Inpatient Management and OBICU Care for Pregnant Patients With Severe COVID-19 Disease

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Abstract: This manuscript will review intensive care management considerations for pregnant patients with severe COVID-19 disease.
Key words: COVID, ICU, pregnancy

Introduction

The management of pregnant women in the intensive care unit (ICU) is many times nuanced and is dependent on the severity of critical illness (ie, sepsis, respiratory failure, hemorrhage). Further, pregnancy status (antepartum, intrapartum, and postpartum) and fetal viability are incredibly important factors and make patient care complex. SARS-coronavirus 19 (COVID-19) has

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pushed intensivist and obstetricians alike to become familiar with respiratory care, mechanical ventilation, and ICU care of the obstetric patient. This chapter will focus on considerations as it relates to this care. The focus of this chapter will center on severe and critically ill COVID-19 infections in pregnancy and its supportive care strategies in the ICU.

DEFINITION

Severe disease of COVID-19 is currently defined as having a respiratory rate > 30 breaths per minute, hypoxemia with oxygen saturation of <94% on room air, or $> 50\%$ lung involvement on imaging.[1] Many times pregnant patients are admitted for at least supplemental oxygen and monitoring in the setting of severe disease. Location of admission is highly dependent

on the hospital and its system as well as the gestational age of the fetus. For instance, where some labor and delivery units have allotted negative pressure rooms on the floor, others may need to exclusively admit to the COVID hospitalist or medicine service. In the absence of hypotension, need for mechanical ventilation, or other signs of organ failure, many of these patients can be monitored on the medicine/COVID wards, labor and delivery, or antepartum units. In the setting of critical disease, defined as multiorgan failure or dysfunction, shock, or respiratory failure requiring mechanical ventilation and/or noninvasive ventilation (NIVV), these patients are usually placed in either intermediate care units or ICUs depending on the level of necessary care.[1]

RISK FACTORS FOR CRITICAL ILLNESS IN PREGNANCY

Pregnant patients are at increased risk for critical illness in pregnancy when compared with nonpregnant counterparts respectively: ICU admission [10.5 vs. 3.9 per 1000 cases; adjusted risk ratio (aRR) = 3.0; 95% confidence interval (CI) = 2.6-3.4]; need for mechanical ventilation (2.9 vs. 1.1 per 1000 cases; aRR = 2.9; 95% CI = 2.2-3.8), receive extracorporeal membrane oxygenation (ECMO) (0.7 vs. 0.3 per 1000 cases; aRR = 2.4; 95% CI = 1.5-4.0), and die (1.5 vs. 1.2 per 1000 cases; aRR = 1.7; 95% CI = 1.2-2.4).[2] These increased risks are further compounded by the racial disparities in medicine that lead to increased severity and infection in black pregnant persons.[3,4]

The transition from hospital admission to higher levels of care can be difficult. However, increased work of breathing, inability to maintain oxygenation > 94%, persistent and frequent fevers, and worsening myalgias can all be early warning signs. Further, scoring systems may be utilized to aid in identifying patients who need escalation of care in COVID-19. These include the Sequential Organ Failure Assessment (SOFA) score, the "quick" or qSOFA, and the modified Early Warning Signs Score.[5] Data are limited in this context when it comes to pregnancy. However, there have been modified scoring systems that take into account clinical characteristics of pregnancy.

The transition to higher levels of care can be difficult and complexities are multifactorial. It is dependent upon the resources available to the perinatal floors and to the hospital. The majority of needs for ICU admission are usually secondary to respiratory failure and need further respiratory support.

RESPIRATORY SUPPORT

Respiratory support varies upon the needs of the patient. The respiratory support in the ICU can vary from escalations to facemask to intubation (Fig. 1). Facemask or "Non-Rebreather" can give a maximum of 15 liters per minute along with Venturi Face Mask. This is usually initially started for transfer or upon admission to allow time for other noninvasive and support. High-flow nasal cannula is commonly used in critical illnesses including respiratory failure or hypoxemia.[6,7] In studies with respiratory failure and acute respiratory distress syndrome (ARDS), high-flow nasal cannula can be used to decrease need for intubation, ventilator days, as well as length of stay.[6] In COVID-19, HiFLO nasal cannula has been successfully used to prevent invasive ventilation and decrease ICU length of stay.[7] Bilevel positive airway pressure and continuous positive airway pressure can also be used in COVID-19. Originally, these modalities were controversial with concern for aerosolization of infection particles. However, this risk is ameliorated with proper use of personal protective equipment.[8] Although pregnancy has not been extensively studied it is not a contraindication to use.

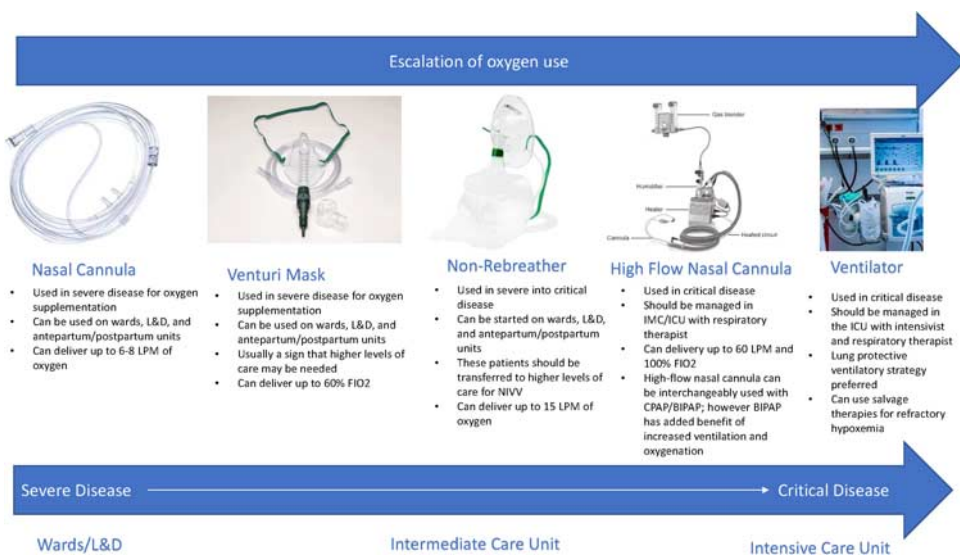Mechanical ventilation is reserved for patients who cannot participate in NIVV.

FIGURE 1. Escalation of care and oxygen use. Figure shows escalation of oxygen use in conjunction with higher levels of care. BiPAP indicates bilevel positive airway pressure; CPAP, continuous positive airway pressure; FIO_2, fraction of inspired oxygen; ICU, intensive care unit; IMC, intermediate care unit; LPM, liters per minute; NIVV, noninvasive ventilation.

This can be secondary to altered mental status, inability to tolerate NIVV, and other forms of organ dysfunction or shock. If mechanical ventilation is needed it should not be delayed for the sake of pregnancy alone.

During escalation of care, the obstetric team and the intensive care team should remain in continuous communication. Multidisciplinary approaches are imperative to successful resuscitations for both the mother and fetus. After intubation, discussions regarding delivery timing and place should be discussed in detail.

Mode of ventilation can be dependent upon institutional practices; however, lung protective ventilation is encouraged even in the setting of third trimester pregnancy. This mode of ventilation involves the use of low tidal volumes in concordance with incremental increases in positive end expiratory pressure and lower fraction of oxygen ratios.[9] This ventilatory maneuver has shown to decrease mortality in nonpregnant populations with ARDS and is

commonly used for COVID-19. Other salvage modes of ventilation, that is, airway pressure release ventilation, can be used in pregnancy as well, even the third trimester.

ADJUNCTS TO RESPIRATORY SUPPORT
In the setting of refractory hypoxemia other modalities and adjuncts should be used. Refractory hypoxemia can be defined as a PaO_2 <70 mm Hg or a *P*/F ratio <150 mm Hg.[1,10] In this setting both prone positioning and neuromuscular blockade can be used in moderate to severe ARDS. Prone positioning still can improve oxygenation and mortality in this patient population; however, the benefit of early neuromuscular blockade remains indeterminate in the setting of lung protective ventilation.[11–13]

Other adjuncts to respiratory support include pulmonary vasodilators (nitric oxide and inhaled prostacyclins.[14,15] Neither of these modalities are considered

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routine treatments in ARDS or critical (or refractory) COVID-19 pneumonia. However, they can be temporizing or salvage therapies as both can both acutely increase oxygenation with waning effects in 48 to 96 hours.[14,15] Because of these waning effects, long-term morbidity and mortality remain unchanged.[14,15] If all of all other modalities have been utilized, one can use ECMO to artificially bypass the lungs (venovenous) and or heart (venous arterial) or other permutations of mechanical circulatory support, venous-arterial-venous ECMO, venovenous+impella, etc.[16] Although often discussed there are general indications for ECMO per Extracorporeal Life Support Organization guidelines:[17]

- Hypoxic (refractory) respiratory failure despite optimal ventilatory strategies.
- Severe hypercapnia (pH 7.2 and $PaCO_2 > 80$ mm Hg for > 6 h).
- Prolonged ventilation > 7 days.
- Cardiogenic shock (refractory to conventional therapies with a cardiac index < 2 L/min/m^2 and central venous oxygen saturation of $<65\%$).
- Murray score > 3.
- Single organ failure with minimal or no comorbidities (ie, no stroke or liver failure).
- Massive pulmonary embolism.
- Bridge to cardiac or lung translation.
- Cardiac arrest.

ECMO should be started or immediately transferred to ECMO centers of excellence for the most improved outcomes. Risks associated with ECMO include high incidences of thrombosis, stroke, hemorrhage, and limb ischemia.

ANTICOAGULATION IN THE CRITICALLY Ill COVID-19 PATIENTS

Anticoagulation regimens using both unfractionated heparin and low-molecular weight heparin have been used in pregnancy. In general, at least prophylactic anticoagulation is advocated for symptomatic COVID-19 patients requiring inpatient admission.[1] However, data for anticoagulation in the critically ill pregnant patient remains less clear. COVID-19 infection, respiratory failure, and pregnancy are all risk factors for venous thrombosis.[18] Thus, many institutions have advocated for full anticoagulation in the patient population based on the high thrombosis risk in critically ill COVID in both the pregnant and nonpregnant states. In the setting of full anticoagulation in pregnancy, unfractionated heparin infusions may be preferred over low-molecular weight heparin based on the risk of need for interventions, preterm birth, and hemorrhage.

THERAPEUTICS

There are multiple therapeutic strategies for COVID-19 severe and critical illness and this remains an evolving topic. Currently, there are numerous regimens that have shown to be effective in the nonpregnant state. Unfortunately, many (or none) of the randomized controlled trials intentionally excluded pregnant women. Thus, much of the data and use is extrapolated from nonpregnant populations. Of note, therapeutics that are currently in use are not contraindicated in pregnancy. The therapeutics are as follows:

- Remdesivir: Remdesivir is an antiviral used for the treatment of patients with severe disease or requiring oxygen supplementation. A randomized controlled trial showed that remdesivir was superior to placebo at shortening the time to recovery in adults hospitalized with COVID-19 infection. The dosage of Remdesivir is usually a 200 mg loading dose on Day 1 followed by 100 mg daily for up to 9 additional days.[19,20]
- Dexamethasone: Dexamethasone is associated with a decreased risk of mortality among people requiring mechanical ventilation and supplemental oxygen in COVID-19. Many institutions use

dexamethasone concomitantly with remdesivir COVID-19 in the setting of severe and/or critical illness. The dosage of dexamethasone is usually 6 mg PO or IV for up to 10 days. If fetal lung maturity is also required in the setting of severe and/or critical COVID-19 infection, dexamethasone can be used for this purpose and the medication is given for 6 mg IM q 12×48 hours and then subsequently for dexamethasone 6 mg IV/PO daily for a total of 10 days.[21]

- Tocilizumab: Tocilizumab is an interleukin-6 inhibitor used to combat COVID-19. Interestingly, tocilizumab appears to be most effective in treating patients who require oxygen but are not yet ventilated. In a randomized controlled trial, it was found that it reduced progression of disease to a composite outcome of mechanical ventilation and death. Usually, tocilizumab is only given once with a 8 mg/kg dosing weight with a maximum of 800 mg.[22]

- Convalescent plasma: convalescent plasma has been frequently used in the context of COVID-19. The hypothesis is that "passive immunization" from a formerly infected individual will jump start the immune system to control and halt the evolution of severe disease. Observational studies have shown promise in morbidity for patients that receive "high titer" convalescent plasma; however, a randomized control trial showed no difference in 30-day mortality or significant clinical benefit.[23]

Therapeutic regimens continue to evolve for patients with COVID-19 and physicians and practitioners should continue to remain up to date on options that can be offered to patients.

ANTENATAL TESTING AND DELIVERY TIMING

In the setting of pregnancy, antenatal testing, and delivery are important aspects in perinatal care. Although there is some guidance in delivery after 32 weeks in the setting of critically ill COVID-19 parturients with refractory hypoxemia, delivery timing remains nuanced and should be individualized.[10] This aspect of care is incredibly nuanced and requires multidisciplinary discussions among obstetrics/maternal fetal medicine, intensivist, anesthesia, and pediatrics. This multidisciplinary team must also include respiratory therapy and nursing in addition to the physician team.

Conclusion

Although complex, the care of critically ill pregnant patients are similar to their nonpregnant counterparts. The mainstay of care is supportive in nature with the addition of appropriate therapeutic options. Particular aspects of pregnancy, that is, antenatal testing and delivery timing, should be individualized. Care teams should have active and daily communication about plans of care and treatment goals.

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