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.

Preferential use of dexamethasone for fetal lung maturation in severe coronavirus disease 2019

INTRODUCTION: As of July 1, 2020, over 10 million cases of coronavirus disease 2019 (COVID-19) and over 500,000 COVID-19–related deaths have been reported to the World Health Organization.[1] The Centers for Disease Control and Prevention found that pregnant women with COVID-19 were more likely to be hospitalized, admitted to the intensive care unit, and require mechanical ventilation when compared with nonpregnant women of reproductive age with COVID-19.[2] Preliminary data from the Randomised Evaluation of COVID-19 Therapy (RECOVERY) trial found that dexamethasone administration was associated with a reduction in 28-day mortality in patients requiring supplemental oxygen or mechanical ventilation.[3] It is unclear if dexamethasone is similarly effective in pregnant women with COVID-19.

CASE STUDY: A 27-year-old Latina primigravida at 30 weeks of gestation presented to the emergency department with an 8-day history of fever, cough, and dyspnea. She tested positive for severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) from a nasopharyngeal swab that was taken 7 days earlier. The patient's medical history included obesity, a sleeve gastrectomy, anemia, and thrombocytopenia. Her outpatient medications included a prenatal vitamin, vitamin B12, and vitamin D. Four of the patient's family members also tested positive for SARS-CoV-2, and she had been self-quarantining at home.

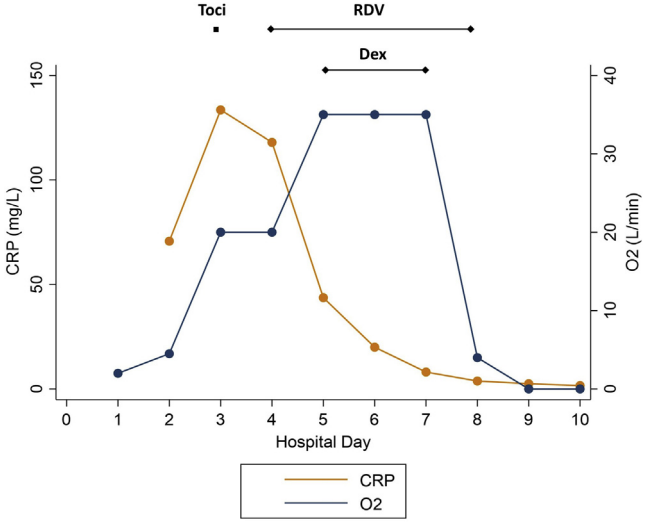
In the emergency department, the patient's temperature was 37°C, heart rate was 102 beats per minute, blood pressure was 106/55 mm Hg, respiratory rate was 25 breaths per minute, oxygen saturation was 94% on room air oxygen, and body mass index was 31 kg/m^2. A repeat nasopharyngeal swab tested positive for SARS-CoV-2, and a chest X-ray showed bilateral infiltrates. Her laboratory results demonstrated lymphopenia and elevated levels of C-reactive protein, D-dimer, and interleukin-6 (Supplemental Table). An obstetrical ultrasound showed normal fetal heart rate and amniotic fluid volume, and the fetal weight was estimated to be 1642 g. The patient was admitted to the inpatient unit and treated with oxygen supplementation through a nasal cannula at a flowrate of 2 L/min, enoxaparin at a dosage of 1 mg/kg/d, and positioning in a modified prone position.

On hospital day 2, her dyspnea worsened, and the oxygen supplementation was increased to a flowrate of 4.5 L/min to meet the target oxygen saturation of ≥95% for pregnancy. Compassionate use of remdesivir was requested and approved by Gilead Sciences (Foster City, CA) and the Food and Drug Administration, but was not immediately available. Owing to an increasing oxygen requirement and evolving cytokine storm, a 400 mg dose of tocilizumab was administered intravenously for off-label use following informed consent (Figure). On hospital day 4, remdesivir was available, and a dose of 200 mg was administered intravenously, followed by subsequent doses of 100 mg daily for 4 days.

On hospital day 5, the patient was transferred to the intensive care unit while receiving oxygen supplementation at a flowrate of 35 L/min through a high-flow nasal cannula with the fraction of inspired oxygen at 60%. Owing to a concern for impending respiratory failure, dexamethasone was administered for fetal lung maturation (4 doses of 6 mg intramuscularly every 12 hours) in preparation for a possible emergent delivery. On hospital day 8, after completion of the dexamethasone course, the patient's oxygen requirement decreased, and the plans for an emergent delivery were discontinued. The patient was transferred out of the intensive care unit, transitioned to room air, and discharged home in a stable condition on hospital day 10.

DISCUSSION: This case study describes a pregnant patient with severe COVID-19 who recovered soon after receiving dexamethasone for fetal lung maturation. When preterm delivery is imminent, antenatal corticosteroids, such as betamethasone and dexamethasone that have similarly efficacies,[4] are administered to the mother to accelerate fetal lung maturity and decrease neonatal mortality.[5] However, there was an initial hesitation to administer corticosteroids

FIGURE
CRP concentration and O2 during hospitalization for COVID-19



CRP, C-reactive protein; *Dex*, dexamethasone; *O_2*, supplemental oxygen requirement; *RDV*, Remdesivir; *Toci*, Tocilizumab. Hospital day 1 = symptom day 8

Dellapiana. Use of dexamethasone for fetal lung maturation in COVID-19. Am J Obstet Gynecol MFM 2020.

in pregnant women with COVID-19 owing to concerns of worsening the disease.[6]

In light of the preliminary findings from the RECOVERY trial, the National Institute of Health recommended using dexamethasone at a dosage of 6 mg/d for up to 10 days in patients with COVID-19 requiring supplemental oxygen.[7] Although a 48-hour course of antenatal corticosteroids is effective for fetal lung maturation, prolonged courses of antenatal corticosteroids are typically not recommended because of a potential adverse impact on long-term childhood neurodevelopment.[8] We administered dexamethasone over 48 hours using the standard dosing for fetal lung maturation, to which the patient responded favorably. We cannot attribute the recovery to dexamethasone alone, as the patient also received tocilizumab and remdesivir, which have shown to have benefits in the treatment of COVID-19 in pregnancy.[9]

We suggest preferential use of dexamethasone (4 doses of 6 mg intramuscularly every 12 hours) over betamethasone when acceleration of fetal lung maturity is indicated for pregnant women with severe COVID-19. When supplemental oxygen or mechanical ventilation is required beyond 48 hours, an additional 8 days of corticosteroids may be considered to mimic the design of the RECOVERY trial, in which administration of prednisolone at a dosage of 40 mg orally once daily or hydrocortisone at a dosage of 80 mg intravenously twice daily for pregnant women is recommended. Methylprednisolone may also be considered because of the limited placental transfer and documented efficacy in cases of acute lung injury,[10] but additional studies are needed to evaluate this approach.

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REFERENCES

1. World Health Organization. WHO coronavirus disease (COVID-19) dashboard. WHO Health Emergency Dashboard. 2020. Available at: https://covid19.who.int/. Accessed July 1, 2020.
2. Ellington S, Strid P, Tong VT, et al. Characteristics of women of reproductive age with laboratory-confirmed SARS-CoV-2 infection by pregnancy status - United States, January 22-June 7, 2020. MMWR Morb Mortal Wkly Rep 2020;69:769–75.
3. RECOVERY Collaborative Group, Horby P, Lim WS, et al. Dexamethasone in hospitalized patients with Covid-19 - preliminary report. N Engl J Med 2020. [Epub ahead of print].
4. Crowther CA, Ashwood P, Andersen CC, et al. Maternal intramuscular dexamethasone versus betamethasone before preterm birth (ASTEROID): a multicentre, double-blind, randomised controlled trial. Lancet Child Adolesc Health 2019;3:769–80.
5. Roberts D, Brown J, Medley N, Dalziel SR. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev 2017;3:CD004454.
6. McIntosh JJ. Corticosteroid guidance for pregnancy during COVID-19 pandemic. Am J Perinatol 2020;37:809–12.
7. National Institutes of Health. COVID-19 treatment guidelines. Corticosteroids 2020. Available at: https://www.covid19treatmentguidelines.nih.gov/dexamethasone/. Accessed June 26, 2020.
8. Räikkönen K, Gissler M, Kajantie E. Associations between maternal antenatal corticosteroid treatment and mental and behavioral disorders in children. JAMA 2020;323:1924–33.
9. Naqvi M, Zakowski P, Glucksman L, Smithson S, Burwick RM. Tocilizumab and remdesivir in a pregnant patient with coronavirus disease 2019 (COVID-19). Obstet Gynecol 2020. [Epub ahead of print].
10. Saad AF, Chappell L, Saade GR, Pacheco LD. Corticosteroids in the management of pregnant patients with coronavirus disease (COVID-19). Obstet Gynecol 2020. [Epub ahead of print].

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