Corticosteroid Guidance for Pregnancy during COVID-19 Pandemic

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The field of medicine is facing an unprecedented challenge rapidly adapting current medical practice in caring for novel coronavirus disease 2019 (COVID-19) patients. The field of obstetrics is no different. Current treatment algorithms and protocols must be evaluated and modified to account for what is being learned and already known about COVID-19. One of our common practices in obstetrics is to give corticosteroids for fetal lung maturity to those at risk of delivering prematurely. Unfortunately, corticosteroid use has been associated with worse outcomes in COVID-19 positive patients. Given this information, it is necessary that obstetricians adjust practice to carefully weigh the fetal benefits with maternal risks. Therefore, our institution has examined the risks and benefits and altered our corticosteroid recommendations.

The novel coronavirus disease 2019 (COVID-19) pandemic is causing a necessary, rapid adjustment within the field of obstetrics. Corticosteroid use is a mainstay of therapy for those women delivering prematurely. Unfortunately, corticosteroid use has been associated with worse outcomes in COVID-19 positive patients. Given this information, it is necessary that obstetricians adjust practice to carefully weigh the fetal benefits with maternal risks. Therefore, our institution has examined the risks and benefits and altered our corticosteroid recommendations.

Key Points
- Corticosteroid use is an important part of prematurity treatment because it provides benefit to the fetus.
- Corticosteroid use may be related with increased morbidity and mortality in novel coronavirus disease 2019 (COVID-19).
- Therefore, during the COVID-19 pandemic, an alteration in current corticosteroid practices is necessary to uniquely weigh the maternal risks and fetal benefits.
In examining the data, there are numerous studies demonstrating neonatal benefit to corticosteroid use.\textsuperscript{3, 4–7} Because of this, it has become the standard of care to give betamethasone (or dexamethasone) to women at risk for delivering pretermly between 23 and 36 weeks of gestation.\textsuperscript{3, 8, 9} In fact, corticosteroids are such an ingrained part of obstetric practice, we give them out more than is truly necessary. In evaluating obstetricians’ use of betamethasone, several studies have examined how poorly steroids are timed (<7 days from administration to delivery) for imminent delivery. Two of these studies found that betamethasone was only given within the effective window 45.4 to 80% of the time.\textsuperscript{10, 11} In this pandemic, given that obstetricians are faced with two patients, mom and baby, it is necessary to balance the risks and benefits for each patient, which means evaluating how and when it is necessary to give them. In examining corticosteroids by gestational age, the absolute risk of neonatal complications and improved neonatal benefit by gestational age should be considered. Travers et al demonstrated that the lowest gestations receive the largest benefit from corticosteroids.\textsuperscript{12} In this large prospective cohort of 117,941 infants, neonatal death before discharge did not demonstrate a statistically significant reduction at or beyond 31 weeks. Additionally, survival without morbidity also did not reach statistical significance after 28 weeks. Given this delicate balance of choosing between neonatal benefit and possible maternal harm, it is prudent that obstetricians become more cautious with their betamethasone administration during this time. Weighing the risks and benefits, our institution has recommended that no women COVID-19 positive or person under investigation (PUI) receive corticosteroids beyond 32/7 weeks. We acknowledge that it may be difficult to determine whether a maternal fever in labor is chorioamnionitis or COVID-19.

| Table 1 | Disease severity and adverse composite outcome in COVID-19 patients treated with systemic glucocorticoids\textsuperscript{1} |
|-----------------------------|-----------------|------------------|-----------------|
| Variable | All patients \(n = 1,099\) \(n (%)\) | Disease severity | Presence of composite primary end point\textsuperscript{a} |
| | | Nonsevere \(n (%)\) | Severe \(n (%)\) | Yes \(n (%)\) | No \(n (%)\) |
| Systemic glucocorticoids | 204 (18.6) | 127 (13.7) | 77 (44.5) | 35 (52.2) | 169 (16.4) |
| Individual aspects of the composite outcomes | | | | | |
| ICU admission | | 33 (16.2%) | | | |
| Invasive ventilation | | 17 (8.3%) | | | |
| ECHMO\textsuperscript{b} | 5/77 (0.5%) | | | | |
| Death | 5 (2.5%) | | | | |

Abbreviations: COVID-19, novel coronavirus disease 2019; ECHMO, extracorporeal membrane oxygenation; ICU, intensive care unit.

\textsuperscript{a}Primary composite endpoint was admission to an ICU, use of mechanical ventilation, or death.

\textsuperscript{b}ECHMO was used in severe patients; % calculated from \(n = 77\).

In this examination, there are numerous studies demonstrating neonatal benefit to corticosteroid use.\textsuperscript{3, 4–7} Because of this, it has become the standard of care to give betamethasone (or dexamethasone) to women at risk for delivering pretermly between 23 and 36 weeks of gestation.\textsuperscript{3, 8, 9} In fact, corticosteroids are such an ingrained part of obstetric practice, we give them out more than is truly necessary. In evaluating obstetricians’ use of betamethasone, several studies have examined how poorly steroids are timed (<7 days from administration to delivery) for imminent delivery. Two of these studies found that betamethasone was only given within the effective window 45.4 to 80% of the time.\textsuperscript{10, 11} In this pandemic, given that obstetricians are faced with two patients, mom and baby, it is necessary to balance the risks and benefits for each patient, which means evaluating how and when it is necessary to give them. In examining corticosteroids by gestational age, the absolute risk of neonatal complications and improved neonatal benefit by gestational age should be considered. Travers et al demonstrated that the lowest gestations receive the largest benefit from corticosteroids.\textsuperscript{12} In this large prospective cohort of 117,941 infants, neonatal death before discharge did not demonstrate a statistically significant reduction at or beyond 31 weeks. Additionally, survival without morbidity also did not reach statistical significance after 28 weeks. Indeed, the number of mothers needed to treat with corticosteroids to prevent one neonatal death is six at 23 to 24 weeks but can increase to 798 women at 34 weeks.\textsuperscript{12} Given this delicate balance of choosing between neonatal benefit and possible maternal harm, it is prudent that obstetricians become more cautious with their betamethasone administration during this time. Weighing the risks and benefits, our institution has recommended that no women COVID-19 positive or person under investigation (PUI) receive corticosteroids beyond 32/7 weeks. We acknowledge that it may be difficult to determine whether a maternal fever in labor is chorioamnionitis or COVID-19.
Given the experience of those in New York with asymptomatic COVID-19 patients at the outset of labor, we recommend treating with antibiotics as is standard for chorioamnionitis, but also treating the patient as a PUI and obtaining a COVID-19 test. We also recommend (see Table 3) a maternal fetal medicine consultation for decisions regarding corticosteroid administration for pregnancies <32 weeks in women at risk of preterm delivery who are COVID-19 positive or PUI as individualization of care is necessary to take into account the unique risks of corticosteroids for the mother versus the benefit for the fetus.

When corticosteroids are not given, tocolysis should also not be undertaken given that the endpoint for tocolysis is to achieve steroid administration. When giving corticosteroids and utilizing tocolysis, consideration for risks and benefits of each tocolytic is prudent. Currently, the most efficacious tocolytic is indomethacin for achieving steroid benefit. While there was concern about nonsteroidal anti-inflammatory drugs (NSAIDs) in the setting of COVID-19, the Food and Drug Administration (FDA) has recently stated that there are no data to suggest NSAID use should be altered at this time. However, if a women is already hypotensive or tachycardic, nifedipine should not be used. Magnesium is a less effective tocolytic than indomethacin and nifedipine, and given the recommendation for conservative fluid management is less than ideal choice. Finally, betamimetics should not be used as they cause significant maternal hypotension, tachycardia, and pulmonary edema which should be avoided in someone who is has COVID-19. The discussions regarding corticosteroid administration and tocolysis should involve a multidisciplinary team including maternal fetal medicine, obstetrics, critical care physician, infectious disease specialists, and neonatologists. These decisions are of critical importance to serve both the interests of the mother and the fetus.

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Conflict of Interest
None declared.

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Table 3 Recommendations for corticosteroid use during the COVID-19 pandemic

- We recommend that no women COVID19 positive or PUI receive corticosteroids beyond 320/7 wk.
- We recommend an MFM consultation for decisions regarding corticosteroid administration for pregnancies <32 wk in women at risk of preterm delivery who are COVID-19 positive or PUI as individualization of care is necessary to take into account the unique risks of corticosteroids for the mother vs the benefit for the fetus.
- We recommend against tocolysis in women who are COVID-19 positive or PUI who are not receiving corticosteroids.

Abbreviations: COVID-19, novel coronavirus disease 2019; MFM, maternal-fetal medicine; PUI, person under investigation.