Successful Treatment of Pregnant and Postpartum Women With Severe COVID-19 Associated Acute Respiratory Distress Syndrome With Extracorporeal Membrane Oxygenation

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Abstract: There are limited data on the use of extracorporeal membrane oxygenation (ECMO) for pregnant and peripartum women with COVID-19 associated acute respiratory distress syndrome (ARDS). Pregnant women may exhibit more severe infections with COVID-19, requiring intensive care. We supported nine pregnant or peripartum women with COVID-19 ARDS with ECMO, all surviving and suffering no major complications from ECMO. Our case series demonstrates high-maternal survival rates with ECMO support in the management of COVID-19 associated severe ARDS, highlighting that these pregnant and postpartum patients should be supported with ECMO during this pandemic. ASAIO Journal 2021; 67;132–136

Key Words: ECMO, extracorporeal membrane oxygenation, COVID, COVID-19, ARDS, pregnancy, peripartum

The pandemic associated with coronavirus SARS-CoV-2 and related clinical disease, COVID-19, has affected over 38 million people worldwide with over one million deaths.1 The hormonal, cardiovascular physiology, and immunomodulatory changes during pregnancy increase susceptibility to respiratory infections and may predispose to severe presentations of the disease.2,3 Additionally, reports of severe COVID-19 infections in pregnant and peripartum women and the fetal effects are emerging.2,4-7

Extracorporeal membrane oxygenation (ECMO) is an invasive support strategy for cardiac, respiratory, or combined cardiorespiratory failure when conventional treatment options have failed. ECMO has been successfully deployed for the management of critical illness in pregnant and postpartum patients, including during the previous pandemic.5-10 The use of ECMO for acute respiratory distress syndrome (ARDS) during the H1N1 pandemic saved many maternal and fetal lives, however, few studies report the use of pregnant and postpartum ECMO during this pandemic.1-8,11

Against this background, we present an international case series of pregnant and peripartum patients managed with ECMO for COVID-19 induced ARDS, with maternal data and data on fetuses and neonates as relevant.

Methods

Pregnant and postpartum patients with a polymerase chain reaction confirmed for SARS-CoV-2 infection supported with ECMO were identified by the collaborating institutions from February until September 2020. Descriptive statistical methods included median (minimum-maximum range) and frequency, n (%). Demographics, maternal pre-ECMO, ECMO characteristics, and neonatal outcomes were described. Adverse events during the ECMO course were also identified. Individual IRB approval was obtained by the collaborating institutions.

Results

Our cohort includes nine patients with median age 30 years (range 22–43 years), five of whom were within 48 hours postpartum, two peripartum, and two pregnant at the time of ECMO initiation. All but two patients reported respiratory symptoms of COVID-19 during the third trimester. All patients had severe ARDS with a median PaO2/FiO2 (PF ratio) of 62 mm Hg (54–100 mm Hg) managed with invasive mechanical ventilation, 5 (56%) with inhaled epoprostenol, and 6 (67%) with prone positioning. Specific COVID-19 therapies before ECMO included remdesivir 4 (44%), ribavirin/lopinavir 2 (22%), convalescent plasma therapy 4 (44%), hydroxychloroquine 4 (44%), azithromycin 6 (67%), anticytokine 2 (22%), and glucocorticoids 5 (56%). Table 1 summarizes maternal characteristics, including comorbidities and COVID-19-related symptoms and therapies.

The median RESP score was 4 [1–6] before ECMO cannulation.12 All patients received venovenous ECMO support, one concurrently with an intra-aortic balloon pump due to elevated left ventricular end-diastolic pressure and signs of biventricular dysfunction. ECMO cannulation strategies varied with three patients undergoing femoral-femoral, three with femoral-internal jugular configuration, and three with
Table 1. Maternal Characteristics

| Center   | patient 1 | patient 2 | patient 3 | patient 4 | patient 5 | patient 6 | patient 7 | patient 8 | patient 9 |
|----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|-----------|
| **Maternal factors** |           |           |           |           |           |           |           |           |           |
| Age (years) | 28        | 30        | 22        | 27        | 34        | 30        | 30        | 36        | 43        |
| Race      | Hispanic  | Hispanic  | Caucasian | African-American | Patient | Declined | Hispanic | Indian | African-American | Caucasian |
| Weight (kg) | 90.7      | 100.0     | 70.0      | 63.2      | 72.0      | 88.5      | 70.0      | 94.5      | 117.1     |
| Comorbidities | Obesity   | Obesity   | None      | None      | Obesity   | None      | Obesity   | None      | Obesity   |
| Pregnancy-related comorbidities | None      | Hypothyroidism | None      | None      | Tonic-clonic seizures | None      | None      | None      | Placenta previa Succenturate placental lobe |
| Maternal COVID-19 |           |           |           |           |           |           |           |           |           |
| Symptom onset (days) | 7         | 6         | 8         | 4         | 4         | 7         | #         | 17        | 6         |
| COVID-19 diagnosis | PCR       | PCR       | PCR       | PCR       | PCR       | PCR       | PCR       | PCR       | PCR       |
| CRP (mg/mL) | 12.1      | 15.5      | 6.7       | #         | 28.94     | 69.1      | 20.9      | 169.5     | #         |
| White-cell count | 7.45      | 7.8       | 8.16      | 4.96      | 41.0      | 7.4       | 16.6      | 26.8      | 12.9      |
| LDH (U/L) | 221       | 486       | 1,100     | 444       | 664       | 296       | 459       | 834       | #         |
| Troponin (ng/mL) | <0.006    | <0.006    | 6.5       | <0.03     | 0.059     | #         | 0.021     | 0.083     | #         |
| Ferritin (ng/mL) | 77        | 429       | 72        | 77.7      | 588       | 72        | #         | #         | #         |
| D-Dimer (mcg/mL) | 1.34      | 4.63      | 15.25     | 2.20      | 2.38      | 0.502     | #         | 3.91      | 12.1      |
| Fibrinogen (mg/dL) | 586       | 537       | 447       | 540       | 765       | #         | 596       | 1,266     | 640       |
| Echo ejection | 60%       | 60%, RV enlarged | 40-45%  | Normal EF | Normal EF | Normal EF | Normal EF | Normal EF | Normal EF |
| Invasive ventilation | Yes      | Yes       | Yes       | Yes       | Yes       | Yes       | Yes       | Yes       | Yes       |
| PEEP/plateau (cm H2O) | 12 / 30 | 14 / 30 | 14 / 31 | 16 / 29 | 10 / 28 | 19 / 28 | 15 / 34 | 16/30 | 16/30 |
| PF ratio prior cannulation | 56       | 55        | 69        | 66        | 100       | 66        | 60        | 54        | 62        |
| Inhaled nitric oxide | No        | No        | No        | No        | No        | No        | No        | No        | No        |
| Inhaled prostacyclin | Yes       | Yes       | Yes       | No        | No        | No        | Yes       | No        | Yes       |
| Prone positioning | Yes       | Yes       | Yes       | No        | No        | Yes        | No        | Yes       | No        |
| COVID-19 targeted therapy before ECMO | 1. HCL | 1. HCL | 1. HCL | Convalescent plasma | 1. Azithromycin | 1. Remdesivir | 1. HCL | 1. Remdesivir | Dexamethasone |
| 2. Azithromycin | 2. Azithromycin | 2. Azithromycin | 3. Convalescent plasma | 2. Remdesivir | 2. Lopinavir | 2. Azithromycin | 3. Dexamethasone |
| 3. Tocilizumab | 3. Tocilizumab | 3. Tocilizumab | 4. Convalescent plasma | Remdesivir | 3. Remdesivir |
| 4. Convalescent plasma | 4. Convalescent plasma | 4. Tocilizumab |
| Systemic steroids | Yes | Yes | Yes | No | No | No | Yes | Yes |
| Gravida/Para | 4/2 | 2/1 | 1/1 | 3/1 | 1/0 | 4/3 | 1/0 | 5/4 | 1/0 |
| Gestational age | 30 + 3 | 35 + 2 | 29 | 33 | 30 | 37 + 3 | 25 + 2 | 32 + 6 | 32 + 6 |
| Delivery | CS | CS | CS | # | CS | CS | CS | CS | CS |

Data not available.

CAD, coronary artery disease; CS, cesarean section; HCL, hydroxychloroquine; HTN, arterial hypertension; PCR, Polymerase chain reaction; PEEP, positive end expiratory pressure; PF ratio, PaO2/FiO2; RV, right ventricle; SLE, systemic lupus erythematosus.
Before hospital discharge. One newborn died among all but one were premature, less than 37 weeks gestation. All newborns were delivered via cesarean section and all but one were premature, less than 37 weeks gestation. Evaluation of the two fetuses for the two patients supported with ECMO for COVID-19 ARDS in peripartum patients remained bleeding. Two of our patients experienced minor bleeding but no major complications during ECMO, alike to the two cases reported. The most common complication reported in ECMO for COVID-19 ARDS was circuit change (15%), which mirrors our complication rate for circuit/oxygenator cloting (22%). Circuit thrombosis may be more common as a result of the combination of pathophysiological alterations of hemostasis during pregnancy, and the anticoagulation protocols, which were the standard practice of each institution and not modified for pregnancy nor COVID-19. Fortunately, vertical transmission of COVID-19 from mother to fetus is rarely reported. None of our infants contracted COVID-19. The majority of our infants were premature, similar to other reports. Not previously reported, the majority of these infants required admission to intensive care, 71% required mechanical ventilation, and one infant is still admitted, and receiving noninvasive positive pressure ventilation. Despite a perilous gestation, the majority of our infants survived.

We recognize that our data and interpretation are limited by the small sample size. However, during this unprecedented pandemic as management strategies and therapies are continually evolving, we felt it important to share the data to help physicians at the bedside.
Table 2. ECMO Characteristics

| Patient/Center | 1/A | 2/A | 3/B | 4/C | 5/D | 6/E | 7/F | 8/B | 9/C |
|----------------|-----|-----|-----|-----|-----|-----|-----|-----|-----|
| Cannulation timing | Postpartum | Postpartum | Postpartum | Pregnancy | Postpartum | At delivery | Postpartum | At delivery | Pregnancy |
| Cannulation type | VV | VV | VV | VV | VV | VV | VV | VV | VV |
| PF ratio prior & RESP score<sup>1</sup> | 56 | 55 | 69 | 66 | 100 | 66 | 60 | 62 |
| Cannulation location | Fem (25F)→Fem (21F) | Fem (19F)→Fem (21F) | Fem (25F)→RU-Dual Lumen (31F) | Fem (23F)→RU (20F) | Fem (25F)→RU (19F) | RU – Dual Lumen (31F) | Fem (29F)→RIJ (24F) | RIJ – Dual Lumen (31F) |
| Anticoagulation on ECMO | Heparin, changed to Bivalirudin due circuit clothing with therapeutic heparin | Heparin, changed to Bivalirudin (suspicion of HIT) | Heparin | Heparin | Heparin | Heparin | Heparin | Heparin |
| Anticoagulation parameters | PTT (60–90s) | PTT (60–90s) | PTT (60–90s)/ Anti-Xa (0.25–0.3)/TEG (R) 2–3 baseline | PTT (60–90s)/ Anti-Xa (0.25–0.3)/TEG (R) 2–3 baseline | Anti-Xa (0.2–0.4) | PTT/TEG (various aims) | PTT (60–90s)/ Anti-Xa (0.25–0.3)/TEG (R) 2–3 baseline | PTT (60–90s)/ Anti-Xa (0.25–0.3)/TEG (R) 2–3 baseline |
| Complications on ECMO | 1. Circuit clotted on Heparin | 1. Inotropes used | 1. Vasodilators used | 1. Surgical site bleeding | 1. Remdesivir continued from before ECMO | 1. Remdesivir—continued from before ECMO | 1. Remdesivir—continued from before ECMO | None |
| | 2. Transient AKI | Right subclavian nerve high-grade stretch injury with foot drop | SIADH | Bacterial pneumonia | Convalescent plasma | Convalescent plasma | Convalescent plasma | None |
| | 3. Oxygenator changed for fibrin deposition | | CINMP | Oxygenator clotted | | | | None |
| ECMO duration (days) | 9 | 11 | 7 | 9 | 10 | 6 | 13 | 57 | 14 |
| Weaned off ECMO | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Yes |
| COVID-19 targeted therapy on ECMO | Remdesivir (started pre-ECMO) | Ribavirin | Placebo arm—Remdesivir (Remdesivir after study unblinded started after decannulation) | Remdesivir—continued from before ECMO | Remdesivir—continued from before ECMO | Remdesivir—continued from before ECMO | Remdesivir—continued from before ECMO | Cytosorb | Systemic steroids |
| | Ribavirin | Convalescent plasma RCT | Convalescent plasma | Convalescent plasma | Convalescent plasma | Convalescent plasma | Convalescent plasma | Systemic steroids | Convalescent plasma |
| Post ECMO complications | Bilateral lower extremities DVT (former ECMO site) | Vaginal bleeding | None | None | None | None | None | 1. Left common femoral vein DVT (former ECMO site) | GBS | None |
| Maternal survival to hospital discharge | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Recannulation 15 days after decannulation, 2nd ECMO run 10 days in duration, vented via trach | Pending | Pending |

<sup>1</sup>Data not available.

AKI, acute kidney injury; CINMP, critical illness polyneuropathy and myopathy; Fem, femoral vein; GBS, Guillain–Barré syndrome; HIT, heparin-Induced thrombocytopenia; RIJ, right internal jugular vein; SIADH, syndrome of inappropriate antidiuretic hormone.
Our case series demonstrates excellent maternal and neonatal survival rates and supports the successful use of respiratory ECMO in the management of COVID-19 associated severe ARDS in pregnant and postpartum patients at high volume ECMO centers. As COVID-19 continues to impact thousands of patients worldwide daily, and despite limited data and resources, pregnancy should not be considered a contraindication for ECMO support for COVID-19 ARDS.

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