# 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.[8–10] 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.[4–8,11]

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 $PaO_2/FiO_2$ (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 to 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

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**Table 1. Maternal Characteristics**

| | patient 1 | patient 2 | patient 3 | patient 4 | patient 5 | patient 6 | patient 7 | patient 8 | patient 9 |
|---|---|---|---|---|---|---|---|---|---|
| Center | A | A | B | C | D | E | F | B | C |
| **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<br>SLE<br>Hypothyroidism | None | None | None | Obesity<br>Asthma | None | Obesity<br>Diverticulitis | Obesity<br>CAD HTN |
| Pregnancy-related comorbidities | None | None | Obesity | Tonic-clonic seizures | None | None | None | None | Placenta previa<br>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 ($\times 10^{-3}/mm^3$) | 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 fraction (EF) | 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 $H_2O$) | 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 | Yes | No | Yes | No |
| Prone positioning | Yes | Yes | Yes | No | Yes | No | Yes | Yes | No |
| COVID-19 targeted therapy before ECMO | 1. HCL<br>2. Azithromycin<br>3. Tocilizumab<br>4. Convalescent plasma<br>5. Remdesivir | 1. HCL<br>2. Azithromycin<br>3. Convalescent plasma<br>4. Tocilizumab<br>5. Ribavirin | 1. HCL<br>2. Azithromycin<br>3. Placebo arm—Remdesivir | Convalescent plasma | 1. Azithromycin<br>2. Remdesivir | 1. Azithromycin<br>2. Convalescent plasma<br>3. Remdesivir | 1. HCL<br>2. Lopinavir | 1. Remdesivir<br>2. Azithromycin<br>3. Dexamethasone | Dexamethasone |
| Systemic steroids | Yes | Yes | Yes | No | 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 | 23 | 33 | 30 | 37+3 | 25+2 | 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, $PaO_2/FiO_2$; RV, right ventricle; SLE, systemic lupus erythematosus.

single-site dual lumen right internal jugular cannulation. Anticoagulation was initiated with unfractionated heparin bolus in 8 (89%) patients (with one not receiving a heparin bolus due to bleeding concerns), with six patients maintained on unfractionated heparin infusion, but three patients changed to bivalirudin targeting institutional thresholds for anti-Xa, partial thromboplastin time, or thromboelastography. Two patients developed thrombotic complications of the membrane oxygenator during ECMO support, managed with oxygenator exchange. One patient developed minor vaginal bleeding during ECMO, and one patient underwent surgical exploration after ECMO decannulation for surgical site bleeding. The median ECMO duration for the first ECMO run was 10 days (range 6–57 days). Our most obese patient (patient 9C) was supported with ECMO flows up to 6.5 L/min without complications and minimal recirculation. Targeted COVID-19 treatment during ECMO included antiviral therapy (remdesivir, ribavirin), and immunomodulatory therapy (convalescent plasma therapy, tocilizumab, Cytosorb). All patients were successfully decannulated from ECMO; however, one patient (9C) required a second 10 day VV-ECMO run (femoral-femoral) postpartum due to worsening respiratory failure. All patients were discharged from the hospital alive, except for two patients still admitted. Further details of the ECMO support are outlined in Table 2.

The two patients with ECMO initiation during pregnancy were electively cannulated in the operating room. While supine positioned, cannulation was directed by fluoroscopy and transesophageal echocardiography. Regular follow-up chest x-rays confirmed cannula positioning. Deliberately both patients were cannulated *via* single-site dual lumen right internal jugular cannula due to potential concern for compression of the uterus and the intraabdominal and pelvic vessels, potentially limiting uterine blood supply. No repositioning of the cannula was required during each of the ECMO runs. Both pregnant patients were able to perform physical therapy and ambulated. Both fetuses were monitored *via* cardiotocography and ultrasound during ECMO support.

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 during pregnancy demonstrated normal fetal growth and no overt fetal compromise. One patient (4C) gave birth 106 days post ECMO cannulation at term gestation, with good APGARS (7/9), the other patient (9C) delivered after completion of the first ECMO run. None of the followed-up newborns had laboratory or clinical evidence suggestive of COVID-19 (Table 3). Maternal breastmilk was not used for any of the newborns except in the one patient, who gave birth 106 days after ECMO decannulation. One newborn died before hospital discharge.

## Discussion

This case series provides insights for pregnant patients supported with ECMO for COVID-19 ARDS. All patients were successfully weaned off ECMO and all except one neonate survived despite maternal distress and preterm delivery. ARDS management, COVID-19 related therapies, as well as ECMO support, did not result in an immediate negative impact on the mothers nor infants. Finally, none of the infants contracted COVID-19 but the majority were premature and required intensive care.

The use of ECMO for pregnant women during the novel coronavirus pandemic can be challenging given the limited data.[4–7] In general, however, pregnant women are younger, healthier, and have close medical follow-up when compared with the general population. This likely contributes to the high survival with the use of ECMO for other indications in peripartum women.[8–10] ECMO for COVID-19 ARDS in peripartum patients is described in two case reports.[5,6] Additionally, two European studies describe 1% of their peripartum patients with COVID-19 requiring ECMO support, however, no details on the patients, ECMO run, nor complications are given.[4,7] Recently, Barbaro et al reported on the successful use of ECMO in COVID-19 in an international cohort study, where 22 patients out of 1,035 were pregnant.[11] Our case series highlights high survival with the support of ECMO for ARDS related to COVID-19 and provides details that may be useful to physicians caring for severely ill pregnant women.

Before the initiation of ECMO, ARDS management for pregnant women followed the clinical practice guidelines for mechanical ventilation in adult patients with ARDS.[13] All patients were treated with high PEEP and low driving pressures, neuromuscular blockade, and 6/9 (67%) with prone positioning.[14] Specific COVID-19 treatment options varied and included systemic glucocorticoids, antiviral, and other immunomodulatory therapeutics. As in the previous pandemic, once conventional intensive therapies were exhausted, ECMO support for ARDS was initiated for these women.[8]

Similar to the general population affected by COVID-19, pregnant women with comorbidities such as obesity, diabetes, and hypertension are at higher risk of serious infection with COVID-19, with 10% needing critical care.[4,7] Comparable to the patient Fiore et al described the majority of our patients were obese.[5] The overall most common complication on ECMO for peripartum patients remains bleeding.[9] Two of our patients experienced minor bleeding but no major complications during ECMO, alike to the two cases reported.[5,6] The most common complication reported in ECMO for COVID-19 ARDS was circuit change (15%), which mirrors our complication rate for circuit/oxygenator clotting (22%).[11] 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.[15] None of our infants contracted COVID-19. The majority of our infants were premature, similar to other reports.[6,15] 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 +IABP (×5 days) | VV | VV | VV | VV | VV | VV |
| PF ratio prior cannulation | 56 | 55 | 69 | 66 | 100 | 66 | 60 | 54 | 62 |
| RESP score[5] | 5 | 3 | 4 | 0 | 6 | 5 | 4 | 4 | –1 |
| Cannulation location | Fem (25F)→ Fem (21F) | Fem (19F)→ Fem (21F) | Fem (25F)→ Fem (21F) | RIJ–Dual Lumen (31F) | Fem (23F)→ RIJ (20F) | Fem (25F)→ RIJ (19F) | RIJ – 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, changed to Bivalirudin (suspicion of HIT) | Heparin |
| Anticoagulation parameters | PTT (60–90s) | PTT (60–90s) | PTT (60–80s)/ Anti-Xa (0.25–0.3)/TEG (R) 2–3 baseline | PTT (60–90s)/ TEG (R) 2–3 baseline | PTT (60–80s) | Anti-Xa (0.2–0.4) | PTT/TEG (various aims) | PTT (60–80s)/ Anti-Xa (0.25–0.3)/TEG (R) 2–3 baseline | PTT (60–90s)/ TEG (R) 2–3 baseline |
| Complications on ECMO | 1. Circuit clotted on Heparin<br>2. Transient AKI<br>3. Oxygenator changed for fibrin deposition | 1. Inotropes used<br>2. Right sciatic nerve high-grade stretch injury with foot drop | 1. Inotropes used<br>2. SIADH<br>3. CINMP | 1. Vasodilators required<br>2. Hyperbilirubinemia | Tension pneumothorax before and on ECMO | 1. Surgical site bleeding<br>2. Bacterial pneumonia<br>3. Oxygenator clotted | None | 1. Inotropes used<br>2. Vaginal bleeding<br>3. Infection | 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 | 1. Remdesivir (started pre-ECMO)<br>2. Systemic steroids | Ribavirin | 1. Placebo arm—Remdesivir (Remdesivir after study unblinded started after decannulation) | Convalescent plasma | 1. Remdesivir—continued from before ECMO<br>2. Convalescent plasma RCT | 1. Remdesivir continued from before ECMO<br>2. Convalescent plasma | 1. Cytosorb<br>2. Systemic steroids | 1. Systemic steroids<br>2. Convalescent plasma | Systemic steroids |
| Post ECMO complications | Bilateral lower extremities DVT (former ECMO site) | Vaginal bleeding | None | None | None | 1. Left common femoral vein DVT (former ECMO site)<br>2. Surgical site exploration for bleeding | GBS | None | Recannulation 15 days after decannulation,<br>2nd ECMO run 10 days in duration, vented *via* trach |
| Maternal survival to hospital discharge | Yes | Yes | Yes | Yes | Yes | Yes | Yes | Pending | Pending |

#Data not available.

AKI, acute kidney injury; CIPNM, 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.

**Table 3. Newborn/Fetal Characteristics at Time of ECMO**

| Patient/Center | 1/A | 2/A | 3/B | 4/C | 5/D | 6/E | 7/F | 8/B | 9/C |
|---|---|---|---|---|---|---|---|---|---|
| Fetal monitoring during ECMO (CTG/US/ other/none) | Postpartum ECMO | Postpartum ECMO | Postpartum ECMO | CTG and US | Postpartum | Postpartum ECMO | Postpartum ECMO | Postpartum ECMO | CTG and US |
| APGAR (1/5 minutes) | 7/8 | 8/9 | 1/3 | * | * | 2/2 | 6/7 | 1/4 | 1/3 |
| Gestational age | 30+3 | 35+2 | 29 | 23 | 33 | 30 | 37+3 | 25+2 | 32+6 |
| Admission to NICU | Yes | * | Yes | * | * | Yes | Yes | Yes | Yes |
| COVID status | Negative | Negative | Negative | * | * | Negative | Negative | Negative | Negative |
| Congenital abnormalities | None | None | None | * | * | None | None | None | PFO |
| Mechanical ventilation | Yes | No | Yes | * | * | Yes | No | Yes | Yes |
| Vasoactives | No | No | Yes | * | * | No | No | Yes | No |
| Newborn survival to hospital discharge | Yes | Yes | No | Yes† | * | Yes | Yes | Pending | Yes |

*Data not available (local IRB restricted use).
†Delivered 106 days post ECMO decannulation.
CTG, cardiotokogram; PFO, persistent foramen ovale; US, ultrasound.

## Conclusion

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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