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Case Report

Preterm neonate delivered to COVID-19 positive mother on ECMO support

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Abstract. Despite ongoing research and recent discoveries, there remains a paucity of data regarding COVID-19 and its implications for pregnant women, particularly its effects on the developing fetus. To date, there are a limited number of articles available regarding the utility of Extra Corporeal Membrane Oxygenation (ECMO) for cardio-respiratory support of pregnant women during the perinatal period. Additionally, there are only a few case reports detailing the delivery management of a baby born to a mother on ECMO support. Here, we report a case of a premature, low birth weight neonate delivered by a 32-year-old woman while on ECMO due to severe acute respiratory distress syndrome resulting from COVID-19 infection.

Keywords: COVID-19, ECMO, premature neonate, SARS CoV-2

1. Background

The 2019 novel coronavirus disease (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a global public health emergency. Despite ongoing research and recent discoveries, there remains a paucity of data regarding COVID-19 and its implications for pregnant women, particularly its effects on the developing fetus. To date, there are a limited number of articles available regarding the utility of Extra Corporeal Membrane Oxygenation (ECMO) for cardio-respiratory support of pregnant women during the perinatal period. Additionally, there are only a few case reports detailing the delivery management of a baby born to a mother on ECMO support. Here, we report a case of a 26-week premature low birth weight (860 gram) neonate delivered by a 32-year-old woman while on ECMO due to severe acute respiratory distress syndrome resulting from COVID-19 infection.

2. Case presentation

At 23 weeks gestation, a 32-year-old G3P2002 woman presented to an outside hospital with a two-day history of fever, chills, headache, and cough in the setting of a recent COVID-19 exposure at work. Her past medical history included two prior cesarean sections, and uneventful current pregnancy. She had positive SARS-CoV-2 detected by PCR. In view of respiratory distress with supplemental oxygen requirement, she was admitted and started on intravenous Remdesivir (200 mg initial dose followed by 100 mg once daily) and Dexamethasone (6 mg daily). On the second day of admission, she experienced acute respiratory decompensation neces-

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sitating invasive mechanical ventilation. In lieu of her worsening clinical status and superimposed pregnancy, the decision was made to transfer her to our facility with access to ECMO and a level 4 Neonatal intensive care unit (NICU).

She was initially admitted to our Medical Intensive care Unit (MICU) where she remained intubated, and Remdesivir (10-day course) and dexamethasone were continued. Due to worsening hemodynamic stability, she was started on vasopressors: Norepinephrine, epoprostenol, and subsequently vasopressin. Vancomycin was started for superimposed bacterial pneumonia. On hospital day 6, she was transferred to Cardiac Surgery Intensive Care Unit (CSICU) for ECMO consideration in view of worsening hypoxic respiratory failure. The decision was made to place her on venovenous (VV) ECMO.

Despite being on ECMO, oxygenation was still a profound challenge. She received a course of remdesivir, methylprednisolone, and antibiotics for secondary bacterial pneumonia (respiratory culture growing methicillin-resistant *Staphylococcus aureus*, and Chest x-ray showing persistent extensive bilateral pulmonary opacities). Her course was complicated by Candida fungemia (*Candida albicans*), acute cholecystitis, severe upper gastrointestinal bleeding requiring multiple packed red blood cells and cryoprecipitate transfusions, atrial fibrillation requiring cardioversion with amiodarone followed by metoprolol and later mechanical cardioversion. During her stay in the CSICU on ECMO, she was kept paralyzed and sedated with various medications such as propofol, fentanyl, and cisatracurium, in addition to other sedatives and paralytics. She also received nitric oxide for hypoxic respiratory failure. Additionally, because of the ECMO, she was also on an unfractionated heparin drip for anticoagulation.

On the 20th day of admission, mom had a spontaneous vaginal delivery of her baby in her sedated, paralyzed state at 26-weeks 2-days gestation. The NICU team arrived expeditiously; the female infant emerged with poor tone, dusky, with primary apnea. She was warmed, dried, and stimulated, with a heart rate less than 60/min requiring Positive pressure ventilation (PPV), with which heart rate increased greater than 100/min. APGAR score was 2,4,5 at 1, 5, and 10 minutes respectively. She was transferred to the NICU and placed on a conventional ventilator. The initial chest x-ray was consistent with respiratory distress syndrome (RDS) and surfactant was administered.

The neonate had tonic-clonic seizure-like movements of her right upper extremity, which was suppressed by phenobarbital load followed by a maintenance dose. Ultrasound head showed "no intraventricular hemorrhage". With the presentation of seizures as well as the mother's history of COVID-19 infection, with superimposed bacterial pneumonia and fungemia, antibiotics (linezolid and cefepime), antifungal (amphotericin), and an antiviral (acyclovir) were started. During the initial stabilization period, the baby became hypotensive, necessitating an epinephrine drip for 48 hours. The echocardiography revealed a large PDA with a left to right flow with systemic pulmonary pressures.

The SARS COV-2 result was negative on days 1 and 3 of life. After 48 hours of negative blood culture and negative HSV swab and HSV PCR, the linezolid and acyclovir were discontinued, followed by the discontinuation of cefepime on DOL 7. Amphotericin was continued for a 14-day course given the maternal history of candida fungemia.

The neonate required multiple blood transfusions during her NICU stay, including three red cell transfusions, two platelet transfusions, and two Fresh frozen plasma (FFP). During the infant's NICU stay, she has been managed for her prematurity, bronchopulmonary dysplasia, apnea of prematurity, metabolic bone disease, history of seizure-like activity, retinopathy of prematurity, and PDA. Her NICU course was complicated by bilateral osteomyelitis of her femurs for which, she is now status post-antibiotic treatment.

At the time of submission of the report, the infant is 117 days old; term corrected gestational age on room air in the bassinet and on full enteral feeds by an orogastric tube. As for the mother, after delivery, the mother's hypoxic state improved, and she was decannulated from ECMO and placed on a mechanical ventilator with tracheostomy on the 11th postpartum day (31st day of admission). She was later transferred to a rehabilitation center, from where she was discharged home without any respiratory support. She exhibits grossly normal verbal and ambulatory skills, though some impairment in short-term memory is noted.

3. Discussion

The use of ECMO is rapidly increasing for adult patients with cardiorespiratory failure [1]. The survival rate in pregnant women on ECMO is 75–80 %,

and 65–70% for the fetus [2, 3]. The decision to use ECMO in pregnancy presents unique challenges. The potential indications for ECMO in pregnancy include acute respiratory distress syndrome due to pneumonia or transfusion-related lung injury, pulmonary embolism, amniotic fluid embolism, cardiomyopathy, and primary pulmonary hypertension with right heart failure [2]. The clinical team must always weigh the risk versus benefit, including the overall risk of using ECMO in pregnant mothers, such as bleeding, nosocomial infections (bloodstream, respiratory, urinary tract, or wound infections), limb ischemia, and venous thromboembolism [4].

Pregnant women with SARS-CoV-2 are more likely to be hospitalized and at high risk for intensive care admission and receipt of mechanical ventilation and when indicated ECMO, compared to nonpregnant women with SARS-CoV-2; however, the mortality rate is similar [5, 6]. The higher morbidity risk among pregnant women with SARS-CoV-2 may be explained by the pregnancy-related physiologic changes, including a shift in CD4+ T cell population toward the Th2 phenotype over Th1, the reduction in total lung capacity due to diaphragmatic splinting by the gravid uterus, and increased risk of thromboembolic events [7]. The predominant maternal complications with SARS-Cov-2 include cardiomyopathy, respiratory failure requiring mechanical ventilation/ECMO, and death.

Delivery while on ECMO may be beneficial for pregnant women. Cesarean section is the most used mode of delivery, and labor induction could be considered when a cesarean cannot be performed, or the fetus has died in utero. A multidisciplinary team including the ECMO team, the obstetrician, anesthesiologist, and ICU doctors is needed in such clinical scenarios. The risk of fetal morbidity and mortality due to premature delivery needs to be weighed against the risk of fetal morbidity due to maternal illness and therapy [8]. The resuscitation of a neonate born to pregnant women with SARS CoV-2 should be performed, as per the American Academy of Program, Neonatal Resuscitation Program (NRP), with slight modifications in respiratory care practices. Everyone in the neonatal resuscitation team should don the personal protective equipment (gown, gloves, N95 respirator mask, a face shield, eye-protection goggles). The necessary precautions need to be taken to decrease the risk of spread of infection, particularly during aerosol-generating procedures such as bag-mask ventilation, endotracheal intubation, invasive ventilator, non-invasive respiratory support (continuous positive airway pressure, high-flow nasal cannula), and suctioning [9, 10].

Our neonatal patient in the case report is consistent with other reports of the low vertical transmission rate of SARS-CoV-2; however, the placenta may be affected in mothers with SARS Co-V2 [4, 5, 11]. Transplacental hematogenous transmission, intrapartum transmission via exposure to maternal infected secretions, and postpartum transmission via respiratory droplets from the mother are possible ways of maternal transmission of SARS CoV-2 to the infant [12]. The risk of neonatal infection is not greater with vaginal delivery, rooming-in with mother, or breastfeeding, provided the respiratory precautions, including wearing the mask, are undertaken. [13, 14].

NICU admissions, prematurity, low birth weight, and cesarean section are common expectations with deliveries in mothers with SARS CoV-2 [15]. The risk of preterm delivery is 20% [5]. The neonate born to a mother with SARS-CoV-2 needs to be tested for reverse transcriptase-polymerase chain reaction (RT-PCR) for SARS-CoV-2 at 24 and 48 to 72 hours of life. Neonates should be assessed for clinical features of SARS-CoV-2 infection, such as fever, cough, nasal congestion, respiratory distress, decreased activity, and feed intolerance. ECMO use during pregnancy theoretically can be associated with a high risk for maternal and fetal bleeding complications [3, 16]. The neonate in this case report had coagulopathy and thrombocytopenia, which normalized after FFP and platelet transfusion, possibly explained by maternal underlying condition and prematurity. The neonate's mother was on long-term unfractionated heparin, which usually does not cross the placenta. Neonatal outcomes of delivery of the mother on ECMO support for SARS CoV-2 are within the limit expected for prematurity.

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Disclosure statement

All authors have no conflicts of interest to disclose.

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