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Oxygen saturation in pregnant individuals with COVID-19: time for re-appraisal?

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Managing pregnant individuals with acute respiratory disease secondary to COVID-19 has been a challenge. Most professional societies including the Society for Maternal-Fetal Medicine recommend keeping O_2 saturation at ≥95% in pregnant individuals. Reaching this target has been increasingly difficult in some patients, especially during the latest wave of infections attributed to the delta variant of SARS-CoV-2. In the absence of adequate supporting data, and in the setting of a reassuring fetal status, we propose that maternal O_2 saturation should be maintained between 92% and 96% for admitted patients with acute respiratory failure who require supplemental O_2. This may prevent unnecessary invasive interventions that might not hold maternal or fetal benefit, specifically at very preterm gestational ages.

Key words: COVID-19, oxygen saturation, pregnancy

Introduction and Current Guidelines

During pregnancy, several professional societies recommend maintaining O_2 saturation (SpO_2) at ≥95%.[1–3] In response to the current COVID-19 pandemic, the Society for Maternal-Fetal Medicine (SMFM) recommends that the target SpO_2 for pregnant individuals should be higher than recommended for the nonpregnant population (SpO_2≥92%). Furthermore, they recommend that inpatient monitoring should be considered for pregnant individuals with moderate or severe signs or symptoms of COVID-19 and for those whose SpO_2 drop below 95% while on room air during exertion. These patients should call their healthcare provider, undergo prompt evaluation, and be considered for inpatient admission, because they may require admission to higher level of care units such as an intensive care unit or a step-down unit.[1]

Other professional societies such as the Royal College of Obstetricians and Gynaecologists and the International Federation of Gynecology and Obstetrics have advocated for the maintenance of SpO_2 at a similar cutoff of ≥95%.[2,3] However, the evidence supporting maintenance of SpO_2 at this cutoff is limited. Meanwhile, the World Health Organization suggests maintaining SpO_2 at 92% to 95% in pregnant individuals with severe respiratory infection secondary to COVID-19.[4]

What is the Evidence Behind Using an O_2 Saturation of ≥95%?

There are no published trials or clinical studies demonstrating that an SpO_2 at or above 95% is necessary for pregnant individuals to maintain adequate fetal oxygenation. Expert opinions suggest initiating supplemental O_2 for pregnant individuals when their SpO_2 falls below 94%, and this is based on known physiological changes that occur during pregnancy such as an increase in the partial pressure of O_2 (PaO_2) and increased O_2 demand.[5] Some of the current guidelines that suggest maintaining an SpO_2 of ≥95%[3,6,7] cite a paper published by Bhatia et al.[8] These authors state that a PaO_2 of 70 mm Hg is required to maintain adequate fetal oxygenation, which they also associate with a maternal SpO_2 of 95%.[8] Bhatia et al[8] make this conclusion on the basis of a study by Catanzarite et al[9] who included 28 women with acute respiratory distress syndrome (ARDS) who required intubation during pregnancy or within 1 week postpartum.[9] This study is limited because it used the older definition of ARDS, included patients only if they were intubated and within 7 days of delivery, and used the birth outcome of perinatal asphyxia, on the basis of historic data, to indicate a causal mechanism of neonatal hypoxia.[9] Applying these data to modern guidelines ignores >20 years of progress that has been made in the management of ARDS and confounding conditions such as the high rate of maternal multisystem organ failure. Although evidence from severe acute respiratory syndrome and COVID-19 suggests that there is a higher rate of fetal growth restriction in cases with severe maternal illness,[10–12] this is likely multifactorial instead of being limited to hypoxemia as the cause. There is no compelling objective evidence that an SpO_2 of 95% is required for adequate fetal oxygenation.

Mallampali et al[13] recommend maintaining the maternal PaO_2 above 60 to 70 mm Hg to avoid adverse effects on uteroplacental perfusion. However, other experts suggest that a PaO_2 of >60 mm Hg (correlating with an SpO_2 of >90%) is a reasonable target for pregnant individuals with acute respiratory failure.[12,14] This is because fetal hemoglobin has a higher affinity for O_2 than adult hemoglobin,

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which makes the fetus more resistant to changes in maternal O_2 saturation and some degree of hypoxia.[15,16] Further support that a PaO_2 of 60 mm Hg is adequate for fetal O_2 delivery is on the basis of data from pregnant individuals living at high altitudes.[17] Although this is a chronic rather than acute exposure to hypoxia (and is accompanied by compensation such as tachypnea and relative polycythemia), most of the pregnant individuals are young and healthy and have a good reserve to tolerate even acute hypoxia.[18]

In an effort to decrease maternal morbidity and mortality, early warning models have been developed to assist in the timely recognition of acutely ill patients,[19−21] with some models including SpO_2 as one of the parameters.[19,20] Unlike other vital sign parameters that could directly be associated with an increased risk for maternal morbidity, the use of SpO_2 at <95% was not (relative risk, 1.3; 95% confidence interval, 0.2−7.9).[19] Shields et al[20] published a maternal early warning tool using different cutoffs for SpO_2. They used an SpO_2 of <90% as a single severe parameter and an SpO_2 of <93% as a nonsevere parameter. However, low SpO_2 (whether <90% or <93%) was a rare occurrence and was seen in <0.1% of included patients.[20] In conclusion, the paucity of clinical data and lack of significance seen in early warning models do not provide sufficient evidence to support using an SpO_2 of ≥95% as a cutoff for pregnant individuals presenting with acute respiratory distress.

Challenges in Maintaining an O_2 Saturation of ≥95%

In nonpregnant individuals with acute respiratory failure secondary to COVID-19, current guidelines recommend starting supplemental O_2 when levels drop below an SpO_2 of 90% (strong recommendation, moderate-quality evidence) and suggest supplemental O_2 use when SpO_2 falls below 92% (weak recommendation, low-quality evidence).[22] In acutely ill patients, high-quality evidence showed that liberal O_2 therapy (median baseline SpO_2 of 96%) is associated with increased mortality.[22] Moreover, practice guidelines for acutely ill patients, including COVID-19 patients with acute hypoxemic respiratory failure, do not recommend administration of supplemental O_2 above an SpO_2 of 96% (strong recommendation, moderate-quality evidence) because it may lead to worse outcomes.[22−24] In pregnant individuals, Pacheco et al[5] also recommend that O_2 therapy should be titrated to avoid SpO_2 levels above 96%. Using a minimum target of 95% for SpO_2 in pregnancy would make it more difficult to titrate O_2 supplementation to avoid an SpO_2 of >96%.

There is a paucity of data to guide the O_2 goals when COVID-19 progresses to ARDS. Generally, the goal is to maintain PaO_2 at 55 to 80 mm Hg on the basis of extrapolation from the original ARDSNet trial[25] and more recent use in the ACURASYS[26] and Reevaluation of Systemic Early Neuromuscular Blockade[27] trials. Although there may be phenotypes of COVID-19−associated ARDS that respond to high amounts of noninvasive supplemental O_2 support, such as heated high-flow nasal cannulas, many of these patients will require invasive mechanical ventilation.[28,29] Indeed, some emerging data suggest that noninvasive positive-pressure ventilation (continuous positive airway pressure or bi-level positive airway pressure) may increase mortality and fail to decrease the rates of intubation in critically ill COVID-19 patients.[30] Other modern therapies for ARDS, such as prone positioning, have been used as alternative interventions to avoid invasive mechanical ventilation and improve oxygenation in COVID-19 patients,[31,32] however, these therapies present unique challenges for pregnant individuals.

The criteria to mechanically ventilate pregnant and nonpregnant individuals are similar. These include airway protection, hypoxia, hypercarbia, and hemodynamic instability.[15] Pregnant individuals infected with the SARS-CoV-2 delta variant are more frequently critically ill, requiring O_2 support more often compared with infection with previous variants.[33,34] In pregnant individuals with acute respiratory failure secondary to COVID-19, guidelines suggest to maintain a target maternal SpO_2 of ≥95% as per professional societies recommendations, whereas for nonpregnant patients, often a target PaO_2 of 55 to 80 mm Hg or an SpO_2 of >90% is recommend. To meet this higher goal, pregnant individuals may need increased O_2 delivery by noninvasive O_2 delivery methods, earlier intubation and mechanical ventilation, increasing fraction of inspired O_2, mean airway pressure, or positive end-expiratory pressure. In addition, pregnant individuals will have cephalad displacement of the diaphragm, increased intraabdominal pressure, which provides mechanical evidence of a disadvantage of oxygenation, and an increased O_2 consumption by the developing fetus. This increased oxygenation target is difficult to achieve, especially in patients with COVID-19 affected by the latest wave of infections attributed to the delta variant of SARS-CoV-2.[33,35] Thus, pregnant patients may be more likely to be exposed to increased invasive interventions when maternal oxygenation goals of 95% are unable to be maintained using noninvasive methods of O_2 supplementation, with potential risks and without clear maternal or fetal benefit.

In its guidance for managing COVID-19 patients, the SMFM suggests delivery at or after 32 weeks' gestation in settings of refractory maternal hypoxemia.[1] Although an SpO_2 cutoff of ≥95% seems reasonable and safe as a target, in most clinical situations, challenges in treating pregnant individuals affected by the most recent COVID-19 wave have raised questions regarding the validity of this recommendation, especially for patients at extreme preterm gestational ages. Designing a randomized controlled trial comparing the clinical outcomes for patients who were maintained at O_2 saturation levels of 92% and 95 %, respectively, would be ideal and might be warranted. However, designing and completing such a trial in a timely fashion with the current COVID-19 wave is unrealistic. Individualized patient care based on maternal clinical

status and gestational age is of utmost importance.

External Fetal Monitoring as a Noninvasive Tool

Fetal oxygenation depends on maternal oxygenation and placental perfusion. Significant disturbances in maternal oxygenation may lead to fetal hypoxia, which is often reflected as a nonreassuring fetal status during fetal heart rate monitoring.[36] External fetal monitoring can be used as an indicator of fetal well-being, and having a reassuring fetal heart rate is associated with adequate oxygenation and perfusion of the fetus.[37,38] Fetal heart rate monitoring can be used as an additional vital sign that may help in the management of the maternal condition and guide the decision to move toward additional invasive interventions if needed. As long as the fetal status is reassuring, tolerating a maternal SpO_2 between 92% and 96% is prudent and might prevent detrimental outcomes associated with invasive interventions that could negatively affect both mother and baby.

Furthermore, tolerating a lower maternal SpO_2 may prevent unnecessary fetal interventions that could happen at time of intubation or extracorporeal membrane oxygenation (ECMO) cannulation, which could be challenging depending on the maternal characteristics. In many instances with difficult intubations, maternal O_2 saturation can transiently drop as low as 60% to 70% and is often associated with changes in variability and decelerations on thr fetal monitor.[39] Sustained nonreassuring fetal status often warrants acute interventions such as emergent cesarean delivery, which carries significant additional morbidity[40,41] to the mother on top of her acute respiratory failure secondary to COVID-19. More so, in cases of very preterm pregnancies, a classical cesarean delivery may be indicated, which carries an increased risk of bleeding[42,43] and long-term implications for future pregnancies.[44,45]

Conclusion

An SpO_2 below 95% in a pregnant individual with COVID-19 should prompt evaluation by a healthcare provider and may require inpatient admission. For pregnant individuals on supplemental O_2 for acute respiratory failure secondary to COVID-19 infection, there is a lack of convincing evidence supporting the current recommended SpO_2 of $\geq$95%. We suggest maintaining SpO_2 in a range of 92% to 96% in critically ill individuals admitted to the hospital on O_2 supplementation.

In the setting of reassuring fetal heart rate monitoring, this could possibly prevent unnecessary invasive interventions including endotracheal intubation with mechanical ventilation and ECMO. This is especially significant when the decision to escalate to these measures is based on the concern for maintaining fetal oxygenation rather than supporting the mother's respiratory status. In these situations, external fetal monitoring can be used as an additional noninvasive tool to monitor the fetal well-being and reserve invasive interventions for maternal respiratory status indications as long as the fetus is not showing signs of distress. ■

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