

# Management of life-threatening acute respiratory syndrome and severe pneumonia secondary to COVID-19 in pregnancy: a case report and literature review

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## Abstract

Through this case, we present the thought process, team-based strategy and sequel of managing a complex, critically ill pregnant with ARDS and COVID-19 pneumonia. This case also confirms the feasibility of using convalescent plasma and ECMO during early postnatal period in acutely ill parturient with respiratory failure.

## TITLE PAGE

**Title** Management of life-threatening acute respiratory syndrome and severe pneumonia secondary to COVID-19 in pregnancy: a case report and literature review

**Short title** Management of critically ill obstetric patient diagnosed with COVID-19

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## Expertise

Our team comprises of, experts from obstetrics, critical care medicine, emergency medicine, infectious disease, clinical pharmacy, health policy and research. We have worked together previously with a proven track record of researching fields of obstetric and perinatal population.

## Case Registration

This case has been registered as a preprint at research square. DOI: 10.21203/rs.3.rs-36328/v1

This case has been presented in accordance with CARE case report guidelines.

## Keywords

COVID-19, maternal, pandemic, perinatal, ECMO, convalescent plasma, pharmacological interventions.

## Key Clinical Message

Evidence based treatment involving multidisciplinary decision making is warranted to treat COVID-19 in pregnancy. This case confirms the feasibility of using convalescent plasma and ECMO during early postnatal period in critically ill patients.

## Background

The novel coronavirus disease 2019 (COVID-19) has been declared as a ‘pandemic outbreak’ and public health emergency of utmost international concern (1). Over 8.2 million confirmed cases and more than 446,392 deaths (as of 17/06/2020), the pandemic continues to harm significant number of people worldwide. Approximately, 5% of the infected cases are complicated by hypoxia and respiratory failure (2). The reported prevalence of severe pneumonia among Chinese patients was as high as 5% with an estimated mortality rate of 2.3 – 3.83% (3-5). Partial immune suppression, physiological and anatomical changes and multiple interaction with the healthcare system during pregnancy, presents an unprecedented challenge in managing this vulnerable population (2,6,7).

Previous infectious outbreaks such as, H1N1 influenza virus, Zika virus, severe acute respiratory syndrome corona virus (SARS-CoV) and Middle East respiratory syndrome corona virus (MERS-CoV) have had significant adverse impact on maternal as well as perinatal outcomes (6,8). Data collated from these patients demonstrated higher rates of intensive care unit admission, intubation, and death compared with non-pregnant patients (7,9). Anecdotal evidence demonstrates 0.1–0.2% of all pregnancies are complicated by respiratory failure (10,11).

Till date, no pharmacological intervention has been proven effective to treat COVID-19. Despite promising outcomes, no high-quality evidence exists for the safety and efficacy of convalescent plasma in treating SARS-CoV2 infection. Inconclusive, limited clinical experience has been reported supporting the use ECMO in the management of COVID-19 (12,13). In the absence of any definitive therapy, the cornerstone of COVID-19 treatment varies from symptomatic ambulatory care management to intensive care treatment (14).

Over the past decade, the healthcare system in Qatar has transformed to a world class public health system providing free or highly subsidized healthcare to all its citizens and residents (15-17). The tiny Arabian Peninsula is also reported to have one of the lowest COVID-19 fatality rates in the world estimating less than 0.07% (18).

## Case Presentation

We present a case of a 33-year old pregnant women at 32 weeks of gestation, was referred to a tertiary care center following 8-day history of malaise, cough, sore throat and shortness of breath. Her past medical history revealed, asthma (>10 years) on inhaled steroids and gestational diabetes. Prior to admission, she was taking vitamins and budesonide and reported no history of allergies to medications. She is non-smoker and no recent travel was reported.

During the current admission, her vital signs were as follows: temperature 37.4°C, heart rate - 98 beats per minute, respiratory rate 25 br/min, blood pressure 98/63 mm Hg, and oxygen saturation (SpO<sub>2</sub>) 90% room air, 96% with nasal canula. She complained of tiredness, lower back ache while breathing, pertinent dry cough and shortness of breath. No obstetric or fetal concerns were noted. All relevant blood tests, nasopharyngeal swab/real-time reverse transcriptase polymerase chain reaction (RtPCR), and chest X-ray were performed (see table 1). Chest X-ray demonstrated patchy ground glass pneumonic infiltrates in both lung fields suggesting clinical correlation for pneumonia (see figure 1). Nasopharyngeal and throat swabs confirmed positive for SARS-CoV-2 infection.

### Insert table 1 : Laboratory values for the first 10 days

Following positive Rt-PCR, on day 1 of the hospital stay the patient was commenced on HMC’s COVID-19 treatment protocol, chloroquine 400 mg once daily for 10 days, azithromycin 500 mg once daily for 10 days, oseltamivir 150 mg twice orally for 10 days, intravenous ceftriaxone 2gm once daily for 10 days. Within few hours, she developed severe hypoxemia and acute respiratory distress (RR: 35 b/min), and was unable to

complete sentences. Considering the maternal acuity and gestational age she was transferred to the intensive care unit of an obstetric specialty care.

The patient was admitted to a negative pressure intensive care room with multi-disciplinary expertise to manage critically ill obstetric patients. Additional oxygen support was provided, non-breather mask 15L/min, with positive end-expiratory pressure (PEEP) at 5 cm H<sub>2</sub>O, and fraction of inspired oxygen (FiO<sub>2</sub>) at 100%. However, no improvement was observed, methylprednisolone 40mg was administered to decrease the host inflammatory responses in the lungs. On day 2, as the patient was not tolerating the non-invasive ventilation (NIV) and complained of uneasiness, shortness of breath with pain while breathing. As a part of the treatment protocol Kaletra® lopinavir/ritonavir (80/20mg) and one dose of Tocilizumab 400mg (for hyper-inflammation caused by cytokine release) were administered. On day 3, considering the deteriorating respiratory functions, a multidisciplinary team including, internists, medical team, obstetric specialty, anesthesiologist decided to intubate her.

As patient required deep sedation to tolerate lung protective ventilation, continuous sedation/analgesia with propofol: 50mcg/kg/min + fentanyl: 5mcg/kg/hr, was administered aiming the Richmond Agitation and Sedation Scale (RASS) (19) more than -4. Despite intubation and other medical interventions, the respiratory functions and static compliance worsened remarkably, and positive end-expiratory pressure (PEEP) and FiO<sub>2</sub> was kept high. The ventilator flow was adjusted as follows, peak pressure: 21mbar, plateau pressure: 20mbar, mean pressure: 14mbar, MV: 10.8L/min, minute volume (MV): 0.8L/min, respiratory rate: 22bpm, VT (tidal volume): 393mL, Resistance (R): 7.6mbar/L/s, Compliance: 119.5mL/mbar, PEEP: 14.7mbar. End-tidal carbon dioxide (EtCO<sub>2</sub>): 29mmHg.

The cardiotocography (CTG) demonstrated no fetal heart acceleration and non-reassuring fetal outcomes anticipated mostly due to maternal hypoxemia. Considering persistent deterioration in maternal respiratory function and signs of fetal distress, it was decided to terminate the pregnancy by cesarean section (C-section). Magnesium sulphate 2gm infusion was commenced for fetal neuroprotection and was monitored for toxicity. The patient underwent an uncomplicated lower segment transverse cesarean section delivering a 1900gms baby boy, with a blood loss of 300ml. As per current recommendations, there was no need for a delayed cord clamping, and the baby was separated from the patient immediately.

On day 4, the patient encountered prolonged QTC intervals anticipated mostly due to hydroxychloroquine /+ Kaletra® lopinavir/ritonavir. Hydroxychloroquine was withheld, and timely monitoring was recommended. The patient encountered life-threatening hypoxia and severe acute respiratory failure post operatively. ECMO team was consulted and veno-venous ECMO bi-femoral cannulation was initiated after consent was obtained from the husband. On day 5, during infectious disease consultation ribavirin was added and 2 units of convalescent plasma was administered to improve her respiratory mechanisms. On day 6, the ECMO team decided to stop cisatracurium and noradrenaline and to wean off sweep gas aiming for oxygen saturation >88% and PH >7.25. Cabergoline 1mg, potent dopamine receptor agonist (to inhibit milk production) was administered to avoid breast engorgement and pain.

On day 14, on ECMO, the liver enzymes were elevated, due to antiviral medications, following which the ribavirin was withheld. The inflammatory markers drastically reduced following administration of methylprednisolone 20mg. On day 18, the patient developed hematuria and hematoma at the C-section wound antibiotics were started, low dose of fibrinogen was replaced. On day 19, the patient developed subcutaneous emphysema due to gram positive galenium bacteria, which was treated cefipime, later changed to piperacillin tazobactam sodium 4500mg. On day 23, following an improved clinical and respiratory functions, ECMO decannulation was performed and was well tolerated. After 24 hrs, the patient was extubated on high flow nasal oxygen (2L), echocardiogram revealed no evidence of infective endocarditis. On day 25, following improved clinical findings, the patient was shifted from the intensive care unit to a step-down unit with continuous monitoring. The patient was clinically stable and was discharged two weeks later.

**Insert Picture 1:** Radiological Findings

**Insert figure 1:** Ventilation flowsheet during hospitalization

## Neonatal summary

Following a preterm delivery, the neonatal APGAR scores documented at 1,5 and 10 minutes were 2, 3, and 7 respectively. However, an hour after delivery, the newborn encountered severe asphyxia and was transferred to neonatal intensive care unit for resuscitation and intubation. The baby received one dose of surfactant and was extubated after 16 hours to nasal continuous positive airway pressure. The newborn was tested twice (14 days interval) for COVID-19 IgG and IgM and was found negative in both the occasions. The baby was discharged on day 14.

## Discussion

We report a multidisciplinary approach to treating and complete recovery of acute respiratory failure and severe pneumonia secondary to SARS-COV2 infection during pregnancy. A plethora of studies have demonstrated the management of mild – moderate cases of SARS-COV2 infection in pregnancy with positive outcomes (2,10,20). However, very few studies have reported the management of critically ill patients, particularly in pregnancy. Pneumonia during pregnancy is often accompanied by hospitalization and critical care management including ventilatory support (20). Although the treatment of pneumonia during pregnancy mirrors that of non-pregnant state, the use of convalescent plasma and ECMO in pregnancy is rare (9,11,21).

The clinical presentations, symptoms and the radiological findings in our case were consistent to previous case reports (3,22,23), of SARS-COV2 infection. A nationwide population-based cohort (n=1942) reported, pregnant women with viral pneumonia (other than COVID-19) demonstrated higher risk of preterm birth, intrauterine growth retardation low birthweight and poor Apgar scores when compared to those without pneumonia (24). Hence, as demonstrated in this case, an early delivery is considered as an alternative for critically ill pregnant women with ARDS.

In terms of therapeutic management, no specific pharmacological agent or vaccine to treat COVID-19 is available (12). Once COVID-19 was confirmed, hydroxychloroquine, azithromycin, oseltamivir, intravenous ceftriaxone and methylprednisolone were administered. Hydroxychloroquine and methylprednisolone are considered safe in pregnancy and have been used extensively to treat COVID-19 (25). However, there is a paucity of evidence regarding the use of antimalarial and antiviral therapy in treating SARS-COV2 infections (26), even in this case, it is unclear if the empirical use of these medications had any role in the recovery of our patient. Tocilizumab (monoclonal antibody IL-6 receptor antagonist) was administered post operatively, due to the deteriorating respiratory functions, hemodynamic instability and persistently elevated inflammatory markers. Several COVID-19 studies have demonstrated improved respiratory functions, and successful recovery in patients receiving one dose, (27-30).

Anecdotal evidence from previous viral infections including Ebola, SARS-CoV, H5N1 avian influenza, and H1N1 influenza suggests the use of convalescent plasma containing neutralizing antibody is effective (31-34). Food and Drug Administration (FDA) has recently approved the use of convalescent plasma to treat critically ill COVID-19 patients (35). A meta-analysis investigating effectiveness of convalescent plasma in SARS coronavirus infection and severe influenza, reported significant reduction in viral loads and mortality (36). In this case the transfusion of convalescent plasma demonstrated improved clinical outcomes, and COVID-19 specific inflammatory markers were significantly improved.

There is a scarcity of evidence behind the use of lung-protective ventilation and ECMO in COVID-19 infection during pregnancy (10). The use of ECMO in pregnancy and postpartum is rare. An estimated 40% of pregnant or postpartum women admitted to ICU are complicated by ARDS or cardiac arrest (37,38). Like previous reports demonstrating improved maternal survival (39,40), the use of VV-ECMO in this patient is expected to have potentially resulted in positive respiratory outcomes and successful recovery. Furthermore, providing adequate rest to lungs using VV-ECMO was necessary to avoid ventilator-associated and oxygen-induced lung injury.

## Conclusion

Through this case, we demonstrate the importance of involving multidisciplinary team in decision making, as balancing maternal complications as well as reassuring fetal wellbeing during such critical period is imperative. We have thus confirmed the feasibility of using convalescent plasma and ECMO during early postnatal period in critically ill obstetric patients with respiratory failure. The use of tocilizumab, convalescent plasma, followed by intensive care management with intubation and ECMO might have potentially contributed to the complete recovery of the mother and the newborn. Whether antimalarials-hydroxychloroquine (in particular), and/or antivirals are effective in treating COVID-19 - remains unknown. Further well-defined studies are necessary to study the effectiveness and safety of plasma transfusion in COVID-19 patients.

## Declarations

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### Conflicting interests

The authors declare that there is no conflict of interest

### Funding

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### Informed consent

Written informed consent was obtained from the patient for their anonymized information to be published in this article and shall be presented on request.

### Ethical approval

Ethical approval to report this case was obtained from the institutional review board at Hamad Medical Corporation.

### Author contribution

All authors have made substantial contribution to the case report. **SY** (Consultant obstetrician) and **MH** (Pharmacy Executive Director) has contributed to the conceptualization of the case report and were responsible for supervision, planning and execution. **SH** is a senior consultant and head of obstetric emergency who was involved in the initial assessment of the case. **ZM** is the primary obstetrician (senior consultant) who was involved in treating the case along with **TR & IB** (obstetric consultant) and **MJ** (specialist obstetrician). **AA** is a senior research fellow and ECMO consultant who managed the case in intensive care unit. **AM** is a senior consultant at the emergency department, involved in the initial management of the case. **MM** is infectious disease consultant and provided valuable input to the manuscript and managing the COVID-19 and related complications. **AT** and **FM** have contributed by interpreting the laboratory and radiological findings. **HS** is consultant neonatologist who managed the newborn in the NICU. **PR** and **WK** are pharmacy administrative, involved in the acquisition of the financial support, scientific review and verification for the validity of content. **BT** is a clinical pharmacy specialist and doctoral researcher who took the lead in writing the manuscript in consultation with **SY, MH, AM, PR, FM**. All authors discussed, reviewed and edited the case report. All authors agreed to the final version prior to its submission.

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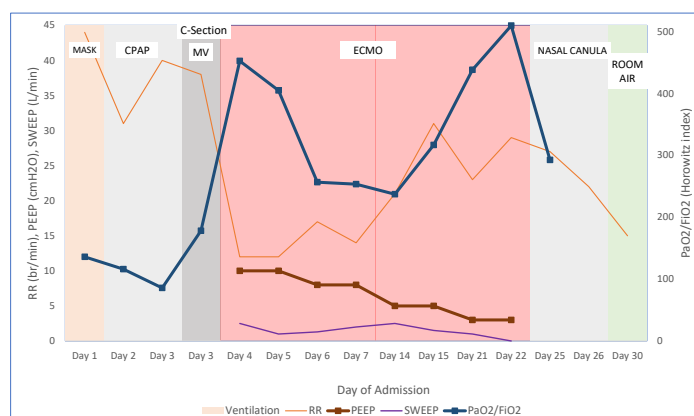
## List of Figures

### Figure 1: Ventilation flowsheet during hospitalization

RR: Respiratory rate (breaths/min), PEEP- Positive end expiratory pressure (centimeters of water), SWEEP- ECMO gas flow (Liters/min), PaO<sub>2</sub>/FiO<sub>2</sub>- Horowitz index – Partial pressure of oxygen arterial/ Fraction of inspired oxygen, ECMO- Extra corporeal membrane oxygenation, MV- Mechanical ventilation

### Picture 1: Chest X-ray demonstrating ARDS

Figure 1



## Hosted file

Figures.pdf available at <https://authorea.com/users/338958/articles/465317-management-of-life-threatening-acute-respiratory-syndrome-and-severe-pneumonia-secondary-to-covid-19-in-pregnancy-a-case-report-and-literature-review>