



COVID-19-Associated Coagulopathy in the Peripartum Setting: A Case Report

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AJP Rep 2022;12:e33–e35.

Abstract

Sepsis-induced coagulopathy (SIC) scoring and D-dimer can be used to recognize COVID-19-induced coagulopathy, but the utility of these is largely unknown in the peripartum setting and leaves anticoagulation guidance unclear. We present the case of a critically ill postpartum patient with COVID-19 infection. This patient presented with clinical signs of COVID-19 infection and developed acute respiratory failure requiring invasive mechanical ventilation and subsequent cesarean delivery at 34 weeks. She initially improved postoperatively but deteriorated after postoperative day 5. She was found to have a very elevated D-dimer of 58 $\mu\text{g}/\text{mL}$ and anticoagulation was escalated to full dosing. She required prolonged mechanical ventilation and deceased after developing gram-positive cocci bacteremia. This case demonstrates that recognition and management of COVID-19-associated coagulopathy can be confusing in the peripartum period and studies are needed to validate D-dimer and SIC scoring in this population of patients.

Keywords

- ▶ COVID-19
- ▶ coagulopathy
- ▶ D-dimer
- ▶ peripartum
- ▶ anticoagulation

The sepsis-induced coagulopathy (SIC) scoring system is a validated tool developed by the International Society of Thrombosis and Haemostasis (ISTH) to facilitate early recognition of disseminated intravascular coagulopathy (DIC). The SIC scoring has also been used to identify coagulopathy in patients with COVID-19.¹ In a retrospective analysis of 449 COVID-19 patients that met SIC criteria or had a markedly elevated D-dimer ($> 3.0 \mu\text{g}/\text{mL}$), a 20% decrease in 28-day mortality was demonstrated in patients receiving prophylactic low-molecular-weight heparin (LMWH) or unfractionated heparin.² The utility of D-dimer and SIC scoring tool has not been validated in the peripartum setting but may still be valuable in recognizing COVID-19-associated coagulopathy as demonstrated in our case.

Case

A 30-year-old inmate and Native American G6P5 at 34 weeks of gestation presented to the emergency room on March 31,

2020 with a cough worsening over 2 weeks. Associated symptoms included fatigue and nausea. She was afebrile but did have tachypnea at 22 respirations per minute and oxygen saturation at 94% on room air. Chest X-ray showed a questionable infiltrate in the periphery of the right lower lobe. Initial laboratory work was significant for absolute lymphopenia at $7,700 \times 10^3/\mu\text{L}$, C-reactive protein (CRP) 8.0 mg/dL, ferritin 72 ng/mL, and procalcitonin 0.11 ng/mL. Initial blood cultures were negative. A nasopharyngeal swab for SARS-CoV-2 by polymerase chain reaction (PCR) was obtained. She was started on azithromycin and ceftriaxone. Her pregnancy was complicated by a history of five prior cesarean sections. She had been recently transferred to Fort Worth, Texas, from a federal facility in South Dakota 2 weeks preceding her admission.

On April 1, 2020, while being monitored on the labor and delivery unit, her tachypnea worsened and she developed profound dyspnea with ambulation. She required 4L/min by nasal cannula to maintain oxygen saturation above 95%.

received
September 23, 2020
accepted after revision
October 8, 2021

DOI <https://doi.org/10.1055/s-0041-1742237>.
ISSN 2157-6998.

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She also developed a fever to 38.3°C. A course of hydroxychloroquine was initiated in conjunction with continued azithromycin. Her respiratory status continued to worsen, so the decision was made to intubate and mechanically ventilate. There was subsequent concern for fetal distress and the decision was made to proceed with delivery. The SARS-CoV-2 PCR result was still pending at this time, but given the high suspicion for the disease, antenatal steroids for neonatal benefit were deferred for concern of potential maternal harm. She had an uncomplicated c-section with a quantitative blood loss of 450 mL. Tranexamic acid was given intraoperatively. The infant was intubated for respiratory distress and sent to the neonatal intensive care unit (NICU). Cord blood gas analysis showed a mild respiratory acidosis, arterial pH 7.13, pO₂ 24, and pCO₂ 79 with a base deficit of 4.7 mmol/L. The infant tested negative for SARS-CoV-2 PCR. The infant was extubated the next day and was stable on room air by the 4th day of life. The infant discharged home with a family member on the 18th day of life.

On postoperative day 3, a positive SARS-CoV-2 PCR resulted. Application for remdesivir was approved on postoperative day 5 and initiated as 200 mg once followed by 100 mg daily for 10 days, and she completed the antiviral course.

Ventilator settings were consistent with ARDSnet protocol guidelines. Ventilation was initially done using assist control (AC)/volume control (VC) with a gradually rising PaO₂/FiO₂ ratio up to 440 by postoperative day 5. Her PaO₂/FiO₂ ratio dropped to 232 on postoperative day 6 and she was transitioned to airway pressure release ventilation (APRV). Of note, her CRP was 12 but increased to 33 on postoperative day 8, and she reached a maximum temperature of 39.9°C. She developed a superficial wound separation 1 week postoperatively and a vacuum-assisted closure device was placed, which was changed every 3 to 4 days depending on positioning. Several attempts were made to wean paralytics; however, it consistently resulted in prolonged episodes of hypoxia. She remained in the prone position and was intermittently supinated as tolerated.

A bronchoscopy was done on postoperative day 12 due to refractory hypoxia, and findings were concerning for diffuse alveolar hemorrhage (DAH). DAH workup including deoxyribonucleic acid (DNA) double-strained (DS) antibodies, anti-neutrophil cytoplasmic antibody (ANCA) vasculitis panel, and glomerular basement membrane antibodies were negative. Tocilizumab was given the same day. The following day, a blood clot developed in her radial artery catheter. A D-dimer resulted as 58 µg/mL. She had a platelet count of 413 × 10⁹/L, international normalized ratio (INR) of 1.29, and a Sequential Organ Failure Assessment (SOFA) score of 4 equating to an SIC score of 3. The decision was made to transition to full anticoagulation using a heparin drip with a goal titration partial thromboplastin time (PTT) of 50 to 80 seconds. Cardiophilin antibodies were negative.

Upon availability, she received convalescent plasma on postoperative day 20. She developed gram-positive cocci bacteremia and deceased after 28 days of mechanical ventilation.

Conclusion

An important mechanism of COVID-19-associated mortality is diffuse alveolar damage, small vessel thrombosis, and thrombotic microangiopathy as demonstrated in autopsies of COVID-19 patients.³ Connors and Levy perspective on anticoagulation management in COVID-19 findings conclude that coagulopathy is related to severity of illness and resultant thromboinflammation as opposed to viral activity.⁴ It is well known that procoagulation factors are increased in pregnancy, resulting in a fivefold increased risk of thromboembolism when compared with nonpregnant women and 60-fold increased risk in the first 3 months after delivery.⁵ These findings suggest that pregnant and postpartum patients may be more susceptible to the thromboinflammatory effects of COVID-19 resulting in worsening illness. This is demonstrated in our case given the deterioration after postoperative day 5. Similar findings are reflected in a case series of two antepartum patients admitted for severe COVID-19 who underwent c-section. Both patients deteriorated on postoperative day 3 and had a D-dimer greater than 2 µg/mL. They improved after receiving full dose anticoagulation.

Interestingly, a person's risk of severe illness from COVID-19 is very similar to the individual risk factors for venous thromboembolism (VTE) in pregnancy. This list includes heart disease, obesity, autoimmune disease, hypertension, and sickle cell disease. Cesarean delivery is also an independent risk factor for VTE with an estimated fourfold increased risk as compared with vaginal delivery.⁶ Cesarean delivery has not been listed as a risk factor for severe illness in COVID-19 infection but, as demonstrated in our case as well as in the aforementioned two case series, it may potentially worsen maternal risk of serious illness particularly when the inflammatory response is at its peak around postoperative days 3 to 5. This suggestion is validated in a cohort of 82 women with a positive SARS-CoV-2 reverse transcription PCR (RT-PCR) and who delivered within 14 days of admission; 13.5% of women undergoing c-section had severe maternal outcomes and 21% had clinical deterioration. Some women who underwent cesarean delivery may have had the confounding factor of preterm delivery for worsening maternal disease, but even after adjusting for this confounder, cesarean delivery remained independently associated with increased risk of clinical deterioration.⁷ This may suggest that women admitted for moderate to severe COVID-19 infection and presence of other risk factors for VTE, including cesarean delivery, should at minimum receive prophylactic anticoagulation and may benefit from escalation to intermediate or full dosing especially if the D-dimer or SIC score is elevated.

We suggest considering use of the SIC score or a markedly elevated D-dimer for early recognition of COVID-19-associated coagulopathy in the peripartum setting. Patients with an elevated SIC score or markedly elevated D-dimer should receive therapeutic anticoagulation as in our case. Despite not having validation of D-dimer or SIC scoring in pregnant or postpartum women, this should not preclude them from aggressive anticoagulation as their risk of VTE and development of severe COVID-19 illness is likely higher than nonpregnant patients.

Conflict of Interest

Dr Roopina Sangha declares the following conflict of interest: received payment or honoraria for lectures, presentations, speakers bureaus, manuscript writing, or educational events from John Peter Smith Hospital, Fort Worth, Texas.

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