

Research Article

Six Critically Ill COVID-19 Pregnant Patients at a Detroit Hospital: A Case Series

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Abstract

Objective: Coronavirus-2019 (COVID-19) can cause viral pneumonia with rapid deterioration into acute respiratory distress syndrome requiring intubation. Pregnant patients with respiratory collapse secondary to COVID-19 present multiple management challenges. We present a case series of 6 pregnant patients with severe COVID-19 infection requiring admission into the intensive care unit. Their clinical course, medical management, and critical care interventions are described.

Methods: This is a retrospective, single-center case series of pregnant women who were infected with COVID-19 and subsequently required critical care. Inclusion criteria were pregnant patients with a positive COVID-19 nasopharyngeal swab and admission to the intensive care unit.

Results: Six pregnant women with severe COVID-19 pneumonia at Henry Ford Hospital required intensive care unit hospitalization. All women were treated with steroids. Standard treatment also included Hydroxychloroquine. There was 1 full-term delivery via cesarean section at 37 weeks and 4 days after intubation due to non-reassuring fetal heart tones remote from delivery with absent variability noted on fetal heart tracing. There were 2 preterm deliveries. One delivery was an urgent cesarean section at 36 weeks and 5 days for non-reassuring fetal heart tones in the setting of preeclampsia with severe features and worsening respiratory compromise from COVID-19 pneumonia. The other delivery was a vacuum-assisted vaginal delivery at 36 weeks and 3 days' gestation following labor induction for a persistent category two fetal heart tracing. All neonates tested negative for COVID-19. All patients survived and were discharged home.

Conclusion: This case series adds to the expanding literature describing the complex care surrounding pregnant patients with severe COVID-19 pneumonia requiring intensive care management. As the pandemic continues, we hope our experience and treatment modalities can contribute to future care of patients.

Keywords: Covid-19; Pregnancy; Delivery; Critical care; Intubation

the intensive care unit. Their clinical course, medical management, and critical care interventions are described.

Introduction

Coronavirus-2019 (COVID-19) can cause viral pneumonia with rapid deterioration into acute respiratory distress syndrome requiring intubation [1]. There have been limited case reports on critically ill pregnant patients with COVID-19. Pregnant patients with respiratory collapse secondary to COVID-19 present multiple management challenges. We present a case series of 6 pregnant patients with severe COVID-19 infection requiring admission into

Methods

This is a retrospective, single-center case series of pregnant women who were infected with COVID-19 that subsequently required critical care. The Henry Ford Health System Institutional Review Board approved this study. After approval, data was extracted from the EPIC (EPIC systems corporation, Verona WI) electronic medical record system by medical record number after the patient was admitted to the intensive care unit (ICU) at a

tertiary care center in Detroit, Michigan. Inclusion criteria were pregnant patients with a positive COVID-19 nasal swab and admission to the intensive care unit and treated between March 1, 2020 and May 1, 2020. There were no exclusion criteria. Data collected included demographics such as race, gestational age, body mass index, and comorbidities. Admission symptoms, COVID-19 exposure, chest radiography, relevant COVID-19 labs, treatment modality, and patient outcomes were all recorded.

Results

Out of 33 pregnant women who tested positive for COVID-19, 6 had severe COVID-19 pneumonia at Henry Ford Hospital requiring intensive care unit hospitalization (mean age, 30 years old; range, 18-37 years old). One woman had a history of obstructive sleep apnea, well-controlled asthma, and uncontrolled type 2 diabetes mellitus; 1 had a history of hypothyroidism and hypertriglyceridemia. Four of 6 patients were morbidly obese (mean Body Mass Index (BMI), 37.26 kg/m²; range 22.37-56.0 kg/m²). Patients' race included 4 African Americans, one Hispanic, and one Arab American individual. Gestational age at time of admission ranged from 23 weeks to 37 weeks and 2 days (Table 1).

Demographics	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Age	35 years old	37 years old	36 years old	29 years old	18 years old	25 years old
Ethnicity	African American	Arab American	African American	Hispanic	African American	African American
Gestational age at presentation	30w 4d	23w 0d	23w 0d	35w	36w5d	37w2d
Comorbidities	Obesity	Obesity, well-controlled asthma, uncontrolled type 2 diabetes mellitus, and obstructive sleep apnea	Obesity, hypothyroidism, and hyperlipidemia	Obesity	None	Prediabetes
BMI (kg/m ²)	35.9	56	41.53	42.4	25.39	22.37

w: weeks; d: days; BMI: Body Mass Index

Table 1: Patient demographics.

Key diagnostic findings included chest x-ray results indicative of viral pneumonia in all 6 patients; decreased absolute lymphocyte count in 4 of 6 patients tested; abnormal liver function tests in 2, and hypertriglyceridemia in 1. Clinical findings seen in all 6 of the patients included shortness of breath and tachycardia; 5 of 6 patients presented with tachypnea; 4 of 6 presented with hypoxia requiring immediate oxygen supplementation; and 2 of 6 patients had a known COVID-19 positive exposure (Table 2).

Clinical Presentation	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Sick contact	Yes	No	Yes	No	No	No
Symptoms	Shortness of breath	Shortness of breath	9 days of cough, myalgia's, and shortness of breath	7 days of cough, fever, and shortness of breath	7 days of shortness of breath, cough, fevers, and headache	2 days of cough, fever and shortness of breath
Vitals	Tachycardia (110 bpm), tachypnea (38 breaths/min), hypoxic (SPO ₂ 90% room air), and afebrile	Tachycardia (129 bpm), tachypnea (40 breaths/min), hypoxic (SPO ₂ 91% room air), and afebrile	Tachycardia (105 bpm), tachypnea (28 breaths/min), hypoxic (SPO ₂ 88% room air), and febrile 39.0°C	Tachycardia (140 bpm), tachypnea (51 breaths/min), hypoxic (SPO ₂ 85% on room air), and afebrile	Tachycardia (110 bpm), tachypnea (26 breaths/min), afebrile, and severe range blood pressures (170s/100s)	Tachycardia (127 bpm) and febrile (38.8°C)

Chest radiography	Interstitial opacities	Hazy/patchy, opacities in both lower lungs	Bilateral airspace densities	Bilateral pulmonary opacities in lower lungs	Diffuse focal consolidation, patchy airspace opacities and interstitial prominence	Patchy bilateral lower lung airspace opacities due to multifocal pneumonia/pneumonitis
Laboratory abnormalities		CRP 9.6 mg/dL	Elevated aspartate aminotransferase 62 International Units/L, total creatine phosphokinase 531 IU/L, CRP 14.7 mg/dL and decreased absolute lymphocytes 0.13 K/uL	Elevated procalcitonin 0.92ng/mL, CRP 6.2 mg/dL, lactate 2.3. EKG: prolonged QTc interval of 520ms		Absolute lymphocytes 0.25 K/uL

CRP: C-Reactive Protein; EKG: Electrocardiogram

Table 2: Clinical Presentation.

All women were treated with steroids, initially intravenous methylprednisolone 40 mg twice a day for 3 days. A shortage quickly developed and oral prednisone 40-80 mg twice a day for 7-10 days was substituted for 4 patients. Standard treatment also included hydroxychloroquine 400 mg oral loading dose for 2 doses and then 200 mg oral twice daily for a total of 5 days. One patient did not receive hydroxychloroquine therapy due to prolonged corrected QT interval of greater than 500 ms; one patient declined hydroxychloroquine due to concern for possible fetal effects; and 4 patients received a full course of hydroxychloroquine as described. Three of 6 patients were treated with antibiotics for superimposed bacterial pneumonia. All 6 patients received venous thromboembolism prophylaxis; 5 patients with preterm gestation received betamethasone secondary to the potential for preterm delivery (Table 3).

Treatment	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
COVID-19 treatment	IV methylprednisolone	Standard hydroxychloroquine and oral prednisone as well as zinc	Standard hydroxychloroquine and oral prednisone	Standard hydroxychloroquine and oral prednisone	Oral prednisone	Standard hydroxychloroquine and IV methylprednisolone
Superimposed bacterial pneumonia	None	Ceftriaxone	None	None	Ceftriaxone and doxycycline	Ceftriaxone and azithromycin
VTE prophylaxis	Enoxaparin 40 mg SQ daily	Heparin 5,000 U SQ every 8 hours	Enoxaparin 40 mg SQ daily	Unfractionated heparin 7,500 mg SQ every 8 hours	Heparin 5000 U SQ every 8 hours	Heparin 5000 SQ every 8 hours
Obstetrics interventions	Betamethasone 12 mg IM, 2 doses 24 hours apart	Betamethasone 12 mg IM, 2 doses 24 hours apart	Betamethasone 12 mg IM, 2 doses 24 hours apart	Betamethasone 12 mg IM, 2 doses 24 hours apart	Betamethasone 12 mg IM, magnesium sulfate IV 6 g bolus followed by 2 g/hour infusion	None
Miscellaneous	None	None	None	None	Lasix 40 mg IV every day for 3 days	None

IV: Intravenous; VTE: Venothromboembolus; SQ: Subcutaneous; IM: Intramuscular

Table 3: Treatment modalities.

All 6 patients received antepartum testing with fetal non-stress tests. The 2 patients who were admitted at 23 weeks' gestational age were monitored for 20 minutes once a day. The remaining 4 patients had fetal non-stress tests every 8 hours. As long as the tracing was reassuring, they would be taken off the monitor. Since our patients were sedated, we did not have expectations to have accelerations while monitoring.

There was 1 full-term delivery via cesarean section at 37 weeks and 4 days after intubation due to non-reassuring fetal heart tones remote from delivery with absent variability noted on fetal heart tracing. There were 2 preterm deliveries. One delivery was an urgent cesarean section at 36 weeks and 5 days for non-reassuring fetal status in the setting of preeclampsia with severe features and worsening respiratory compromise from COVID-19 pneumonia. The other preterm delivery was a vacuum-assisted vaginal delivery at 36 weeks and 3 days' gestation following labor induction for a persistent category 2 fetal heart tracing. All neonates were tested for COVID-19 via a nasopharyngeal swab at 24 hours of life and had negative test results. One infant remained hospitalized for 7 days for respiratory distress and suspicion of sepsis. The other 2 infants were discharged on hospital day 2. All patients were discharged home in stable condition (Table 4).

Hospital Course	Case 1	Case 2	Case 3	Case 4	Case 5	Case 6
Respiratory support	High flow nasal cannula	Mechanical ventilation	Mechanical ventilation	Mechanical ventilation	Mechanical ventilation	Mechanical ventilation
Days intubated	0	14	7	8	3	2
Maximum ventilatory settings	N/A	PEEP 18 cm H ₂ O, FiO ₂ 100%	PEEP 12 cm H ₂ O, FiO ₂ 100%	PEEP 10 cm H ₂ O, FiO ₂ 70%	PEEP 10 cm H ₂ O, FiO ₂ 50%	PEEP 8 cm H ₂ O, FiO ₂ 40%
Days hospitalized	9	17	11	13	8	7
Delivery	No	No	No	Yes, induction was performed at 36 weeks, 3 days' gestational age for category 2 FHT. Delivery resulted in a vacuum assisted vaginal delivery.	Yes, urgent cesarean section for severe range blood pressures refractory to interventions in setting of preeclampsia with severe features. Patient intubated prior to delivery, then transferred to intensive care unit.	Yes, urgent cesarean section for persistent category II FHT following intubation. Patient was intubated prior to delivery, and 2 prolonged decelerations were noted on FHT. Patient was found to be shivering with absent variability noted on FHT.
Outcome	Discharged on room air.	Patient left against medical advice on hospital day 17 and was on 3 L nasal cannula at that time.	Discharged on room air.	Patient diagnosed with preeclampsia without severe features. Patient discharged postpartum day 3 on room air.	Discharged postpartum day 8 on room air. Patient discharged with labetalol 800 mg TID and nifedipine XL 60 mg.	Discharged on postoperative day 4 on room air
N/A: Not Available; PEEP: Positive End-Expiratory Pressure; FHT: Fetal Heart Tracing; TID: Three Times a Day.						

Table 4: Hospital course.

Discussion

COVID-19 has been associated with acute respiratory failure leading to acute respiratory distress syndrome. While the treatment of acute respiratory distress syndrome in pregnancy generally mirrors the non-pregnant population, it remains unclear if COVID-19 pneumonia in pregnancy has a single characteristic clinical course or is more variable. Recent literature has proposed different clinical 'phenotypes' of COVID-19 pneumonia depending on infection severity, ventilatory responsiveness, and time elapsed from onset of disease [1]. Optimal intensive care interventions and ventilatory support settings require an appreciation of the potential variable clinical course of COVID-19 pneumonia, particularly in pregnancy.

The physiologic changes of pregnancy are important to account for in the setting of respiratory collapse and mechanical ventilation. The normal compensated respiratory alkalosis of pregnancy (PCO_2 28-32 mm Hg) should influence the selected respiratory rate. Studies show that 'permissive hypercapnia' (up to 50 mm Hg) has not been associated with adverse fetal effects [2]. A target PaO_2 of 70 mm Hg is appropriate during pregnancy, in contrast to 55-80 mm Hg in the non-pregnant state and facilitates maintenance of maternal oxygen saturation at greater than 95%. These targets guide ventilator FiO_2 parameters.

Fetal considerations, particularly in the perivable gestational age window, often complicate clinical decision making. The guiding principle that optimal management of maternal status is also optimal management for the fetus is too often not adhered to. We have too little experience with respiratory collapse requiring mechanical ventilation for COVID-19 pneumonia to determine if delivery (regardless of route) facilitates maternal resuscitation or hinders it.

Given these uncertainties, it is critical to have a conversation with the patient, or her surrogate decision maker (durable power of attorney) if the patient is incapacitated, regarding interventions for fetal indications, especially in patients at an early gestational age. Counseling should highlight the balance of risk and benefit for maternal status and fetal status but should accentuate the precept that a disassociation between maternal and fetal interests is rare. A multidisciplinary approach with neonatology consultation is also valuable under these critical circumstances to provide information regarding fetal prognosis and wishes for neonatal resuscitation in the perivable gestational age window. It is also important to discuss, and prepare for, the possibility of perimortem cesarean section if maternal cardiac arrest occurs.

Immediate delivery prior to intubation was only considered in one of our patients. This individual also had coexisting preeclampsia with severe features at 36 weeks and 5 days' gestation. Given the diagnosis of preeclampsia with severe features we recommended

delivery. While attempting an induction of labor the patient became unstable requiring increasing oxygen requirements with a mixed clinical picture of COVID-19 pneumonia and pulmonary edema secondary to the preeclampsia. The decision was then to deliver expeditiously via cesarean section prior to intubation and transfer to the surgical intensive care unit. Delivery prior to intubation was not considered in any of the other patients. In most cases the desaturation happened quickly and maternal stabilization took precedence. The goal of our team was to not deliver unless fetal distress was noted on antepartum testing.

Oral hydroxychloroquine has been recommended at our institution for all COVID-19 patients requiring treatment. The Maternal Fetal Medicine team counseled obstetric patients about hydroxychloroquine use in pregnancy when applicable. The American College of Obstetrics and Gynecology recommends use of hydroxychloroquine when indicated; it is a low-risk drug in pregnancy despite its ability to cross into placental circulation [3]. It is uncertain whether our institution's empiric use of hydroxychloroquine and prednisone facilitated our patients' recovery. Currently, there is no treatment for COVID-19 approved by the U.S. Food and Drug Administration. Our institution's empiric uses of hydroxychloroquine and prednisone is based upon novel studies that indicated its potential benefit as a treatment for severe COVID-19 infection [4-7].

Antivirals were not considered for any of our patients. At the time of these individuals' admissions our institution had started to offer antiviral therapy to severe COVID-19 cases, however pregnancy was made an exclusion criteria. Currently the diagnosis of pregnancy is no longer an exclusion criteria and if a pregnant patient met criteria for antiviral treatment they would be treated accordingly.

The use of proning appeared crucial in 2 of our patients. Placing an individual in the prone position allows for recruitment of alveoli and corrects ventilation perfusion mismatch, which occurs in acute respiratory distress syndrome [8]. Patients selected for this treatment continued to be hypoxic despite optimizing mechanical ventilation in the supine position. The criteria for pregnant patients to be placed in prone positioning are the same as non-pregnant individuals [9]. Clinicians previously were hesitant to place pregnant patients in the prone position because of uncertainty regarding fetal response. During the 2009 influenza pandemic, however, many pregnant patients underwent prone ventilation as rescue therapy. Case reports described successful proning in pregnancy without apparent adverse maternal or fetal effects [10].

Only one patient was transferred to an outside facility for potential nitric oxide treatment and Extracorporeal Membrane Oxygenation (ECMO). This individual continued to worsen and deoxygenate every time she was placed in the supine position.

After review of records and discussion with providers from the outside facility, the patient never required nitric oxide treatment nor ECMO. Clinical improvement occurred without any change in treatment.

It is important to notice that many of the risk factors that increase the risk of severe COVID-19 infection in the non-pregnant patient are mirrored in the pregnant patient. Most critically ill patients in this case series were obese and African American. Review of the demographics of patients hospitalized with COVID-19 revealed that the African American population is disproportionately affected [11,12]. Additionally, studies also illustrate an inverse correlation between age and BMI, indicating that younger patients with severe disease were more likely to be obese [13]. These characteristics are imperative to identify those at high risk for severe disease given the potential for rapid clinical deterioration and need for mechanical ventilation.

In conclusion, this case series adds to the expanding literature describing the complex care surrounding pregnant patients with severe COVID-19 pneumonia requiring intensive care management. As the pandemic continues, we hope that our experience helps to inform the care of these critically ill patients.

Authors' Data Availability Statement

All data collected has been shared in this project within the tables. Data became available from March to May of 2020, we collected data as patients were admitted.

Ethical Statement

No ethical board was needed for this study. The study was approved by the Henry Ford Health System Institutional Review Board.

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References

1. Gattinoni L, Chiumello D, Caironi P, Busana M, Romitti F, et al. (2020) COVID-19 pneumonia: different respiratory treatments for different phenotypes? *Intensive Care Med* 46: 1099-1102.
2. Ma J, Ye H (2016) Effects of permissive hypercapnia on pulmonary and neurodevelopmental sequelae in extremely low birth weight infants: a meta-analysis. *Springerplus* 5: 764.
3. Sperber K, Hom C, Chao CP, Shapiro D, Ash J (2009) Systematic review of hydroxychloroquine use in pregnant patients with autoimmune diseases. *Pediatr Rheumatol Online J* 7: 9.
4. Wang M, Cao R, Zhang L, Yang X, Liu J, et al. (2020) Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) *in vitro*. *Cell Res* 30: 269-271.
5. Gao J, Tian Z, Yang X (2020) Breakthrough: chloroquine phosphate has shown apparent efficacy in treatment of COVID-19 associated pneumonia in clinical studies. *Biosci Trends* 14: 72-73.
6. Colson P, Rolain JM, Lagier JC, Brouqui P, Raoult D (2020) Chloroquine and hydroxychloroquine as available weapons to fight COVID-19. *Int J Antimicrob Agents* 55: 105932.
7. Russell B, Moss C, George G, Santaolalla A, Cope A, et al. (2020) Associations between immune-suppressive and stimulating drugs and novel COVID-19-a systematic review of current evidence. *Ecancermedicalscience* 14: 1022.
8. Corneji RA, Diaz JC, Tobar EA, Bruhn AR, Ramos CA, et al. (2013) Effect of prone positioning on lung protection in patient with acute respiratory distress syndrome. *Am J Respir Crit Care Med* 188: 440-448.
9. Guerin C, Reignier J, Richard JC, Beuret P, Gacouin A, et al. (2013) Prone positioning in severe acute respiratory distress syndrome. *N Engl J Med* 368: 2159-2168.
10. Samanta S, Samanta S, Wig J, Baronia AK (2014) How safe is the prone position in acute respiratory distress syndrome at late pregnancy? *Am J Emerg Med* 32: 687.e1-3.
11. Garg S, Kim L, Whitaker M, O'Halloran A, Cummings C, et al. (2020) Hospitalization rates and characteristics of patients hospitalized with laboratory-confirmed coronavirus disease 2019 - COVID-NET, 14 states, March 1-30, 2020. *MMWR Morb Mortal Wkly Rep* 69: 458-464.
12. Gold JA, Wong KK, Szablewski CM, Patel PR, Rossow J, et al. (2020) Characteristics and clinical outcomes of adult patients hospitalized with COVID-19 - Georgia, March 2020. *MMWR Morb Mortal Wkly Rep* 69: 545-550.
13. Kass DA, Duggal P, Cingolani O (2020) Obesity could shift severe COVID-19 disease to younger ages. *Lancet* 395: 1544-1545.