Severe Maternal Morbidity and Neonatal Mortality After COVID-19 Infection: Case Report

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ABSTRACT

Background: Maternal coagulopathy and adverse fetal effects are both possible results of COVID-19 infection during pregnancy. This case demonstrates the potentially fatal outcomes when both occur simultaneously.

Case Presentation: A 39-year-old multiparous woman at 31 weeks gestation presented with mild COVID-19 symptoms and decreased fetal movement. Evaluation included a biophysical profile with 2/8 scoring and fetal heart rate tracing that developed a terminal bradycardia. She underwent an emergent cesarean delivery that was complicated by disseminated intravascular coagulation (fibrinogen <60mg/dL, platelets 34, international normalized ratio [INR] 2.1) and maternal hemorrhage requiring massive transfusion. The neonate ultimately required prolonged resuscitation with Apgar scores of 0/0/0 at 1, 5, and 10 minutes and passed away on day 6 of life.

Conclusions: Even in the absence of severe symptoms, maternal COVID-19 infection during pregnancy can cause a maternal systemic and placental reaction that can lead to serious maternal morbidity, as well as fetal or neonatal morbidity and mortality.

BACKGROUND

Pregnant patients are at increased risk for morbidity and mortality secondary to COVID-19 infection; however, only approximately 30% have accepted vaccination.[1] This case details an unvaccinated pregnant woman with mild COVID-19 symptoms who underwent emergent delivery for nonreassuring fetal status via cesarean delivery, which was complicated by severe coagulopathy recognized in the operating room and neonatal demise. This is a reminder to clinicians and patients alike to take seriously the severity of COVID-19 infection during pregnancy. Though fetal and neonatal morbidity are common with maternal COVID-19 infection, this is typically due to maternal decompensation and depressed cardiovascular and respiratory systems.[2] Similarly, coagulopathy secondary to COVID-19 infection during pregnancy is well-documented, but this generally leads to maternal morbidity and mortality rather than fetal.[3] We present a unique case in which COVID-19 infection, without significant maternal respiratory symptoms, caused a maternal coagulopathy and placental inflammatory response leading to nonreassuring fetal status such that she underwent emergent delivery with massive hemorrhage and prolonged neonatal resuscitation with subsequent neonatal demise.

CASE PRESENTATION

A 39-year-old woman gravida 4 para 3 at 31 weeks of gestation presented reporting 1 day of decreased fetal movement. She had been diagnosed with COVID-19 infection 5 days prior to presentation. She was tested following a close exposure (positive test by a family member) and then developed mild symptoms, including several days of cough, myalgias, and chills with no fevers or shortness of breath. Her symptoms had resolved by the time of presentation. She had an uncomplicated pregnancy prior to this diagnosis and had initiated prenatal care in the first trimester. Despite counseling, she had declined the COVID-19 vaccination

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multiple times throughout pregnancy. The fetal anatomic survey at 19 weeks of gestation was normal.

On initial examination, maternal vital signs and oxygen saturation levels were normal. Her prepregnancy body mass index was 23. Cardiopulmonary exam revealed normal lung sounds bilaterally. The fetal heart rate tracing demonstrated fetal tachycardia with a baseline of 165, minimal variability, and an isolated spontaneous deceleration (Figure 1). A biophysical profile was performed and noted to be 2/8 (+2 for fluid). She received 1 dose of betamethasone for fetal lung maturity and was admitted to labor and delivery for continued monitoring. After 2 hours of continuous fetal monitoring, the fetal heart rate tracing suddenly developed recurrent deep decelerations. Fetal heart rate variability was absent (Figure 2). An emergent cesarean delivery was recommended.

A primary low-transverse cesarean delivery via Pfannenstiel incision was performed under general anesthesia after obtaining informed consent. Approximately 100 cc of frank blood was encountered upon entry into the peritoneal cavity. The etiology of this was unclear, but further impaired hemostasis throughout the procedure and lab values that returned later in the procedure indicate this was most likely due to coagulopathy. There was no evidence of uterine rupture or injury. There was also no evidence of placental abruption. The patient delivered a male infant from the vertex presentation with a birthweight of 2240 grams and Apgar scores of 0, 0, and 0 at 1, 5, and 10 minutes. This is approximately the 97th percentile for weight; the patient did have a normal O'Sullivan glucose test and overall normal fetal anatomy survey at 20 weeks gestation consistent with early ultrasound. The infant was resuscitated, intubated, and taken to the neonatal intensive care unit (NICU). Bleeding from the hysterotomy was initially brisk due to atony and she

Figure 1. Initial Fetal Heart Rate Tracing

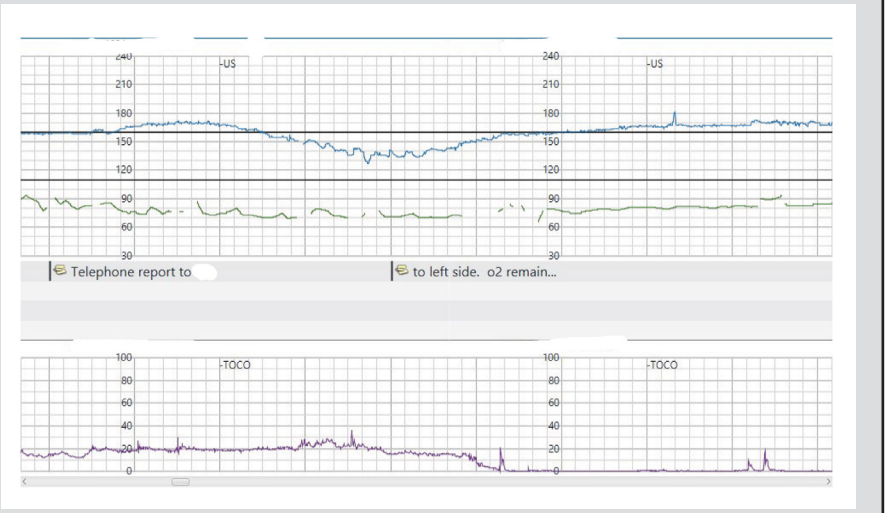
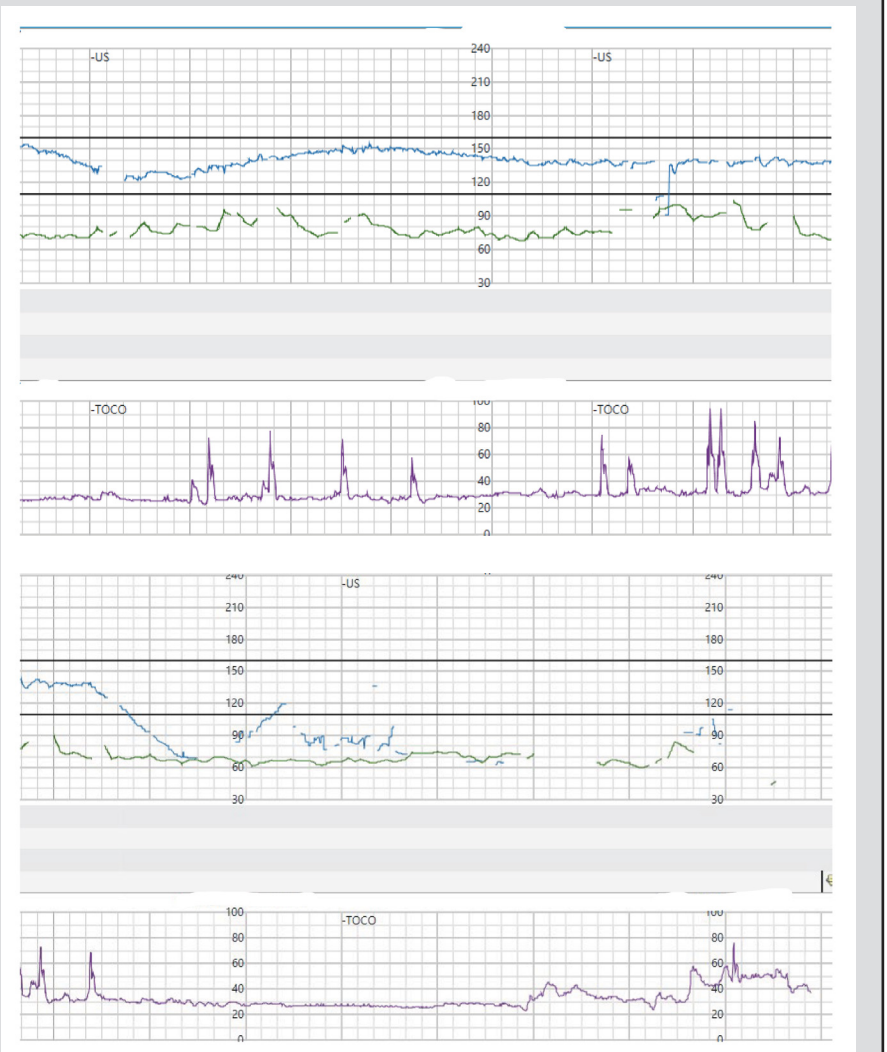


Figure 2. Fetal Heart Rate Tracing Immediately Prior to Cesarean Delivery



was given 1 g of tranexamic acid (TXA) and 200 mcg of Methergine, in addition to Pitocin and uterine massage. The hysterotomy was closed in running-locked fashion with continued bleeding noted along the length of the incision, despite improved uterine tone. At this time, laboratory workup returned with a platelet level of 41 (Table 1). A disseminated intravascular coagulation (DIC) panel was added on to her initial blood draw. At this time, the massive transfusion protocol was initiated. Transfusion of 1 unit of packed red blood cells and 1 unit of platelets was ordered and initiated. Hemostasis along the hysterotomy was rendered with additional suture placement and left-sided O'Leary suture placement. The abdomen was closed and the procedure concluded. Total quantified blood loss was 2,286 cc. The DIC panel resulted with critically low fibrinogen, international normalized ratio (INR) of 2.3, and partial thromboplastin time of 57 seconds (Table 1). She was given an additional unit each of blood and platelets, as well as 2 units of cryoprecipitate and 1 unit of fresh frozen plasma. Placental pathology showed trophoblastic necrosis and intervillous fibrin and inflammation with no signs of placental abruption. Due to laboratory capabilities, COVID-19 polymerase chain reaction was unable to be performed on the placenta. In total, she received 2 units of packed red blood cells, 2 units of platelets, 2 units of cryoprecipitate, and 1 unit of fresh frozen plasma.

Table 1. Maternal Laboratory Values

	HD 1 14:43	HD 1 16:18	HD 1 21:50	HD 1 23:12	HD 2 03:00	HD 2 19:42	HD 2 06:45	HD 4 10:55
Hemoglobin (g/dL)	12.6		8.8	8.8		7.8	7.4	8.1
Platelets (plt/mL)	34	41	46	45	88	126	127	240
INR		2.3	1.2		1.1			
Fibrinogen (mg/dL)		<60	188		206			
D-Dimer (mcg/mL)		>20	19.63		8.41			
Kleihauer-Betke test	0% fetal RBC							
Urine protein: creatininer ratio						0.12		

Abbreviations: HD, hospital day; INR, international normalized ratio; RBC, red blood cell.

Table 2. Neonatal Laboratory Values

	DOL 1 17:42	DOL 2 04:12	DOL 2 18:20	DOL 3 05:39	DOL 3 18:02	DOL 4 05:40	DOL 4 17:30	DOL 5 06:23
Hemoglobin (g/dL)	17.5	12.3	13.6	12.0	11.9	8.4	12.4	12.3
Platelets (plt/mL)	215	143	131	110	96	84	55	140
INR	4.3	4.1	2.5	2.1	1.7	1.6	1.5	1.4
Fibrinogen (mg/dL)	137	234	241	260	294	256	279	291
D-Dimer (mcg/mL)	>20	19.22						

Abbreviations: DOL, day of life; INR, international normalized ratio.

The patient was extubated 1 hour after conclusion of the procedure and transferred to the intensive care unit (ICU). Vital signs were stable and within normal limits. She met routine postoperative milestones and was transferred back to labor and delivery for continued recovery on postoperative day 1. Laboratory values were initially trended every 6 hours in the ICU until she was deemed clinically stable, and then laboratory draws were drawn daily to monitor improvement. She remained admitted through postoperative day 6 due to slow return to ambulation but ultimately was discharged home in stable condition.

Early identification of severe hypoxic-ischemic encephalopathy and intraventricular hemorrhage secondary to neonatal DIC gave the infant a poor prognosis. He tested negative for COVID-19 infection, and aside from poor tone, no gross abnormalities were noted on physical exam. There were also no signs of hydrops on exam or imaging, and the first hemoglobin immediately after delivery was 17.5 but dropped to 12.3 at approximately 10 hours of life (Table 2). His platelets were 215 initially and trended downward over the first 72 hours of life to a nadir of 55. Initially, the patient and her partner desired full resuscitative interventions, despite poor prognosis. On day-of-life 6, neonatal resuscitative efforts were withdrawn, and the infant died 4 hours later. Neonatal diagnoses from NICU imaging studies, laboratory values, and clinical presentation included profound disseminated intravascular coagulopathy and grade IV intracranial hemorrhages.

DISCUSSION

Though fetal and neonatal morbidity are not unusual with maternal COVID-19 infection during pregnancy, this is commonly due to maternal decompensation and depressed cardiovascular and respiratory systems.[2,4] Similarly, coagulopathy as a result of COVID-19 infection during pregnancy is well-documented, but this generally leads to much more significant maternal morbidity and mortality than fetal.[3,5-6] This is a case where COVID-19 infection, even without maternal respiratory symptoms, caused a severe reaction that led to catastrophic outcomes for both mother and newborn: acute maternal coagulopathy leading to spontaneous intraperitoneal bleeding and hemorrhage requiring massive transfusion protocol and ICU admission for the mother and a placental reaction that led to uteroplacental insufficiency, manifesting as a terminal bradycar-

dia and subsequent delivery of a neonate that required extensive resuscitation and ultimately died.

The pathologic study of the placenta revealed a premature placenta with "trophoblastic necrosis and intervillous fibrin and inflammation, without findings of placental abruption." This finding is consistent with the reported cases of intrauterine fetal demise that were attributed to a possible COVID-19 infection.[7] The pathophysiology of this has not been entirely elucidated, but it appears that COVID-19 infects trophoblastic cells outlining placental villi, which causes necrosis of trophoblastic tissue. This ischemia leads to uteroplacental insufficiency, which can lead to fetal hypoxia and, ultimately, intrauterine fetal demise or terminal bradycardia, as in this case. It is important to note that this is a placental reaction, or a placentitis, as many of these cases—including this one—had a neonate who tested negative for COVID-19 infection.

Similar studies of placental pathology after COVID-19 infection show evidence of hypoxia-induced maternal vascular malperfusion, with a small number of these cases also showing evidence of the acute inflammatory reaction demonstrated here.[8,9] Inflammatory placental reactions are common, such as in cases of infection with cytomegalovirus or *Treponema pallidum*.[10] These infections are usually "clinically silent" and have not been associated with adverse outcomes in most studies.[11] Other viruses, such as Zika virus, have been shown to cause similar placental reactions, including irregular fibrin deposition, though not with the severity of placentas studied after COVID-19 infection.[12]

There are several reasons this case is unique. This represents further evidence of possible placental effects of the COVID-19 virus, even though studies have demonstrated that the virus itself is not able to cross the placental barrier.[13-14] It provides further evidence of the need for more study on the possible effects of COVID-19 in pregnancy. Most importantly, it highlights the potential devastating outcomes of maternal COVID-19 infection and the need to continue to take every measure possible to reduce the spread of COVID-19. It is well-documented in the literature that COVID-19 vaccines reduce the risk of contracting the virus.[15-17] In patients who are vaccinated and experience a breakthrough infection, disease severity is significantly reduced. From a statistical perspective, the risk of having an outcome such as the one described in this case is reduced if the overall risk of contracting COVID-19 is lower.

The second unique aspect of this case is the patient's rapid change in clinical status. Even in a patient with mild symptoms of the virus and no changes in vital signs, catastrophic coagulopathy can develop rapidly with no other precipitating factors. It is crucial for clinicians to remember that patients with COVID-19 can deteriorate quickly, and constant vigilance is necessary. It provides evidence to clinicians to not only be monitoring maternal cardiovascular and pulmonary status, but to also ensure that hematologic parameters remain normal.

Finally, pregnant patients must be counseled on the possible adverse fetal outcomes of COVID-19. Since COVID-19 is generally not vertically transmitted,[18,19] patients may assume that their fetus may not be affected by COVID-19 infection. This unique and tragic case demonstrates that even in the absence of respiratory concerns, maternal COVID-19 can cause significant morbidity for both mother and fetus, including maternal, fetal, or neonatal death.

Data are limited, but some authorities have suggested that pregnant women in the third trimester should have at least 1 ultrasound to assess fetal amniotic fluid volume at least 14 days after symptom resolution or more than 21 days from prior fetal biometry ultrasound.[20] There have been no published reports on ultrasound findings of placentitis with COVID-19 infection. There has been no consensus recommendation at our institution at this writing, but many clinicians are recommending a follow-up ultrasound within 1 month and once or twice weekly antenatal testing after diagnosis in the third trimester.

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