NEWS AND VIEWS

Perinatal outcomes of pregnant women with severe COVID-19 requiring extracorporeal membrane oxygenation (ECMO): a case series and literature review

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Abstract

Purpose Pregnant women with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection have a higher risk of hospitalization, admission to intensive care unit (ICU) and invasive ventilation, and of acute respiratory distress syndrome (ARDS). In case of ARDS and critical severe coronavirus disease 2019 (COVID-19), the use of extracorporeal membrane oxygenation (ECMO) is recommended when other respiratory support strategies (oxygen insufflation, non-invasive ventilation [NIV], invasive ventilation through an endotracheal tube) are insufficient. However, available data on ECMO in pregnant and postpartum women with critical COVID-19 are very limited.

Methods A case series of three critically ill pregnant women who required ECMO support for COVID-19 in pregnancy and/or in the postpartum period.

Results The first patient tested positive for COVID-19 during the second trimester, she developed ARDS and required ECMO for 38 days. She was discharged in good general conditions and a cesarean-section [CS] at term was performed for obstetric indication. The second patient developed COVID-19-related ARDS at 28 weeks of gestation. During ECMO, she experienced a precipitous vaginal delivery at 31 weeks and 6 days of gestation. She was discharged 1 month later in good general conditions. The third patient, an obese 43-year-old woman, tested positive at 38 weeks and 2 days of gestation. Because of the worsening of clinical condition, a CS was performed, and she underwent ECMO. 143 days after the CS, she died because of sepsis and multiple organ failure (MOF). Thrombosis, hemorrhage and infections were the main complications among our patients. Neonatal outcomes have been positive.

Conclusion ECMO should be considered a life-saving therapy for pregnant women with severe COVID-19.

Keywords COVID-19 · SARS-CoV-2 · Pregnancy · ECMO · ARDS

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Introduction

Coronavirus disease 2019 (COVID-19) is a respiratory disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), a virus first described in December 2019 and classified in the same subgroup as the severe acute respiratory syndrome coronavirus 1 and the Middle East respiratory syndrome coronavirus [1]. Pregnant women are considered a high-risk group for SARS-CoV-2 infection. In fact, physiological changes occurring during pregnancy on the immune, respiratory and cardiovascular systems and on coagulation may promote disease progression [2]. Prognostic factors for poor outcome during severe COVID-19 in pregnancy include advanced maternal age (OR 1.8), high

body mass index [BMI] (OR 2.4), preeclampsia [PE] (OR 6.4), pre-existing diabetes (OR 2.5) and chronic hypertension (OR 2) [3]. Compared with non-pregnant women of reproductive age, pregnant women with COVID-19 are less likely to report symptoms; however, they seem to be more likely to need hospitalization, admission to an intensive care unit (ICU) and invasive ventilation and to experience acute respiratory distress syndrome (ARDS) [4, 5]. Based on the severity of the disease, patients may require different respiratory support strategies that are gradually escalated until the highest treatment needed, such as oxygen insufflation, non-invasive ventilation [NIV] including high-flow nasal oxygen therapy, invasive ventilation through an endotracheal tube and extracorporeal membrane oxygenation (ECMO). In case of ARDS and critical COVID-19, the World Health Organization (WHO) recommends the use of ECMO, when other treatment options are insufficient [1, 6]. During ECMO, blood is drained, diverted to a membrane system and then returned to the patient, providing respiratory and/or hemodynamic support. The ECMO circuit consists of a venous drainage cannula, a blood pump, an oxygenator and a reinfusion cannula, which may be positioned either in the arterial or venous circulation. In the first case, the circuit is called veno-arterial (VA) ECMO and guarantees both cardiac and respiratory support, whereas in the latter case, it is called veno-venous (VV) ECMO and provides only respiratory assistance [7].

Although the use of ECMO for critical cardiopulmonary failure has been rising over the past few years in general population [8], its role in pregnant and postpartum patients remains controversial. A recent meta-analysis on the use of ECMO in pregnant and postpartum patients with H1N1-related ARDS demonstrated maternal and fetal survival rates of more than 60% [9]. Other studies revealed that pregnant and peripartum patients supported on ECMO for different indications had survival rates ranging from 70 to 80% [10–12], that are better than the survival rates reported for ECMO consistent with the ones observed in the general population [13]. Iatrogenic complications associated with ECMO in pregnant patients were consistent with the general population including bleeding, deep venous thrombosis and vascular complications, while the most commonly reported fetal complications are preterm delivery and neonatal intensive care unit (NICU) admission [14]. Data on ECMO in pregnant and postpartum women with critical COVID-19 are scant. In these case series, we report maternal and fetal outcomes of three critically ill women who required ECMO support for COVID-19 during pregnancy and/or postpartum period.

Case 1

A 27-year-old Chinese gravida 2 para 1 at 18 weeks and 6 days of gestation without significant past medical history, except for episodes of uncomplicated urinary tract infections (UTIs) and a previous CS, presented to our hospital reporting 3 days of cough, fever and dyspnea. She had a positive nasopharyngeal (NP) polymerase chain reaction (PCR) test for SARS-CoV-2 2 days before admission. In the previous pregnancy, 7 years before, she underwent a CS at term for labor dystocia. Before COVID-19, the present pregnancy had been uncomplicated. On admission, chest radiography (CXR) showed patchy infiltrates suggestive of pneumonia. She was treated with oxygen, Low-Molecular-Weight-Heparin (LMWH) at prophylactic dose (4000 IU), ceftriaxone and paracetamol. During the second day from admission, her condition worsened, and she was transferred to the COVID-center of our tertiary care institution. On COVID-center admission, she was tachypneic and diaphoretic. Increased levels of serum procalcitonin [PCT] (5.81 ng/ml, normal range < 0.5 ng/ml) and bilateral basal lung opacification at chest ultrasound made suspicion of bacterial superinfection. She was placed on high-flow nasal cannula (HFNC) [fraction of inspired oxygen [FiO_2] 80%–40 Lt/min] and treated with dexamethasone, pantoprazole, LMWH, piperacillin-tazobactam and azithromycin. Despite HFNC, oxygen saturation (SaO_2) was 76–78%, and the respiratory rate (RR) was 45–50 breaths per minute (bpm). Several attempts of NIV were performed to improve SaO_2; however, she poorly tolerated NIV. Lung's capacity for gas exchange was compromised as suggested by the arterial oxygen partial pressure (PaO_2)/fractional inspired oxygen ($FiO2$) [P/F] ratio < 100. Because of severe ARDS according to Berlin criteria which categorizes ARDS as mild (P/F 201–300), moderate (P/F 101–200), and severe ($P/F < 100$) [15], the patient was transferred to the ICU. On arrival, she was intubated and proned according to the COVID-center protocol [16, 17]. Given worsening hypoxia on maximum ventilatory support, the patient was placed on VV-ECMO. At this time, she was 19 weeks and 6 days pregnant. As methicillin-resistant Staphylococcus aureus (MRSA) was isolated in the Broncho-Alveolar Lavage (BAL) fluid, Vancomycin therapy was administered for 15 days. Abdominal ultrasound showed findings suggestive for cholecystitis, subsequently regressed, and of right grade I–II hydroureteronephrosis, stable in subsequent controls. During ECMO, fetal conditions were monitored two times per week with ultrasound: fetal growth and feto-maternal Doppler velocimetry were normal and appropriate for gestational age. Moreover, an ultrasound scan at 21 weeks and 2 days of gestation was performed to check for fetal anomalies, showing normal fetal anatomy.

In the following weeks, there was a slow and gradual recovery of respiratory function. Since episodes of psychomotor agitation occurred during sedation weaning, olanzapine therapy was started. In preparation for sedation weaning, the patient underwent tracheostomy and ECMO support was interrupted after 38 days. Echocardiogram performed after ECMO removal documented fibrinous deposits in the right atrium; therefore, LMWH at anticoagulant dosage (8000 IU/die) was continued until delivery. After 1 month, her PCR NP swab for SARS-CoV-2 resulted negative. At 27 weeks and 1 day of gestation, the patient was transferred to our obstetrics ward. At admission, she was alert, conscious, cooperative, stable, and oriented for times on minimal breathing support with oxygen therapy (1 L/min). Obstetric ultrasound showed an appropriate for gestational age fetus (AGA) with normal fetal-placental Doppler velocimetry and normal amniotic fluid index, although a slight reduction in the growth velocity of abdominal circumference was documented. After 2 days of hospitalization, the patient voluntarily discharged against our advice and was followed up on an outpatient clinic for high-risk pregnancies, in collaboration with pulmonologists and cardiologists. At 33 weeks and 5 days of gestation, the transesophageal ultrasound confirmed the presence of a thrombus near the oval fossa of about 15 mm × 19 mm, without obstruction of the caval outlets. At 37 weeks and 1 day of gestation, she was admitted again to our obstetric ward to perform a scheduled CS because of the previous CS, after the suspension of LMWH which was resumed in the postpartum period at therapeutic dose. The puerperium was uncomplicated, and the patient was discharged, with her baby, 5 days after delivery, planning cardiological and gynecological follow-up visits.

At delivery, the baby weighed 2670 g (Fenton 36%) and the Apgar at 1 and 5 min was 9 and 9, respectively. The neonate did not show any complications, his NP swabs for SARS-CoV-2 were negative and he was discharged in good general condition.

Case 2

A 38-year-old gravida 2 para 1 women, without significant past medical history and reporting a previous uncomplicated pregnancy resulted in a spontaneous vaginal delivery at term, presented at 28 weeks and 4 days of gestation endorsing fever and myalgia from 6 days. She was admitted because of the onset of dyspnea and a positive PCR NP swab for SARS-CoV-2. Before COVID-19, the pregnancy was complicated by gestational diabetes (GDM) in good compensation with diet. C-reactive protein [CRP] and D dimer were elevated at the first evaluation and lung ultrasound showed signs of bilateral basal interstitial disease. At the time of admission, she underwent NIV (FiO$_2$ 65% and positive end expiratory pressure [PEEP]6 cm H$_2$O) and she was treated with LMWH, paracetamol and intravenous dexamethasone (8 mg daily) because of severe COVID-19. Because of the worsening respiratory conditions (*P/F* 120), the onset of tachypnea (RR30 bpm) and the increase of inflammation indices (CRP 239 mg/L [normal range < 5 mg/L], PCT 30, 90 ng/ml [normal range < 0.5 ng/ml]), she was transferred to the ICU where she was intubated and proned. Doppler ultrasound showed thrombosis of the left basilica and subclavian vein. Given worsening hypoxia on maximum ventilatory support, the patient was placed on VV-ECMO via bilateral femoral veins at 30 weeks and 1 day of gestation. In the following days, a further worsening of the pulmonary function occurred with a gradual reduction in lung volumes and complete dependence from ECMO. Because of the onset of pleural effusion on CXR, a right chest drain was placed. As a methicillin-susceptible Staphylococcus aureus (MSSA) was isolated in the BAL fluid, antibiotic therapy with oxacillin was administered. At 30 weeks and 6 days of gestation, a copious hemoptysis occurred, and the patient underwent tracheostomy. During the hospitalization, serial obstetric ultrasound examinations were performed, showing normal fetal growth, amniotic fluid and Doppler velocimetry of the umbilical and middle cerebral arteries. After preterm prelabor rupture of the membranes (PPROM), the patient experienced a precipitous premature vaginal delivery at 31 weeks 6 days of gestation. The obstetric and neonatal teams were quickly alerted for maternal and newborn care. The obstetric team recorded a blood loss of 700 cc; however, postpartum hemorrhage was probably more severe as blood loss was not quantitatively assessed before its arrival. Postpartum hemorrhage was treated with uterotonics (oxytocin) and instrumental revision of uterine cavity, as tissue residues were suspected on ultrasound scan. Because of the severe condition of the patient, we avoided prostaglandins use and we preferred to reduce bleeding by placing the Bakri Balloon which was removed after 24 h. Cabergoline was also administered to inhibit lactation. After delivery, there was a progressive improvement of vital signs and daily ECMO weaning attempts were performed with definitive decannulation on the twentieth day postpartum. The weaning from sedatives was difficult because of several episodes of psychomotor agitation and anxiety for which antidepressant therapy with paroxetine was undertaken. Antibiotic therapy with vancomycin was started the day before the delivery and continued for up 15 days because of the increase of inflammation indices, the onset of fever and the isolation of MRSA in the BAL fluid. Moreover, tazobactam-piperacillin therapy was administered from ICU admission up to 5 days postpartum due to the isolation of Escherichia coli in blood cultures and BAL fluid.

Thrombotic complications worsened in the postpartum period. In particular, thrombosis of the right jugular vein

extended to the homolateral anonymous vein up to its confluence with the superior vena cava and thrombosis on the right side of the ECMO cannula in the subhepatic tract of the inferior vena cava were reported. The computed tomography pulmonary angiogram (CTPA) also revealed a pulmonary embolism associated with an infarction area affecting the posterior basal segment of the right lower lobe. Therefore, anticoagulant therapy with warfarin (2.5 mg daily) was started and continued for up to 3 months after delivery. At the last Doppler ultrasound before discharge, recanalization of the right subclavian vein and minimal thrombosis of the internal jugular vein were described. The patient was discharged about 1 month after delivery in good clinical condition and good respiratory exchange ($P/F > 300$) with autonomous hemodynamics.

At the time of delivery, the baby weighed 1880 g (83% Fenton) and was promptly managed with cardiopulmonary resuscitation. Due to continued poor oxygenation and intermittent respiratory effort, the infant was intubated. The 1- and 5-min Apgar's scores were 1 and 7, respectively. Immediately after delivery, he was transferred to NICU and was extubated the following day. His need of oxygen progressively decreased until the fifth day of life when he was completely weaned. Because of high International Normalized Ratio (INR) value, the neonate was transfused with concentrated red blood cells and fresh frozen plasma. Brain Neonatal Magnetic Resonance Imaging (MRI) 1 month after birth showed normal cerebral findings [18]. Swabs for SARS-CoV-2 were all negative and the neonate was discharged at 37th days of life in good general condition, stable vital parameters and with a weight of 4150 g.

Case 3

A gravida 2 para 1 43-year-old pregnant woman with pre-pregnancy BMI of 38 was admitted to our obstetric ward at 38 weeks and 2 days of gestation reporting cough for 1 week and a positive PCR NP swab for SARS-CoV-2 from the day before. This was a pregnancy obtained by heterologous ICSI. On the admission, the patient was eupneic, SaO_2 in ambient air was 98%, the blood pressure (BP) 139/85 mmHg and the RR 14 bpm. The following day, the patient experienced worsening of symptoms including the onset of dyspnea. Therefore, the obstetrician's team opted for delivery via CS taking into account the unfavorable Bishop's score as well as the patient's multiple obstetric risk factors for severe COVID-19 (obesity and advanced maternal age).

At the time of delivery, the baby weighed 3080 g (53% Fenton). The 1- and 5-min Apgar's scores were 9 and 10, respectively. The neonate tested positive for SARS-CoV-2 14 days after delivery, without any clinical consequence, and

was discharged at 34th days of life in good general condition, stable vital parameters and negative SARS-CoV-2 swab.

On hospital day 5, maternal condition deteriorated: the dyspnea worsened and the SaO2 was 88% on ambient air. Arterial blood gas (ABG) demonstrated a pH of 7, 48, partial pressure of carbon dioxide (pCO_2) of 31 mmHg and partial pressure of oxygen (pO_2) of 54 mmHg. CXR showed parenchymal thickening in the right apical and basal areas. The patient was treated with oxygen (nasal cannulas, 4 l/min), LMWH 6000 IUx2/die, and cabergoline to inhibit lactation. Because of the respiratory failure associated with respiratory alkalosis, she was transferred to the COVID-19 center of our institution. On admission, the patient appeared oriented, cooperative with a SaO2 of 95% (4 l O_2/min) and a RR of 21 bpm. Lung ultrasound showed the presence of A lines at the left apex, several small subpleural thickenings and confluent B lines in bilateral mid-basal area. Oxygen therapy with a Venturi mask and intravenous steroids (dexamethasone 8 mg/die) were administrated. Despite the ongoing therapy, the patient showed a progressive worsening of respiratory exchanges and she needed the use of NIV. Therapy with tocilizumab was also performed. Because of the further worsening of respiratory exchanges and the worsening of parenchymal thickening at CXR, the patient was transferred to the ICU after 7 days. On the arrival, she was proned, sedated and intubated. Because of the ARDS ($P/F < 100$) and the deterioration of clinical parameters, she was placed on VV-ECMO. In the following days, blood exams showed a progressive increase of inflammation indices, anemia with signs of hemolysis, thrombocytopenia, low level of antithrombin and fibrinogen, and a deterioration of liver and renal function. Pseudomonas aeruginosa, Klebsiella oxytoca, and Klebsiella aerogenes were isolated from blood cultures and *Acinetobacter baumannii* from bronchial aspirate samples; therefore, targeted antibiotic and antifungal therapy was administered. Due to the progressive worsening of renal function, the patient underwent dialysis with continuous renal replacement therapy (CRRT). Pleural drainages were also placed for the detection of bilateral pleural effusion. Chest computed tomography (CT) showed pleural empyema and a right thoracotomy was performed. Dehiscence of the thoracotomy incision was then treated with Vacuum Assisted Closure Therapy (Vac Therapy) and by removing the necrotic tissues from the wound site. Several episodes of oral and thoracotomy bleeding occurred. Electroencephalography (EEG) traces were substantially suppressed, and abnormal somato-sensory evoked potentials (SSEPs) were documented (waveform with low voltage and increased latency were recorded on the left hemisphere; the components of the brachial plexus, cervical spinal and lemniscal plexus on this side are not recognizable). During hospitalization, the respiratory function was totally supported by ECMO, the patient was repeatedly transfused with

concentrated red blood cells for severe anemia and hemo-dynamics was supported by noradrenaline and dobutamine. 143 days after the CS, the patient died because of sepsis and multiple organ failure (MOF).

Discussion

We described three cases of severe ARDS in pregnancies complicated by SARS-CoV-2 infection. Due to severe respiratory failure, two of them required ECMO during pregnancy and one in the postpartum period. In the two cases who underwent ECMO during pregnancy, excellent results were obtained. In the first case, ARDS occurred in the second trimester and the patient remained in ECMO for 38 days. She returned to normal respiratory function and delivered at term. In the second one, ECMO was required in the third trimester. The patient experienced a spontaneous delivery at 31 weeks and 6 days of gestation, and she was discharged about 1 month later in good general conditions. It was described that both COVID-19 [19, 20] and ECMO [14, 21] are risk factors for preterm labor; therefore, clinicians should remain vigilant for the possibility of spontaneous preterm labor in these patients. These two patients had no risk factors for severe COVID-19; on the contrary, the last patient, infected with SARS-CoV-2 during the third trimester and undergoing ECMO in the postpartum period, was obese and of advanced age. She had a worse clinical course and she died 143 days after CS because of sepsis and MOF.

Although a recent large prospective multicenter study showed that ICU admission due to COVID-19 during pregnancy may happen without identifiable risk factors [1], it is well known that obesity, hypertension, diabetes mellitus, maternal age greater than 40 years, and third-trimester pregnancy infection are the main risk factors for death and severe disease [22]. Therefore, admission, preferably at a center that has obstetrics services and an adult and neonatal ICU, should be considered in COVID-19 pregnant women with risk factors for decompensation, not only in case of severe disease, but also in case of mild and moderate one [23]. It is also known that CS may increase postpartum complications, including infection, hemorrhage and thromboembolic disorders [24]. Martínez-Perez et al. [25] found that CS in COVID-19 patients was associated with an increased risk for clinical deterioration compared to vaginal birth (22% vs 5%). Therefore, CS may have contributed to worsening the clinical condition of the third patient. Tables 1 and 2 summarize baseline maternal characteristics and the course of the infection in our patients, respectively.

ECMO in pregnant patients requires an accurate evaluation of risks and benefits for both mother and fetus. In fact, ECMO is associated with serious maternal complications, including bleeding (due to both the continuous

Table 1 Baseline maternal characteristics of our pregnant women with severe COVID-19

	CASE 1	CASE 2	CASE 3
Age	27	38	43
Parity	G2P1	G2P1	G2P1
Conception	Spontaneous	Spontaneous	ICSI (embryo-donation)
BMI (Kg/m^2)	23	22	38
Comorbidities	–	–	Obesity
Pregnancy diseases	–	GDM	–

anticoagulation and platelet dysfunction), thromboembolism (due to thrombus formation within the extracorporeal circuit), neurologic injury, hemolysis, thrombocytopenia, cannulation-related complications (e.g., vessel perforation, arterial dissection, distal ischemia, and incorrect location), pulmonary hemorrhage and cardiac thrombosis [26]. In our case series, the first patient experienced cardiac thrombosis, the second one bleeding (postpartum hemorrhage) and thromboembolism and the third one bleeding, hemolysis and thrombocytopenia (Table 3). Moreover, all patients experienced infectious complications; in particular, sepsis worsened the clinical condition of the third patient. Infections are common during ECMO and have a significant impact on the mortality rate. It was reported that the prevalence of hospital-acquired infections during ECMO is about 10–12%; however, bacterial superinfections are quite common in patients with severe COVID-19 disease independently from ECMO [27]. According to the available literature, our data showed that the risk of infections increases along the duration of the ECMO treatment. Other ECMO-specific factors predisposing to infections include the severity of illness in ECMO patients, the high risk of bacterial translocation from the gut, and ECMO-related impairment of the immune system [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 rate with the use of ECMO in peripartum women [28]. However, risk factors for severe COVID-19 (obesity, advanced age, pre-existing diabetes and chronic hypertension) could be also associated with worse outcomes after ECMO, as for the last patient of our case series.

As mentioned above, thrombosis is one of the most common and feared complications of ECMO support. In fact, ECMO requires contact between blood and nonendothelial surfaces and results in coagulation and fibrinolytic pathway activation and a complement-mediated inflammatory response. Heparin is the current international standard for anticoagulation during ECMO [26]. However, there is no consensus on heparin monitoring or therapeutic targets and considerable inter-institutional variability exists [29].

Table 2 COVID-19 infection course in our patients

	CASE 1	CASE 2	CASE 3
Gestational age of COVID-19 infection (weeks)	18 + 6	28 + 4	38 + 2
Symptoms (admission)	Cough, fever, dyspnea	Fever, myalgia, dyspnea	Cough, dyspnea
Treatment	O2, LMWH, dexamethasone, antibiotics, paracetamol	O2, LMWH, dexamethasone, antibiotics, paracetamol	O2, LMWH, dexamethasone, antibiotics, antifungal, paracetamol, tocilizumab
Gestational age of ECMO support (weeks)	19 + 6–26 + 2	30 + 1–20th day postpartum	1 week postpartum until death (143 days after CS)
Maternal death	No	No	Yes

Table 3 ECMO complications in our pregnant women with severe COVID-19

	Case 1	Case 2	Case 3
Infection	×	×	×
Thromboembolism	–	×	–
Bleeding	–	×	×
Hemolysis	–	–	×
Thrombocytopenia	–	–	×
Pulmonary hemorrhage	–	×	–
Cardiac thrombosis	×	–	–
Neurologic injury	–	–	×
Complications of cannulation	–	–	–

Table 4 Perinatal outcomes

	Case 1	Case 2	Case 3
Gestational age of delivery (weeks)	37 + 1	31 + 6	38 + 3
Type of delivery	CS	Vaginal	CS
Neonatal weight (g)	2670	1880	3080
Apgar 1–5'	9–9	1–7	9–10
NICU admission	No	Yes	No
NP swabs	Negative	Negative	Positive

COVID-19 and ECMO may further enhance hypercoagulability in pregnant individuals, with a consequent greater risk for thromboembolism [30]; therefore, standardized protocols for the use of the antithrombotic therapy in pregnant women on ECMO should be created.

Fetal survival after maternal ECMO is reported to be around 70% [14]. The most common fetal complications include preterm delivery and premature rupture of membranes (PROM) and NICU admission [14, 28], while available data about the risk of bleeding in the neonate are conflicting [11, 14, 31]. Our experience confirmed the increased risk of preterm birth during ECMO. Moreover, elevated INR values were found in the second neonate, who was born preterm. We hypothesize that, due to the necessity for anticoagulation of the mother while on the ECMO circuit, the neonates had prolonged exposure of in utero anticoagulant [32]. However, it cannot be concluded that it is an effect of maternal ECMO since vitamin K deficiency is a common finding in preterm infants and heparin does not cross the placenta [33]. Therefore, evaluation for abnormal coagulation studies may be advisable in neonates born from mothers underwent ECMO. Current evidence shows that the risk of vertical transmission of SARS-CoV-2 is low [34]. Among our cases, all neonates had negative swabs for SARS-CoV-2 at the time of delivery, but the third one tested positive after 14 days, whereas he had no post-natal contact with the mother. Because of the lack of a standardized definition, vertical transmission cannot be excluded in the last case. In accordance with the data reported by the Italian Obstetric Surveillance System (ItOSS) [35], neonatal outcomes of our case series are reassuring as all infants had no short-term clinical consequences and were discharged in good general condition (Table 4).

Society for Maternal–Fetal Medicine (SMFM) guidelines [36] state that ECMO is not in and of itself an indication for delivery; however, delivery may be indicated for immediate life-threatening obstetrical concerns to either the mother or fetus/neonate, though ECMO should not be delayed to effect a delivery if no such immediate obstetrical indications exist. Moreover, in case of critically ill COVID-19 parturient with refractory hypoxemia despite mechanical ventilation, these guidelines recommend different management based on gestational age: delivery after 32 weeks of gestation and ECMO before 32 weeks of gestation. Since the success of ECMO as a salvage therapy is often dependent on its early use, potential transfer to an ECMO expert center should be considered in patients with critical disease failing conventional therapy [23]. Moreover, the timing of delivery in pregnant women in ECMO should be decided based on the maternal and fetal conditions and on gestational age [36].

Conclusion

Pregnancy represents a risk factor for infections. As COVID-19 continues to impact thousands of patients worldwide daily, including pregnant women, and despite limited data and resources, pregnancy should not be considered a contraindication for ECMO support for COVID-19 ARDS. In fact, ECMO may increase the survival rates of both mother and fetus and should be considered a life-saving therapy for pregnant women with severe COVID-19. However, it is important to better understand the best strategies in management and therapies considering the dyad mother–fetus.

Selection of ECMO type, cannulation strategies, timing of ECMO implantation, and subsequent management are experience related and challenging due to the lack of guidelines. Prospective observational studies with long-term outcome follow-up would be useful to further clarify current findings.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

Consent to participate Informed consent was obtained from all individual participants included in the study.

Consent to publish The participant has consented to the submission of the case report to the journal.

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