

1 **Care of critically ill pregnant patients with COVID-19: a case series**

2

3 Adi HIRSHBERG MD<sup>1</sup>, Adina R. KERN-GOLDBERGER MD MPH<sup>1</sup>, Lisa D. LEVINE  
4 MD MSCE<sup>1</sup>, Rebecca PIERCE-WILLIAMS DO,<sup>3</sup> William R. SHORT MD MPH,<sup>2</sup>  
5 Samuel PARRY MD,<sup>1</sup> Vincenzo BERGHELLA MD,<sup>3</sup> Jourdan E. TRIEBWASSER MD  
6 MA,<sup>1</sup> Sindhu K. SRINIVAS MD MSCE<sup>1</sup>

7

8 <sup>1</sup>Department of Obstetrics & Gynecology, Maternal Child Health Research Center,  
9 University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania,  
10 USA; <sup>2</sup>Department of Internal Medicine, Division of Infectious Diseases, Hospital of the  
11 University of Pennsylvania, Philadelphia, Pennsylvania, USA; <sup>3</sup>Department of Obstetrics  
12 and Gynecology, Division of Maternal-Fetal Medicine, Sidney Kimmel Medical College  
13 of Thomas Jefferson University, Philadelphia, Pennsylvania, USA

14

15 Corresponding author:

16 Adi Hirshberg, MD

17 Hospital of the University of Pennsylvania Division of Maternal-Fetal Medicine

18 3400 Spruce St, 2<sup>nd</sup> Floor

19 Philadelphia, PA 19104

20 [Adi.Hirshberg@penntermedicine.upenn.edu](mailto:Adi.Hirshberg@penntermedicine.upenn.edu)

21 Disclosure: The authors report no conflict of interest.

22 Word count: Manuscript – 1485

23

24 Key words/phrases:

25 Coronavirus, COVID-19, critical care, intensive care unit, maternal morbidity, maternal

26 mortality, mechanical ventilation

27 **Objective:**

28 The global pandemic from novel coronavirus disease, COVID-19, is spreading rapidly  
29 throughout the United States and major metropolitan areas, such as Philadelphia, are  
30 seeing dramatically rising infection rates. Though pregnant women are not more severely  
31 affected than non-pregnant patients,<sup>1</sup> a portion of obstetric patients will nevertheless  
32 require intensive care similar to their non-pregnant counterparts. Here we review five  
33 cases of critical COVID-19 disease<sup>2</sup> during pregnancy as well as general management  
34 principles.

35

36 **Study design:**

37 This is a retrospective, multi-center case series of symptomatic pregnant women with  
38 positive SARS-CoV-2 testing requiring critical care.

39

40 **Results:**

41 The clinical courses of five women with critical COVID-19 disease, all requiring  
42 mechanical ventilation, are described below and summarized in Table 1. SARS-CoV-2  
43 testing was done via RT-PCR of nasopharyngeal swab unless otherwise specified.

44

45 Case 1: A 28 year old G1P0 with chronic kidney disease and hypertension developed  
46 worsening dyspnea on the sixth day of outpatient monitoring of confirmed COVID-19  
47 illness. She presented to the hospital at 31 weeks' gestation with fever and dyspnea.  
48 Chest imaging demonstrated multifocal pneumonia and she required oxygen (O<sub>2</sub>) at 2  
49 L/min to maintain saturation >95%. On hospital day (HD) 3, she had worsening hypoxia

50 to 80%, requiring 6 L/min O<sub>2</sub>. Antenatal corticosteroids were administered, and given  
51 concern for further decompensation, the decision was made to proceed with intubation  
52 and delivery under controlled settings. She had an uncomplicated cesarean delivery and  
53 recovered in the intensive care unit (ICU) with acute respiratory distress syndrome  
54 (ARDS). She completed courses of hydroxychloroquine and remdesivir and was  
55 ultimately extubated on postoperative day 17 after a slow wean. She was discharged four  
56 days later with two consecutive negative SARS-CoV-2 tests prior to discharge.

57

58 Case 2: A 33 year old G6P5005 with mild asthma presented at 26 weeks' gestation with  
59 worsening fevers and respiratory symptoms for ten days. Her O<sub>2</sub> saturation was 83%  
60 requiring O<sub>2</sub> at 5 L/min and chest imaging demonstrated multifocal pneumonia. SARS-  
61 CoV-2 testing resulted positive. She was transferred to the ICU with increasing oxygen  
62 requirement and intubated several hours later. Given early gestational age and maternal  
63 acuity, continuous fetal heart monitoring was not initiated. Antenatal corticosteroids were  
64 deferred due to concern for worsening viral shedding. Her course has been complicated  
65 by ARDS, septic shock, and inferior vena cava thrombus on therapeutic anticoagulation.  
66 She has completed courses of hydroxychloroquine and remdesivir, as well as antibiotics  
67 for superimposed bacterial pneumonia. She has required vasopressor support and stress  
68 dose steroids for sepsis (using dexamethasone for adjunctive fetal benefit). She was  
69 placed in prone position for worsening hypoxemic respiratory failure and acidosis on HD  
70 3 and 8 with improvement and was cannulated for extracorporeal membrane oxygenation  
71 (ECMO) if required for further deterioration. She remains critically ill, although  
72 ventilatory support has been weaned to tracheostomy collar. Daily fetal heart tone checks

73 with intermittent biophysical profiles have been reassuring. Delivery is being considered,  
74 although may be deferred due to significant maternal improvements and early gestational  
75 age.

76

77 Case 3: A 39 year old G4P3003 with hypertension, obstructive sleep apnea, and insulin-  
78 dependent diabetes presented at 28 weeks' gestation with two weeks of fever, cough, and  
79 worsening dyspnea. She was febrile, tachypneic, and hypoxic to 86% on arrival with  
80 positive SARS-CoV-2 testing and multifocal pneumonia on chest imaging. She was  
81 transferred to the ICU for worsening dyspnea, intubated, and transferred to our tertiary  
82 care facility for ARDS. She received antibiotics for superimposed bacterial pneumonia,  
83 hydroxychloroquine, remdesivir, and therapeutic anticoagulation. She was placed in  
84 prone position on HD 7 for worsening hypoxemic respiratory failure, at which point  
85 antenatal corticosteroids were administered. Fetal evaluation with daily heart tones was  
86 normal. She underwent uncomplicated repeat cesarean delivery on HD 15 at 30 weeks  
87 and 2 days in the setting of persistent, but stable, critical illness requiring mechanical  
88 ventilation. She was extubated on postoperative day 5 (HD 20) and transitioned to high  
89 flow nasal cannula.

90

91 Case 4: A 27 year old G3P0202 presented at 30 weeks of gestation with four days of  
92 myalgias, fatigue, productive cough, and fever. She was tachycardic (>130 beats per  
93 minute) on arrival with chest imaging demonstrating multifocal pneumonia. SARS-CoV-  
94 2 testing was positive. She was started on hydroxychloroquine and transferred to the ICU  
95 for impending respiratory failure with intubation two days later, at which time she

96 received betamethasone and was started on remdesivir. Daily fetal heart tones were  
97 normal. Blood cultures grew *Proteus mirabilis* and she received broad spectrum  
98 antibiotics for superimposed pneumonia. Ventilatory settings could not be weaned  
99 significantly and arterial blood gas demonstrated persistent acidemia. She underwent  
100 uncomplicated primary cesarean delivery on HD 9 due to declining respiratory status.  
101 She was extubated on HD 15 and discharged home on room air five days later.

102

103 Case 5: A 35 year old G4P2012 presented at 25 weeks' gestation with nine days of fever,  
104 cough, and progressive dyspnea. She was febrile and tachypneic with imaging  
105 demonstrating multifocal pneumonia. She was admitted for suspected COVID-19  
106 pneumonia, treated with hydroxychloroquine and antibiotics, and transferred to the ICU  
107 for impending respiratory failure and intubation. Initial SARS-CoV-2 testing resulted  
108 negative twice, though she remained critically ill requiring vasopressor support. Empiric  
109 oseltamivir was initiated and due to increasing likelihood of delivery, antenatal  
110 corticosteroids were administered. A third inpatient SARS-CoV-2 test (from tracheal  
111 aspirate) resulted positive and remdesivir was started. She was successfully extubated on  
112 HD 8, weaned to room air on HD 11, and discharged two days later with close outpatient  
113 follow up.

114

115

## 116 **Discussion**

117 The volume of pregnant patients requiring critical care thus far appears to be higher in  
118 Philadelphia hospitals than in other published accounts. A report early in the pandemic  
119 from Singapore chronicled 55 total cases in the literature of pregnant patients with

120 COVID-19 disease, with no instances of mortality and only one of mechanical  
121 ventilation,<sup>3</sup> while other reviews have uncovered only three additional cases of critical  
122 illness in pregnancy.<sup>4,5</sup> The early American experience with COVID-19 in pregnancy has  
123 been characterized by a case series in New York, reporting a total of two critical cases,  
124 both postpartum.<sup>1</sup>

125

126 While the majority of patients, including pregnant women, can be managed on an  
127 outpatient basis, our experience suggests that obstetric patients with COVID-19, both  
128 with and without comorbidities, can have severe disease in the antepartum period.  
129 Potential worsening of respiratory symptoms up to 14 days after onset can occur in  
130 pregnant women, as evidenced by intubation timing ranging from 7-14 days from  
131 symptom onset in our cases.

132

133 Critical care management of the COVID-19 obstetric patient should generally be guided  
134 by the same principles as for the non-pregnant adult population and is contingent upon  
135 effective multidisciplinary care. The National Institutes of Health published updated  
136 treatment guidelines for COVID-19, including special considerations for pregnant  
137 women.<sup>6</sup> Important considerations include early detection of severe illness and  
138 individualized decisions surrounding use of adjunctive medications, as pregnant women  
139 are not included in many current clinical trials exploring treatment options for COVID-  
140 19. Various oxygen delivery methods, including high flow nasal cannula, noninvasive  
141 positive pressure ventilation, and endotracheal intubation, can all be utilized safely in  
142 pregnancy. Prone ventilation, while technically challenging in later pregnancy, can be

143 implemented with appropriate support for the gravid abdomen, even in the third trimester.  
144 Venovenous extracorporeal membrane oxygenation (ECMO) has been used in non-  
145 pregnant adults with COVID-19. Although not used in our cases, ECMO has been  
146 utilized in pregnancy to support oxygenation for H1N1 influenza and refractory ARDS  
147 and should be considered an alternative rescue strategy for COVID-19. With recent data  
148 suggesting high incidence of thrombotic complications in ICU patients with COVID-19  
149 infection and the known hypercoagulable state of pregnancy, high-prophylactic and  
150 therapeutic dosing of anticoagulation in critically ill pregnant patients should be strongly  
151 considered as well.

152

153 Unique to pregnancy are decisions surrounding fetal monitoring, administration of  
154 antenatal corticosteroids, and delivery, all of which should be individualized, as there is  
155 no evidence yet to guide specific management in this particular disease. Nonetheless,  
156 fetal monitoring in COVID-19 pregnant patients should follow the same considerations  
157 as in other critical illness and should be considered only after fetal viability, when  
158 delivery would not compromise maternal health, or as a noninvasive measure of maternal  
159 status. Although prolonged exposure to high-dose corticosteroids is theoretically  
160 associated with adverse patient outcomes from COVID-19 based on early reports,  
161 corticosteroid courses for fetal lung maturity are short and should be administered with a  
162 high likelihood of early preterm delivery. For intubated patients with COVID-19, timing  
163 of delivery must balance maternal and neonatal risk and benefit, with delivery considered  
164 a potential tool to improve ventilation due to physiologic changes associated with  
165 pregnancy.

166

167 At present, limited data are available on critically ill pregnant women with COVID-19, as  
168 evidenced by varying management of our five cases. Clinical recommendations will  
169 surely continue to evolve as we learn more about this disease in pregnant and non-  
170 pregnant adults. As the pandemic unfolds and more microbiologic, pharmacologic, and  
171 clinical information about COVID-19 comes to light, it is important to consider the  
172 unique needs of critically ill pregnant patients in formulating specific guidelines and  
173 treatment plans.

174

175

176

177 References:

- 178 1. Breslin N BC, Gyamfi-Bannerman C, et al. . COVID-19 infection among  
179 asymptomatic and symptomatic pregnant women: Two weeks of confirmed  
180 presentations to an affiliated pair of New York City hospitals. *American Journal  
181 of Obstetrics & Gynecology MFM*. 2020.
- 182 2. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the  
183 Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report  
184 of 72314 Cases From the Chinese Center for Disease Control and Prevention.  
185 *JAMA*. 2020.
- 186 3. Dashraath P, Jing Lin Jeslyn W, Mei Xian Karen L, et al. Coronavirus Disease  
187 2019 (COVID-19) Pandemic and Pregnancy. *Am J Obstet Gynecol*. 2020.
- 188 4. Mullins E, Evans D, Viner RM, O'Brien P, Morris E. Coronavirus in pregnancy  
189 and delivery: rapid review. *Ultrasound Obstet Gynecol*. 2020.
- 190 5. Zaigham M, Andersson O. Maternal and Perinatal Outcomes with COVID-19: a  
191 systematic review of 108 pregnancies. *Acta Obstet Gynecol Scand*. 2020.
- 192 6. (NIH) NIOH. COVID-19 Treatment Guidelines.  
193 <https://covid19treatmentguidelines.nih.gov/introduction/>. Published 2020.  
194 Accessed.
- 195
- 196

197 Table 1:

	Case 1	Case 2	Case 3	Case 4	Case 5
Age (years)	29	33	39	27	35
Race/ Ethnicity	Asian	Caucasian	Hispanic	Black	Caucasian
BMI kg/m <sup>2</sup>	24.6	27.8	42.5	34.7	32
Admission GA	31w2d	26w0d	28w3d	30w3d	25w2d
Chief Complaint	Fever, dyspnea	Fever, cough, dyspnea	Fever, cough	Fever, cough, dyspnea	Fatigue, cough, rhinorrhea, headache, fever, dyspnea
Medical comorbidities	Chronic kidney disease (C1q nephropathy), hypertension (on ACE inhibitor prior to pregnancy)	Mild, intermittent asthma	Obesity, hypertension, insulin- dependent diabetes	Hypertension (no medication)	obesity
Notable admission laboratory results	Elevated creatinine (patient baseline)	None	Elevated CRP and lactic Acid	Thrombocytopenia	Elevated amniotransferases
Number of days from symptom onset to intubation	9	10	14	7	9
Adjunctive therapy	HCQ, remdesivir	HCQ, remdesivir	HCQ, remdesivir	HCQ remdesivir	HCQ, remdesivir
Antenatal steroids and hospital day administered	Betamethasone, HD 3	Dexamethasone, HD 3,4	Betamethasone, HD 7,8	Betamethasone, HD 3,4	Betamethasone, HD 1,2
Additional clinical details	Intubated at 31w4d, extubation HD 16	Intubated at 26w1d, Prone ventilation	Intubated at 28w3d, prone ventilation	Intubated at 30w5d, bacteremia, extubated HD	Intubated at 25w2d, extubation HD 6 with

	with reintubation, final extubation HD 20, discharged HD 24	(X 2), tracheostomy 29w1d, suspected inferior vena cava thrombus	(X 1), extubated on HD 19	15, discharged HD 20	reintubation, final extubation HD 8, discharged HD 13
Delivery	Yes	No	Yes	Yes	No
Indication	Maternal		Maternal	Maternal	
Gestational age	31w4d		30w2d	31w3d	
Mode	Cesarean		Cesarean	Cesarean	
Neonatal birthweight (grams)	1500		2110	1845	
Apgars	9,9		8,9	2,4,4	
Neonatal SARS-CoV-2 PCR result at 24 HOL	negative		negative	negative	

198 BMI – body mass index, GA – gestational age, HD - Hospital day , HOL- hours of life