Case Report

A Postpartum Death Due to Coronavirus Disease 2019 (COVID-19) in the United States

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BACKGROUND: Limited U.S. reports of pregnant women with coronavirus disease 2019 (COVID-19) infection describe a few critical cases and no maternal mortality.

CASE: A 36-year-old patient at 37 weeks of gestation presented with shortness of breath, fever, cough, and sore throat for 1 week. Within 3 hours of admission, she experienced respiratory distress, required intubation, and underwent cesarean delivery and transfer to the intensive care unit. She subsequently decompensated, with multiorgan failure, sepsis, and cardiopulmonary arrest within 36 hours, despite aggressive supportive care and investigational therapies.

CONCLUSION: A pregnant patient with COVID-19 infection can experience a rapid onset of critical complications that may prove fatal, despite an indolent presentation. The pathogenesis leading to rapid deterioration is unknown.

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Teaching Points

1. The initial presentation of pregnant patients with COVID-19 infection may not be indicative of the ultimate severity of disease.
2. The pathophysiology of progression toward severe and critical illness in COVID-19 infection in pregnancy requires further investigation.
3. The current treatment for COVID-19 infection in pregnancy is supportive. Investigational treatments may be considered in severe cases.

Our understanding and management of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or coronavirus disease 2019 (COVID-19) infection in pregnancy is continually being updated as more is learned about the disease.[1–3] A recent report from affiliated academic hospitals in the borough of Manhattan, New York, suggests that overall clinical outcomes in pregnant patients do not differ from those in nonpregnant patients.[2] Eighty-six percent of their patients with confirmed infection had mild disease, fewer than 10% had severe disease, and fewer than 5% (two patients) were admitted to the intensive care unit (ICU) with critical illness. One patient remained admitted and intubated at the time of the report's publication; the other had been discharged home.

In the absence of effective treatments, the mainstay of clinical management of COVID-19 infection in pregnancy is supportive care.[3] Investigational trials are ongoing for medications for use in severe or critical COVID-19 infections and include antiinflammatory medications, such as anakinra[4] and hydroxychloroquine,[5] to reduce acute tissue injury or antiviral medications, such as remdesivir or lopinavir–ritonavir, to inhibit SARS-CoV-2 viral replication.[6] With the exponential rise of new COVID-19 cases and the potential for severe morbidity or mortality, further understanding of the pathophysiology is required. We report a case of postpartum maternal mortality in the borough of Queens, New York, the epicenter of COVID-19 infection within New York City. Clinical and laboratory findings demonstrate the rapid progression of the patient's disease, which resulted in postpartum mortality within 36 hours of admission, despite aggressive supportive care and administration of multiple investigational drugs. The patient's family provided written informed consent for publication of this report and accompanying images.

CASE

The patient was a 36-year-old woman who presented at 37 weeks of gestation with symptoms of subjective fevers, dry cough, and a sore throat for 1 week. Decreased fetal movement and worsening shortness of breath for the previous 3 days prompted a hospital evaluation. She reported no recent sick contacts or travel outside the

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United States. Her past obstetric history was uncomplicated, with three full-term vaginal deliveries and a first-trimester spontaneous abortion. She was obese (body mass index [BMI, calculated as weight in kilograms divided by height in meters squared] 30) and had a history of appendectomy and abdominoplasty but no other significant medical history.

She presented to the hospital primarily due to worsening shortness of breath. On arrival, her symptoms prompted concern for COVID-19 infection. Hence, she was given a surgical mask, and COVID-19 Person Under Investigation precautions were initiated per Centers for Disease Control and Prevention guidelines.[1] This included airborne, contact, and droplet precautions, with all staff caring for the patient using appropriate personal protective equipment. Nasopharyngeal testing for COVID-19 infection was performed. However, at the time of presentation, no rapid testing was available. The positive polymerase chain reaction test results would not be known until after the patient's death 36 hours after admission. After an initial 2-hour emergency department isolation and assessment in a specially designated area for Person Under Investigation patients, she was transferred to the obstetrics unit for further evaluation, with appropriate precautions. All patient care rooms on the labor and delivery unit are single occupancy; a select few have been designated for COVID-19 isolation, with personal protective equipment available as needed. Consultations with maternal-fetal medicine, infectious disease, and critical care specialists were obtained before transfer.

On arrival to the obstetric floor, the patient's temperature was 98.0°F, pulse 100 beats per minute, blood pressure 127/66 mm Hg, respiratory rate 36 breaths per minute, and oxygen saturation 90–92% despite 15 L of oxygen by a non-rebreather mask. Breath sounds were clear bilaterally, without wheeze or rhonchi. Chest radiographs from the emergency department showed moderate air space opacities and focal consolidations suggesting pneumonia (Fig. 1A). Laboratory tests (Table 1) included a normal admission white blood cell count; however, a mild leukocytosis later developed, with an elevation in the erythrocyte sedimentation rate. A nonstress test was reactive.

One hour after admission to the obstetric floor, the patient's respiratory status acutely deteriorated. An acute change in clinical status was demonstrated by worsening tachypnea (respiratory rate 45 breaths per minute), hypoxia (77% oxygen saturation), and increased work of breathing despite high-flow oxygen (15 L) by a non-rebreather mask. She was intubated immediately thereafter. To further improve maternal ventilation, a cesarean delivery was performed to reduce intra-abdominal pressure. The cesarean delivery itself was uncomplicated, with delivery of a 2,747-g female neonate with Apgar scores of 5 and 9 at 1 and 5 minutes. Fetal cord arterial gases were not requested because the fetal heart rate tracing was reactive before delivery and the 5-minute Apgar score was 9. There was no evidence of neonatal or intra-amniotic infection. The newborn was assessed in the radiant warmer away from the mother owing to the mother's Person Under Investigation status. After assessment and clearance by the pediatricians, the newborn was transferred to the nursery in stable condition. Polymerase chain reaction testing of the neonate was subsequently negative. The placenta was evaluated by pathologists and demonstrated no histopathologic findings.

After delivery, the patient was transferred to the ICU for continued ventilation and supportive care. Anakinra, hydroxychloroquine, and azithromycin were initiated simultaneously by the infectious disease consultants owing to the severity of the patient's overall condition. Anakinra, an interleukin (IL)-1 receptor antagonist typically used in rheumatoid arthritis, was given as an investigational drug to potentially reduce mortality from hyperinflammation and cytokine storm in severe COVID-19 infections.[4] An investigational combination of hydroxychloroquine, a common antimalarial and antiinflammatory medication, and azithromycin, a common macrolide antibiotic, was also given to potentially decrease the SARS-CoV-2 viral load and increase elimination of infection.[5] The critical care physicians initiated piperacillin–tazobactam and vancomycin antibiotics for presumed sepsis on admission. Vitamin C 1,500 mg every 6 hours was also ordered to prevent oxidative tissue damage.

Subcutaneous heparin was started for thromboprophylaxis on arrival to the ICU. However, approximately 17 hours after delivery, the patient demonstrated evidence of acute renal failure, with progressive hyperkalemia, worsening metabolic acidosis (Table 1), and development of anuria. Arterial blood gasses confirmed worsening and severe metabolic acidosis. A follow-up chest radiograph demonstrated increases in lung consolidation and opacities (Fig. 1B). IL-2 and IL-6 levels were each obtained once during the ICU admission. Both values were notably elevated as the patient continued to decompensate, with findings of septic shock including marked hypotension, tachycardia, tachypnea, and fever. Elevation of interleukins also suggested the possibility of cytokine storm and possible benefit for anakinra[4] therapy as previously described. The D-dimer level was 28-fold greater than the upper limit of normal, suggesting a developing coagulopathy and increased risk of mortality.[7] Liver function tests and troponin and lactate levels also rose significantly, signifying multiple organ failure. Despite aggressive supportive measures including ventilation, multiple pressors, and the investigational drug therapies, the patient ultimately had a cardiopulmonary arrest and died within 36 hours of initial presentation.

DISCUSSION

This case involving a pregnant woman with COVID-19 infection demonstrates a rapid and severe onset of respiratory distress, multiple organ failure, and cardiopulmonary arrest, which ultimately led to death. Initially, the patient's oxygenation was suboptimal despite a non-rebreather mask with high-flow oxygen.

Table 1. Laboratory Results During the Patient's 36-Hour Hospitalization

Variable	Reference Range	ED Initial Presentation	ICU 4 h After Admission, 1 h Postpartum	ICU 16 h After Admission, 13 h Postpartum	ICU 19 h After Admission, 16 h Postpartum	ICU 23 h After Admission, 20 h Postpartum	ICU 27 h After Admission, 24 h Postpartum
IL-2 receptor CD25 soluble (pg/mL)	Less than 12.0				1,552*		
IL-6 (pg/mL)	Less than 5.0				79*		
Erythrocyte sedimentation rate (mm/h)	0.0–29.0	85*	79*				
Troponin I (ng/mL)	Less than 0.045		0.96*		3.12*		
D-dimer (ng/mL)	Less than 229.0	6,512*					
PT (sec)	10.0–12.9	10.6	10.9				
INR (ratio)	0.88–1.16	0.94	0.97				
PTT (seconds)	60.0–70.0	30.1†	30.6†				
pH	7.35–7.45				7.34†	7.2†	7.0†
pCO_2 (mm Hg)	32.0–46.0				39	36	48*
PO_2 (mm Hg)	74.0–108.0				58†	59†	80
HCO3 (mmol/L)	23.0–27.0				21†	14†	11†
Base excess (mmol/L)	−2.0–2.0				−4.2†	−13†	−19†
O_2 saturation (%)	Greater than 95%				90†	84†	89†
FiO_2	21–100				70	100	100
Lactate dehydrogenase (units/L)	140.0–280.0	568*	616*				
Lactic acid (mmol/L)	0.7–2.0		5*		4*		
Sodium (mmol/L)	135.0–145.0	137	139	137	140	140	
Potassium (mmol/L)	3.5–5.3	4.2	3.6	7.2*	5.5*	5	
Chloride (mmol/L)	96.0–108.0	110*	109*	108	109*	110*	
Carbon dioxide (mmol/L)	22.0–31.0	19†	17†	18†	22	15†	
Blood urea nitrogen (mg/dL)	7.0–18.0	14	13	20*	23*	25*	
Creatinine (mg/dL)	0.50–1.3	1.16	1.41*	2.08*	2.34*	2.84*	
Glucose (mg/dL)	70.0–99.0	80	126*	40†	68†	105*	
Anion gap (mmol/L)	8.0–16.0	8	13	11	9	15	
Calcium, total serum (mg/dL)	8.4–10.5	8.2†	7.9†	7.2†	6.5†	6.4†	
Glomerular filtration rate (mL/min)	Greater than 60	61	48†	30†	26†	20†	
Total protein, total serum (g/dL)	6.0–8.3	7.3	7.1	6.1	4.7†		
Albumin (g/dL)	3.5–5.0	1.9†	1.7†	1.5†	1.2†		
Aspartate aminotransferase (units/L)	10.0–40.0	98*	99*	565*	1,317*		
Alanine aminotransferase (units/L)	10.0–60.0	42	38	147*	314*		
Alkaline phosphatase (units/L)	40.0–120.0	225*	240*	232*	194*		
White blood cell count (per mm^3)	3.80–10.5	5.83	11.5*		9.81		
Hemoglobin (g/dL)	11.5–15.5	12.3	12.4		11.4†		
Hematocrit (%)	34.5–45.0	36.8	39		35.1		
Platelet count (K/uL)	150.0–400.0	199	179		40†		

ED, emergency department; ICU, intensive care unit; IL, interleukin; PT, prothrombin time; INR, international normalized ratio; PTT, partial thromboplastin time.

* The value for the patient was above normal range.

† The value for the patient was below range.

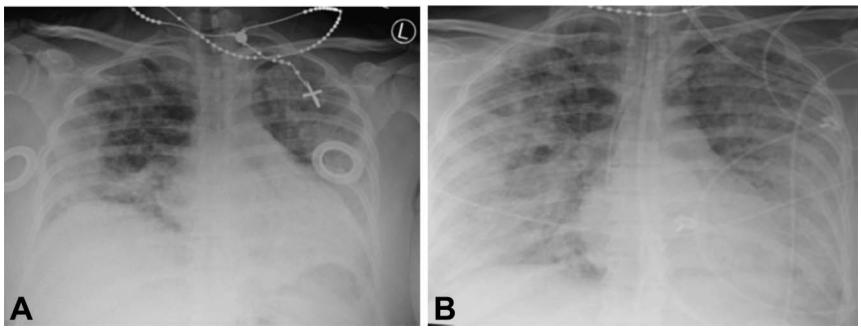

Fig. 1. A. Chest radiograph obtained during the initial emergency department evaluation. **B.** Postpartum chest radiograph on intensive care unit admission.

Vallejo. Postpartum Mortality Due to COVID-19. Obstet Gynecol 2020.

Outside of pregnancy, placement of the patient in a prone position may open dead air spaces within the lung, thereby improving oxygenation. This may limit the use of a non-rebreather mask, which could contribute to aerosolization of viral particles. However, this prone maneuver is contraindicated in a 37-week term pregnant patient. Achieving adequate ventilation in the term pregnant patient may require delivery to reduce intra-abdominal pressure and upward displacement of the diaphragm. Because this patient experienced acute respiratory distress, intubation was performed initially, followed by cesarean delivery; the decision for cesarean delivery should be made on an individualized basis and not simply because of intubation and mechanical ventilation.

In the absence of proven therapies for COVID-19 infection, supportive respiratory care is initiated,[3] and investigational drugs may be considered for more serious cases.[4–8] However, all purported medications for improving outcomes in COVID-19 infection, including antiinflammatory drugs such as anakinra[4] and hydroxychloroquine–azithromycin[5] and antiviral therapies such as remdesivir and lopinavir–ritonavir[6] combination, are currently under investigation, and their benefit is unclear. Recent data from these limited studies do not include outcomes for pregnant patients. Acute microangiopathic events resulting in hypoxic tissue injury may be marked by D-dimer elevation.[7] Evidence of this process is suggested by the preliminary autopsy, which showed bilateral thromboses in the maternal gonadal veins and numerous small thromboses within thin-walled uterine vessels. No pulmonary emboli or deep venous thrombi were seen. On the other hand, cytokine storm resulting in inflammatory tissue injury may be evident with significantly increased interleukin values.[8] Together, these phenomena may ultimately result in a rapid onset of multiple organ failure just before maternal death. The exact mechanisms of these processes require further investigation.

REFERENCES

1. Centers for Disease Control and Prevention. Interim infection prevention and control recommendations for patients with suspected or confirmed coronavirus disease 2019 (COVID-19) in healthcare settings. Available at: https://www.cdc.gov/coronavirus/2019-ncov/hcp/infection-control-recommendations.html. Retrieved April 16, 2020.
2. Breslin N, Baptiste C, Gyamfi-Bannerman C, Miller R, Martinez R, Bernstein K, et al. COVID-19 infection among asymptomatic and symptomatic pregnant women: two weeks of confirmed presentations to an affiliated pair of New York City hospitals. Am J Obstet Gynecol MFM 2020 [Epub ahead of print].
3. Poon LC, Yang H, Kapur A, Melamed N, Dao B, Divakar H, et al. Global interim guidance on coronavirus disease 2019 (COVID-19) during pregnancy and puerperium from FIGO and allied partners: information for healthcare professionals Int J Gynaecol Obstet 2020 [Epub ahead of print].
4. Monteagudo A, Boothby A, Gertner E. Continuous intravenous anakinra infusion to calm the cytokine storm in macrophage activation syndrome. ACR Open Rheumatol 2020 [Epub ahead of print].
5. Gautret P, Lagier JC, Parola P, Hoang VT, Meddeb L, Mailhe M, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. Int J Antimicrob Agents 2020 [Epub ahead of print].
6. Sanders JM, Monogue ML, Jodlowski TZ, Cutrell JB. Pharmacologic treatments for coronavirus disease 2019 (COVID-19): A review. JAMA 2020 [Epub ahead of print].
7. Dolhnikoff M, Duarte-Neto AN, de Almeida Monteiro RA, Ferraz da Silva LF, Pierre de Oliveira E, Nascimento Saldiva PH, et al. Pathological evidence of pulmonary thrombotic phenomena in severe COVID-19. J Thromb Haemost 2020 [Epub ahead of print].
8. Henderson LA, Canna SW, Schulert GS, Volpi S, Lee PY, Kernan KF, et al. On the alert for cytokine storm: immunopathology in COVID-19. Arthritis Rheumatol 2020 [Epub ahead of print].

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