitoring should be based on balancing the family’s expectation/desires for neonatal outcomes and the clinical situation.<sup>68</sup> As such, fetal monitoring should not be performed until a joint neonatology/MFM consultation has occurred. With advances in neonatal care and improved access to neonatal ICU, neonatal survival rates have progressively improved over time in the 22–24-week periviable period.<sup>68</sup>

In the critically ill previable parturient, fetal heart auscultation at daily to weekly intervals is appropriate to confirm the pregnancy remains present; however, before viability, management plans should not deviate because of fetal status. Once the fetus is viable, fetal monitoring should be used to not only assure fetal health but also as yet another hemodynamic parameter to ensure placental perfusion.<sup>69</sup> The frequency of fetal monitoring needs to be individualized, and flexible, based on maternal acuity and decompensation. Recognizing practice vary by institution, a minimum of daily monitoring is recommended for the critically ill. Often, until maternal stability has been established or in the mechanically ventilated or ECMO patient, continuous monitoring is recommended.<sup>67</sup>

### ***Timing of Delivery***

---

The decision to proceed with delivery in the critically ill parturient needs to be balanced with (1) potential benefit toward maternal status and (2) risk of prematurity. In the setting of reassuring fetal monitoring and maternal stability, delivery is seldom recommended. In cases whereby ventilation cannot be optimized, consideration for delivery is appropriate to improve respiratory mechanics.<sup>70</sup> Decision making around delivery needs to include critical care medicine, neonatology, MFM, and obstetrics anesthesia. Delivery location should be prioritized to a labor and delivery suite; however, if delivery in the critical care setting is needed, multidisciplinary advanced planning is critical to ensure all resources are available for both the mother and neonate. In our practice, delivery in the ICU should be limited to perimortem cesarean delivery or whereby maternal/fetal status does not allow for any delay. Therefore, while in the ICU preparations should be made for imminent delivery in case of emergency (**Box 1**).

**Box 1****Recommended obstetric and neonatal supplies for delivery in adult ICU****Maternal**

Cesarean Delivery Kit  
 Vaginal Delivery Kit (if plan to deliver in ICU)  
 Uterotonic Medications<sup>a</sup> (Pitocin, Misoprostol, Methylergometrine)  
 Uterine Balloon<sup>a</sup>

**Neonatal**

Baby Warmer  
 Neonatal Code Cart  
 Oxygen Blender  
 Neonatal Transport Isolette

<sup>a</sup> Available to treat unexpected postpartum hemorrhage

As mentioned above, any parturient with a viable fetus should receive a course of glucocorticoids for fetal lung maturity if critical status presents before 34 weeks gestation.<sup>71</sup> Based on expert opinion from the current pandemic, the following should be considered in terms of timing of delivery. From the point of viability to 31w6d, delivery should be reserved for cases whereby maternal status continues to rapidly deteriorate or when fetus status is nonreassuring despite interventions. Beyond 32 weeks, delivery should be strongly considered in cases requiring mechanical ventilation or ECMO, after a course of glucocorticoids for fetal lung maturity. If maternal status deteriorates beyond 34 weeks, delivery is recommended.<sup>57</sup> It is important to note that mode of delivery (cesarean vs induction of labor) should be determined by standard obstetrics principles if both maternal and fetus status allow.<sup>66,67,70</sup>

Maternal cardiac arrest should prompt decision for urgent (less than 5 minutes) perimortem cesarean delivery. A perimortem cesarean delivery should be performed wherever the arrest occurred; as such, preparing for delivery in the critical care setting is highly recommended. This delivery is performed to maximize maternal resuscitative efforts, most notably, improving cardiac return by decompressing the inferior vena cava of the gravid uterus allowing for more effective CPR.<sup>72</sup>

### **Postpartum**

---

Despite delivery occurring, pregnancy physiology continues for many weeks postpartum.<sup>8</sup> Irrespective of gestational age at the time of delivery, there is a physiologic autotransfusion from the utero-placental unit into maternal circulation resulting in increased visceral perfusion and flow. This autotransfusion results in increased pulmonary pressures and the resultant increased risk of pulmonary edema.<sup>8,73</sup> In addition, an increase in catecholamines and fluid shifts during the postpartum period make the lungs particularly vulnerable to capillary leak.<sup>73</sup>

The other significant consideration during the postpartum state is the increased risk of VTE. The increased thrombogenic state continues for up to 12 weeks postpartum, with the first 6 weeks carrying the highest risk of thromboembolism.<sup>74</sup> With the added risk associated with severe COVID-19, the postpartum critically ill patient should be considered high risk for thromboembolism and appropriate prophylaxis should be administered. As mentioned earlier, adjusted risk-based prophylactic dosing is recommended in critically ill patients, this recommendation still holds true for the postpartum patient.<sup>66,75</sup>

Lastly, lactation issues often arise in critically ill postpartum patients, and COVID-19 is no exception. The benefits of breastfeeding are well established, and every effort should be made to support this activity if it is consistent with the patient's wishes. In addition to the well-known benefits of breastfeeding, breast milk from postpartum patients with COVID-19 has been shown to contain both anti-SARS-CoV-2 IgA and IgG, providing passive immunity to the vulnerable newborn.<sup>76</sup> Consultation with MFM, lactation, pharmacy, and neonatology should occur to confirm medication compatibility with breastfeeding. Providing assistance with pumping or hand expression of milk by nursing staff, lactation, or family is critical to ensure adequate milk production and continue supply.<sup>77</sup>

## SUMMARY

The pregnant patient is at increased risk for severe COVID-19 disease. Although there are limited data, management should focus on the early identification of critically ill patient for triage to the ICU. Standard therapy includes medical management with steroids and maintenance of an oxygenation saturation of at least 95%. The deteriorating patient requires special consideration with the application of therapies such as proning, sedation/analgesia, paralysis, and VV-ECMO. Furthermore, particular attention to fetal monitoring, timing of delivery, and preparation for postpartum issues are essential.

## DISCLOSURE

The authors have no financial conflicts of interest to disclose

## REFERENCES

1. Zambrano LD, Ellington S, Strid P, et al. Update: characteristics of symptomatic women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status - United States, January 22-October 3, 2020. *MMWR Morb Mortal Wkly Rep* 2020;69(44):1641-7.
2. Ko JY, DeSisto CL, Simeone RM, et al. Adverse pregnancy outcomes, maternal complications, and severe illness among US delivery Hospitalizations with and without a coronavirus disease 2019 (COVID-19) Diagnosis. *Clin Infect Dis* 2021;73(Suppl 1):S24-31.
3. Pierce-Williams RAM, Burd J, Felder L, et al. Clinical course of severe and critical coronavirus disease 2019 in hospitalized pregnancies: a United States cohort study. *Am J Obstet Gynecol MFM* 2020;2(3):100134.
4. Easter SR, Gupta S, Brenner SK, et al. Outcomes of critically ill pregnant women with COVID-19 in the United States. *Am J Respir Crit Care Med* 2021;203(1):122-5.
5. Allotey J, Stallings E, Bonet M, et al. Clinical manifestations, risk factors, and maternal and perinatal outcomes of coronavirus disease 2019 in pregnancy: living systematic review and meta-analysis. *BMJ* 2020;370. <https://doi.org/10.1136/bmj.m3320>. m3320.
6. Panagiotakopoulos L, Myers TR, Gee J, et al. SARS-CoV-2 infection among hospitalized pregnant women: Reasons for admission and pregnancy Characteristics - Eight U.S. Health care centers, March 1-may 30, 2020. *MMWR Morb Mortal Wkly Rep* 2020;69(38):1355-9.
7. Galang RR, Newton SM, Woodworth KR, et al. Risk factors for illness Severity among pregnant women with confirmed severe acute respiratory syndrome

- coronavirus 2 infection-Surveillance for emerging Threats to mothers and Babies Network, 22 state, local, and Territorial health Departments, 29 March 2020-5 March 2021. *Clin Infect Dis* 2021;73(Suppl 1):S17–23.
8. Ouzounian JG, Elkayam U. Physiologic changes during normal pregnancy and delivery. *Cardiol Clin* 2012;30(3):317–29.
  9. Wastnedge EAN, Reynolds RM, van Boeckel SR, et al. Pregnancy and COVID-19. *Physiol Rev* 2021;101(1):303–18.
  10. Hegewald MJ, Crapo RO. Respiratory physiology in pregnancy. *Clin Chest Med* 2011;32(1):1–13.
  11. Donders F, Lonnee-Hoffmann R, Tsiakalos A, et al. ISIDOG recommendations Concerning COVID-19 and pregnancy. *Diagnostics (Basel)* 2020;10(4). <https://doi.org/10.3390/diagnostics10040243>.
  12. Committee on Obstetric P. Committee Opinion No. 713. Antenatal corticosteroid therapy for fetal maturation. *Obstet Gynecol* 2017;130(2):e102–9.
  13. American College of O, Gynecologists' Committee on Practice B-O. Practice Bulletin No. 171: management of preterm labor. *Obstet Gynecol* 2016;128(4):e155–64.
  14. Saccone G, Berghella V. Antenatal corticosteroids for maturity of term or near term fetuses: systematic review and meta-analysis of randomized controlled trials. *BMJ* 2016;355:i5044. <https://doi.org/10.1136/bmj.i5044>.
  15. Saad AF, Chappell L, Saade GR, et al. Corticosteroids in the management of pregnant patients with coronavirus disease (COVID-19). *Obstet Gynecol* 2020;136(4):823–6.
  16. Group RC, Horby P, Lim WS, et al. Dexamethasone in hospitalized patients with Covid-19. *N Engl J Med* 2021;384(8):693–704.
  17. Gynaecologists RCoOa. Coronavirus (COVID-19) infection In Pregnancy - Version 14. 2021;
  18. Halscott TV, J and the SMFM COVID-19 Task Force. Management considerations for pregnant patients with COVID-19. 2020;
  19. Heit JA, Kobbervig CE, James AH, et al. Trends in the incidence of venous thromboembolism during pregnancy or postpartum: a 30-year population-based study. *Ann Intern Med* 2005;143(10):697–706.
  20. Pomp ER, Lenselink AM, Rosendaal FR, et al. Pregnancy, the postpartum period and prothrombotic defects: risk of venous thrombosis in the MEGA study. *J Thromb Haemost* 2008;6(4):632–7.
  21. Malas MB, Naazie IN, Elsayed N, et al. Thromboembolism risk of COVID-19 is high and associated with a higher risk of mortality: a systematic review and meta-analysis. *Eclinicalmedicine* 2020;29:100639. <https://doi.org/10.1016/j.eclinm.2020.100639>.
  22. Bikdeli B, Madhavan MV, Jimenez D, et al. COVID-19 and thrombotic or thromboembolic disease: Implications for Prevention, Antithrombotic therapy, and follow-up: JACC state-of-the-Art review. *J Am Coll Cardiol* 2020;75(23):2950–73.
  23. Middeldorp S, Coppens M, van Haaps TF, et al. Incidence of venous thromboembolism in hospitalized patients with COVID-19. *J Thromb Haemost* 2020;18(8):1995–2002.
  24. Investigators R-C, Investigators AC-a, Investigators A, et al. Therapeutic anticoagulation with heparin in critically ill patients with Covid-19. *N Engl J Med* 2021;385(9):777–89.
  25. COVID-19 Treatment Guidelines Panel. Coronavirus disease 2019 (COVID-19) treatment guidelines. National Institutes of Health. Available at: <https://www.covid19treatmentguidelines.nih.gov/>. Accessed September 29 2021.

26. Wang M, Cao R, Zhang L, et al. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell Res* 2020;30(3): 269–71.
27. Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the treatment of Covid-19 - Final report. *N Engl J Med* 2020;383(19):1813–26.
28. Veklury (remdesivir). [package insert]. Gilead Sciences, Inc.; 2021.
29. Burwick RM, Yawetz S, Stephenson KE, et al. Compassionate Use of remdesivir in pregnant women with severe Covid-19. *Clin Infect Dis* 2020. <https://doi.org/10.1093/cid/ciaa1466>.
30. Salama C, Han J, Yau L, et al. Tocilizumab in patients hospitalized with Covid-19 pneumonia. *N Engl J Med* 2021;384(1):20–30.
31. Somers EC, Eschenauer GA, Troost JP, et al. Tocilizumab for treatment of mechanically ventilated patients with COVID-19. *Clin Infect Dis* 2021;73(2):e445–54.
32. Horby P, Staplin N, Haynes R, et al. Tocilizumab in COVID-19 therapy: who benefits, and how? - Authors' reply. *Lancet* 2021;398(10297):300.
33. Investigators R-C, Gordon AC, Mouncey PR, et al. Interleukin-6 receptor Antagonists in critically ill patients with Covid-19. *N Engl J Med* 2021;384(16): 1491–502.
34. Pacheco LD, Saad AF, Saade G. Early acute respiratory support for pregnant patients with coronavirus disease 2019 (COVID-19) infection. *Obstet Gynecol* 2020; 136(1):42–5.
35. Schwaiberger D, Karcz M, Menk M, et al. Respiratory failure and mechanical ventilation in the pregnant patient. *Crit Care Clin* 2016;32(1):85–95.
36. Tolcher MC, McKinney JR, Eppes CS, et al. Prone positioning for pregnant women with hypoxemia due to coronavirus disease 2019 (COVID-19). *Obstet Gynecol* 2020;136(2):259–61.
37. Lapinsky SE. Acute respiratory failure in pregnancy. *Obstet Med* 2015;8(3): 126–32.
38. Campbell LA, Klocke RA. Implications for the pregnant patient. *Am J Respir Crit Care Med* 2001;163(5):1051–4.
39. Lapinsky SE, Posadas-Calleja JG, McCullagh I. Clinical review: ventilatory strategies for obstetric, brain-injured and obese patients. *Crit Care* 2009;13(2):206.
40. Devlin JW, Skrobik Y, Gelinas C, et al. Clinical practice guidelines for the Prevention and management of Pain, Agitation/sedation, Delirium, Immobility, and Sleep Disruption in adult patients in the ICU. *Crit Care Med* 2018;46(9):e825–73.
41. Oxford-Horrey C, Savage M, Prabhu M, et al. Putting it all Together: clinical considerations in the care of critically ill obstetric patients with COVID-19. *Am J Perinatol* 2020;37(10):1044–51.
42. Pacheco LD, Saade GR, Hankins GD. Mechanical ventilation during pregnancy: sedation, analgesia, and paralysis. *Clin Obstet Gynecol* 2014;57(4):844–50.
43. Alhazzani W, Moller MH, Arabi YM, et al. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19). *Crit Care Med* 2020;48(6):e440–69.
44. Guerin C, Reignier J, Richard JC, et al. Prone positioning in severe acute respiratory distress syndrome. *N Engl J Med* 2013;368(23):2159–68.
45. Kenn S, Weber-Carstens S, Weizsaecker K, et al. Prone positioning for ARDS following blunt chest trauma in late pregnancy. *Int J Obstet Anesth* 2009;18(3): 268–71.
46. Samanta S, Samanta S, Wig J, et al. How safe is the prone position in acute respiratory distress syndrome at late pregnancy? *Am J Emerg Med* 2014;32(6): 687 e1–3.

47. Schnettler WT, Al Ahwel Y, Suhag A. Severe acute respiratory distress syndrome in coronavirus disease 2019-infected pregnancy: obstetric and intensive care considerations. *Am J Obstet Gynecol MFM* 2020;2(3):100120.
48. Vibert F, Kretz M, Thuet V, et al. Prone positioning and high-flow oxygen improved respiratory function in a 25-week pregnant woman with COVID-19. *Eur J Obstet Gynecol Reprod Biol* 2020;250:257–8.
49. Pozos CKP DT, Deloya TE, Perez NOR, et al. Severe acute respiratory distress syndrome in pregnancy. Review of the literature and two cases report. *Med Crit* 2019;33(4):209–14.
50. Rossaint R, Falke KJ, Lopez F, et al. Inhaled nitric oxide for the adult respiratory distress syndrome. *N Engl J Med* 1993;328(6):399–405.
51. Akaike T, Maeda H. Nitric oxide and virus infection. *Immunology* 2000;101(3):300–8.
52. Colasanti M, Persichini T, Venturini G, et al. S-nitrosylation of viral proteins: molecular bases for antiviral effect of nitric oxide. *IUBMB Life* 1999;48(1):25–31.
53. Saura M, Zaragoza C, McMillan A, et al. An antiviral mechanism of nitric oxide: inhibition of a viral protease. *Immunotechnology* 1999;10(1):21–8.
54. Garren MR, Ashcraft M, Qian Y, et al. Nitric oxide and viral infection: Recent developments in antiviral therapies and Platforms. *Appl Mater Today* 2021;22. <https://doi.org/10.1016/j.apmt.2020.100887>.
55. Keyaerts E, Vijgen L, Chen L, et al. Inhibition of SARS-coronavirus infection in vitro by S-nitroso-N-acetylpenicillamine, a nitric oxide donor compound. *Int J Infect Dis* 2004;8(4):223–6.
56. Safaee Fakhr B, Wiegand SB, Pincirolli R, et al. High concentrations of nitric oxide Inhalation therapy in pregnant patients with severe coronavirus disease 2019 (COVID-19). *Obstet Gynecol* 2020;136(6):1109–13.
57. Naoum EE, Chalupka A, Haft J, et al. Extracorporeal life support in pregnancy: a systematic review. *J Am Heart Assoc* 2020;9(13):e016072.
58. Hou L, Li M, Guo K, et al. First successful treatment of a COVID-19 pregnant woman with severe ARDS by combining early mechanical ventilation and ECMO. *Heart Lung* 2021;50(1):33–6.
59. Larson SB, Watson SN, Eberlein M, et al. Survival of pregnant coronavirus patient on extracorporeal membrane oxygenation. *Ann Thorac Surg* 2021;111(3):e151–2.
60. Barrantes JH, Ortoleva J, O'Neil ER, et al. Successful treatment of pregnant and postpartum women with severe COVID-19 associated acute respiratory distress syndrome with extracorporeal membrane oxygenation. *Asaio J* 2021;67(2):132–6.
61. Badulak J, Antonini MV, Stead CM, et al. Extracorporeal membrane oxygenation for COVID-19: Updated 2021 guidelines from the extracorporeal life support Organization. *Asaio j* 2021;67(5):485–95.
62. Fina D, Matteucci M, Jiritano F, et al. Extracorporeal membrane oxygenation without systemic anticoagulation: a case-series in challenging conditions. *J Thorac Dis* 2020;12(5):2113–9.
63. Kurihara C, Walter JM, Karim A, et al. Feasibility of Venovenous extracorporeal membrane oxygenation without systemic anticoagulation. *Ann Thorac Surg* 2020;110(4):1209–15.
64. ACOG Practice Bulletin No. 106: Intrapartum fetal heart rate monitoring: nomenclature, interpretation, and general management principles. *Obstet Gynecol* 2009;114(1):192–202.

65. Meschia G. Fetal oxygenation and maternal ventilation. *Clin Chest Med* 2011; 32(1):15–9.
66. Crozier TME. General care of the pregnant patient in the intensive care Unit. *Semin Respir Crit Care Med* 2017;38(2):208–17.
67. Rose CH, Wyatt MA, Narang K, et al. Timing of delivery with coronavirus disease 2019 pneumonia requiring intensive care unit admission. *Am J Obstet Gynecol MFM* 2021;3(4):100373.
68. Obstetric care consensus No. 6: periviable birth. *Obstet Gynecol* 2017;130(4): e187–99.
69. Poon LC, Yang H, Kapur A, et al. Global interim guidance on coronavirus disease 2019 (COVID-19) during pregnancy and puerperium from FIGO and allied partners: Information for healthcare professionals. *Int J Gynaecol Obstet* 2020; 149(3):273–86.
70. Lapinsky SE. Management of acute respiratory failure in pregnancy. *Semin Respir Crit Care Med* 2017;38(2):201–7.
71. Roberts D, Brown J, Medley N, et al. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. *Cochrane Database Syst Rev* 2017;3:CD004454.
72. Oxford CM, Ludmir J. Trauma in pregnancy. *Clin Obstet Gynecol* 2009;52(4): 611–29.
73. Chen L, Jiang H, Zhao Y. Pregnancy with COVID-19: management considerations for care of severe and critically ill cases. *Am J Reprod Immunol* 2020;84(5): e13299.
74. Kamel H, Navi BB, Sriram N, et al. Risk of a thrombotic event after the 6-week postpartum period. *N Engl J Med* 2014;370(14):1307–15.
75. Susen S, Tacquard CA, Godon A, et al. Prevention of thrombotic risk in hospitalized patients with COVID-19 and hemostasis monitoring. *Crit Care* 2020; 24(1):364.
76. Pace RM, Williams JE, Jarvinen KM, et al. Characterization of SARS-CoV-2 RNA, Antibodies, and Neutralizing capacity in milk produced by women with COVID-19. *mBio* 2021;(1):12. <https://doi.org/10.1128/mBio.03192-20>.
77. Dauphinee JD, Amato K, Kiehl E. Support of the breast-feeding mother in critical care. *AACN Clin Issues* 1997;8(4):539–49.