Access this article online

Quick Response Code:

Website: www.pogsjournal.org

DOI: 10.4103/pjog.pjog_31_24

Successful use of hemoperfusion in a pregnant woman with COVID-19 critical infection

Jean Michael Losaria Castillo[1], Lara Marie David Bustamante[1], Bianca King de la Vega[1]

Abstract:

COVID-19 is an infectious disease caused by the severe acute respiratory syndrome coronavirus 2. Although not well established, COVID-19 infection carries a great effect on pregnant patients with increased severity compared to the nonpregnant population. Cytokine storm is a severe immune reaction and is one of the pathogeneses of COVID-19 infection. Studies have shown the benefit of hemoperfusion in managing cytokine storm, but the use in the pregnant population remains limited. We report the case of a 41-year-old pregnant woman at 25 weeks and 5 days age of gestation infected with COVID-19 presenting with difficulty of breathing and desaturation and then underwent hemoperfusion which improved her clinical condition.

Keywords:

COVID-19, cytokine storm, hemoperfusion, pregnancy

Introduction

In 2020, the World Health Organization declared COVID-19, a novel coronavirus disease that originated in China, as a pandemic.[1] This is an infectious disease caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2 virus) and is transmitted from person to person via aerosol droplets and contact routes. This infection affects different people in different ways and most will develop mild-to-moderate symptoms that may include fever, cough, anosmia, ageusia, sore throat, headache, body malaise, diarrhea, and in severe cases, difficulty of breathing.[1]

This virus threatens the general population; however, there are some special populations that are at higher risk for susceptibility and severe disease such as pregnant women. The effect of COVID-19 infection on pregnant women and neonate is not well established, but recent studies have shown an increased risk of preterm delivery and stillbirth and pregnant patients with comorbidities such as obesity and diabetes are likely to have an even higher risk of severe illness.[2] Studies have shown that pregnant women with COVID-19 have a significantly higher chance of being admitted to the intensive care unit (ICU) and might require mechanical ventilatory support compared to nonpregnant women with COVID-19.[3]

Cytokine storm is an event wherein excess inflammatory cytokines are released in the body, leading to organ dysfunction and eventual morbidity or mortality. This phenomenon is thought to account for the pathogenicity of severe COVID-19.[4]

There are several approaches to control excessive inflammation in COVID-19

[1]Department of Obstetrics and Gynecology, College of Medicine, Philippine General Hospital, University of the Philippines Manila, Manila, Philippines

Address for correspondence:
Dr. Jean Michael Losaria Castillo, Department of Obstetrics and Gynecology, College of Medicine, Philippine General Hospital, University of the Philippines Manila, Manila, Philippines.
E-mail: jlcastillo7@up.edu.ph

Submitted: 18-Jun-2024
Revised: 15-Aug-2024
Accepted: 19-Aug-2024
Published: 27-Sep-2024

How to cite this article: Castillo JM, Bustamante LM, De la Vega BK. Successful use of hemoperfusion in a pregnant woman with COVID-19 critical infection. Philipp J Obstet Gynecol 2024;48:202-7.

infection and one of which is hemoperfusion. Hemoperfusion is an extracorporeal blood purification procedure that uses a cartridge to filter molecules such as cytokines, toxins, and pathogens. However, the mechanisms by which hemoperfusion exerts beneficial effects in the context of COVID-19 infection remain poorly understood.

Case Report

A 41-year-old gravida 5 para 3 (3012) at 25 weeks and 5 days age of gestation sought consult at the emergency room of a tertiary hospital for dyspnea. She had an 11-day history of a sore throat, nonproductive coughing, and undocumented fever. Her COVID-19 rapid antigen tested positive and eventually developed new-onset dyspnea with desaturations. History revealed that she was unvaccinated for COVID-19.

She was awake, ambulatory, and in cardiorespiratory distress. She had a blood pressure of 130/70 mmHg, was tachycardic with a heart rate of 133 beats per min, tachypneic with a respiratory rate of 36 cycles per min, afebrile at 36.6°C, and with desaturations as low as 87% on room air.

Physical examination showed decreased breath sounds on bilateral basal lung fields. On abdominal examination, she had a fundic height of 22 cm, with an estimated fetal weight of 1.0–1.2 kg, cephalic in presentation with good fetal heart tones at the hypogastric area. On internal examination, the patient had normal external genitalia, a smooth parous vagina, and a closed, posterior, uneffaced cervix, with the corpus enlarged corresponding to the gestational age.

The patient tested positive for COVID-19 on reverse-transcription polymerase chain reaction (RT-PCR) testing and chest X-ray showed signs of pneumonia. Blood workup showed a white blood cell count of 9.00×10^9/L with neutrophilic predominance, hemoglobin of 106 g/L, hematocrit of 34, and platelet count of 381×10^9/L. Chemistry results showed elevated liver enzymes, with aspartate aminotransferase (AST) at 2.08× and alanine aminotransferase (ALT) at 1.23× the normal levels. Inflammatory markers showed increased levels of ferritin at 390 ng/mL, lactate dehydrogenase at 491 U/L, high-sensitivity C-reactive protein at 115.05 mg/L, interleukin-6 level at 123, and D-dimer at 0.89 ug/mL with a normal procalcitonin at 0.21 ng/mL. Urinalysis results showed pyuria and bacteriuria.

On her 1st hospital day (day 12 of illness), the patient had persistent tachypnea and was shifted to high-flow nasal cannula at 40 LPM with FiO2 of 100%. The COVID-19 investigational drug remdesivir was started, and tocilizumab was procured. Fetal well-being studies (biophysical profile, biometry, fetal heart tones monitoring) were done regularly during the course of her admission [Figure 1].

On her 4th hospital day (day 15 of illness), when ongoing her first dose of tocilizumab infusion, she experienced an adverse drug reaction and developed sudden-onset chills, difficulty of breathing, and desaturation. The patient was eventually intubated and hooked to a mechanical ventilator.

Figure 1: Fetal well-being studies

Biometry (preadmission) - November 8, 2022
- Single live intrauterine pregnancy, in cephalic presentation, with good cardiac and somatic activities
- 19 weeks and 2 days
- Placenta is anterior high lying grade I
- Adequate amniotic fluid volume (3.3 cm SVP)

Baseline biometry (admission) - September 27, 2021, hospital day 2
- Single live intrauterine pregnancy, in cephalic presentation, with good cardiac and somatic activities
- 26 weeks by composite sonar aging
- Placenta is anterior high lying grade I
- BPP is 8/8 with adequate amniotic fluid volume
- EFW is 927 g AGA

BPP/biometry (MICU) - October 7, 2022, hospital day 12
- Single live intrauterine pregnancy, in cephalic presentation, with good cardiac and somatic activities
- 27 4/7 weeks by composite sonar aging
- Placenta is anterior high lying grade II
- BPP is 8/8 with high normal amniotic fluid volume (20 cm)
- EFW is 1117 g AGA

BPP (6 days posthemoperfusion) - October 15, 2021, hospital day 20
- Single, live, intrauterine pregnancy
- BPP 10/10 with normal AFI (13.6 cm)
- Placenta is anterior, high lying, grade II

BPP/biometry - October 19, 2022, hospital day 24
- Single, live, intrauterine pregnancy, cephalic, with good cardiac and somatic activities
- 28 1/7 by composite sonar aging
- Placenta is anterior, high lying, grade II
- BPP 10/10 with normal AFI (10.0 cm)
- Sonographic EFW is AGA (1257 g, 39th percentile)

Congenital anomaly scan/BPP/biometry/Doppler studies (prior to discharge) - October 25, 2022, hospital day 30
- Single, live intrauterine pregnancy, breech, with good cardiac and somatic activities
- 29 1/7 by composite sonar aging
- Placenta is anterior, high lying, grade II
- BPP 10/10 with normal AFI (13.1 cm)
- Sonographic EFW is AGA (1499 g, 72nd percentile, 40 g/day)
- Provisional congenital anomaly scan showed negative results
- Doppler studies show normal for both uterine and umbilical arteries

MICU: Medical intensive care unit, BPP: Biophysical profile, EFW: Estimated fetal weight, AGA: Appropriate for gestational age, AFI: Amniotic fluid index, SVP: Single vertical pocket

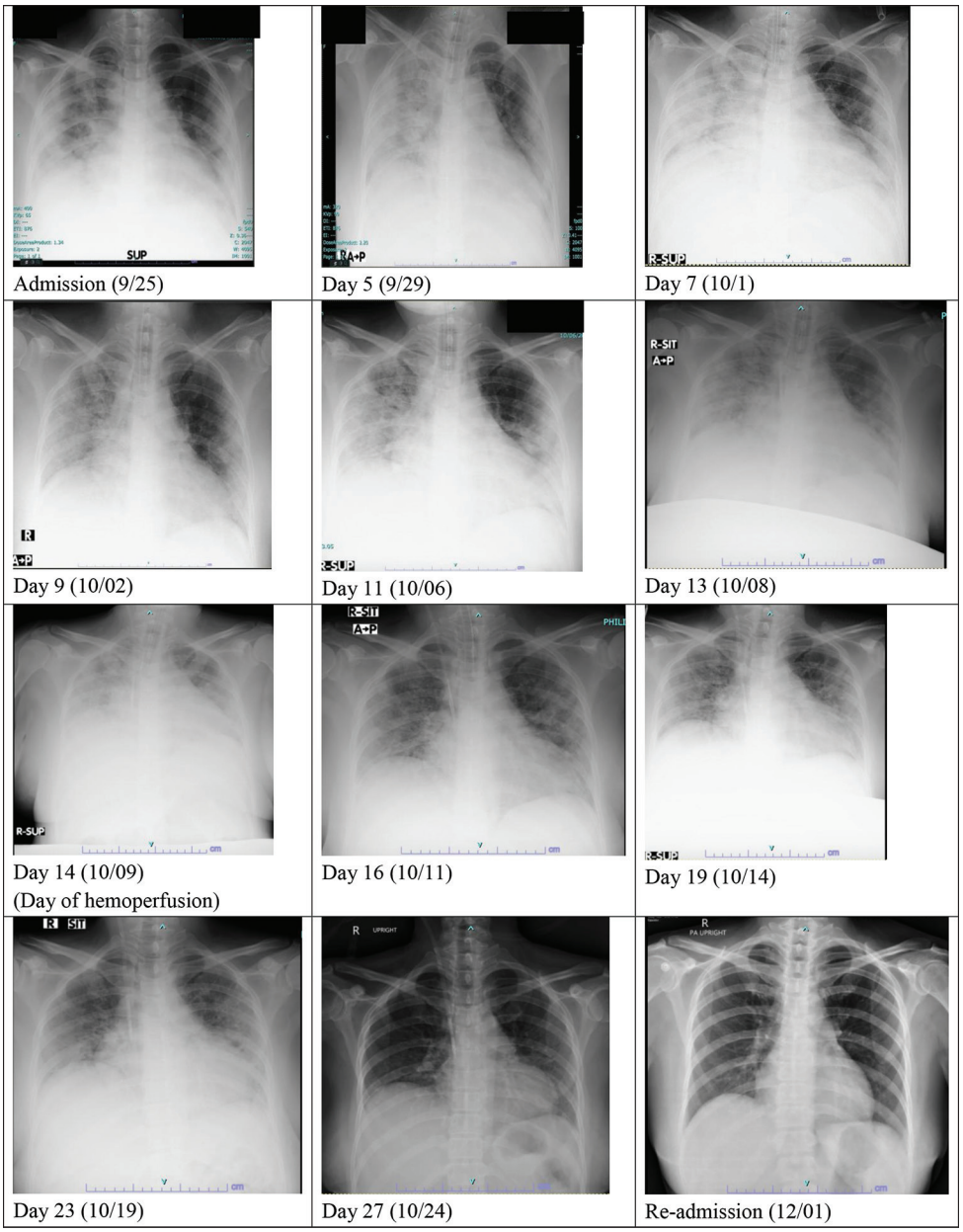

Figure 2: Serial Chest X-ray examinations

Ancillary tests were ordered: a 12-lead electrocardiogram revealing sinus tachycardia; a bedside POCUS Echo showing concentric remodeling, a visual ejection fraction of 55%, adequate wall motion contractility, and an enlarged right ventricle; and a computed tomography scan of the pulmonary artery showing a pulmonary embolism in the arterial branch supplying the anteromedial basal segment of the left lower lobe, along with bilateral ground-glass densities, consolidations, and interlobular septal thickening. The patient was eventually transferred to the COVID ICU on her 6th hospital day (day 17 of illness).

Given the worsening COVID status and her adverse reactions to other investigational drugs, a multidisciplinary conference (pulmonary medicine, endocrinology, cardiology, nephrology, perinatology, and infectious disease) was held on her 11th hospital day (day 22 of illness). Given the limited options (continuing treatment with remdesivir or proceeding with hemoperfusion), increasing inflammatory markers, and poor response to current management, the benefits (improved clinical response) and risks (possible complications of internal jugular catheter insertion and hemoperfusion) were carefully explained, and consent was obtained. The patient then underwent hemoperfusion on her 14th hospital day (day 25 of illness), one cycle lasting 2 h, using the MG series (MG350) hemoperfusion cartridge. Following one cycle of hemoperfusion, inflammatory markers showed

Figure 3: Inflammatory markers

Markers	HD 2	HD 4	HD 8	HD 9	HD 11	HD 15	HD 19	HD 20	HD 26
Ferritin (ng/mL) 6.24–137	390		307	1170		580	237		219
LDH (U/L) 120–246	491	481	275	117	434		243		230
HsCRP (mg/L) 1–3	115	126	42.55			51.65	39.5		3.38
IL-6 (pg/mL) 0–50	123	123			63	24			
Procalcitonin (ng/mL) <0.25	0.21	0.31	2.86		0.47	0.19	0.35	<0.05	

LDH: Lactate dehydrogenase, HsCRP: High-sensitivity C-reactive protein, IL-6: Interleukin-6, HD: Hospital day

decreasing trends immediately post-procedure and continued to decline on subsequent hospital days. Serial chest X-ray studies indicated peripheral clearing of the infiltrates, suggesting improvement [Figures 2 and 3].

Repeat COVID-19 RT-PCR on her 16th hospital day (day 27 of illness) showed negative results. She was eventually transferred to the general ward on her 24th hospital day (day 35 of illness), where she underwent pulmonary rehabilitation exercises and physical therapy sessions. The patient was discharged on her 33rd hospital day at 30 weeks and 6 days age of gestation.

She had regular follow-ups with the obstetrician-gynecologist at the outpatient department and was readmitted for preterm labor at 36 weeks and 4 days of gestation. She delivered a live baby girl via spontaneous vaginal delivery at 35 weeks by pediatric aging, weighing 2490 g, appropriate for gestational age, with an APGAR score of 6, improving to 9. The patient had an unremarkable course postpartum and both the mother and the baby were eventually discharged.

Case Discussion

SARS-CoV-2 is a positive-sense, enveloped, single-stranded RNA virus and is the causative agent of COVID-19.[4] It enters the human cell by utilizing the angiotensin-converting enzyme 2 receptors and targets type II alveolar cells, myocardial cells, and renal proximal tubule cells among others. This may trigger a cytokine storm that will ultimately end up causing multiorgan failure and death.[5]

Cytokine storm causes a severe inflammatory response, in which cytokines are released rapidly in great amounts in response to infection, with multiple studies showing pregnant women having a higher risk for severe COVID-19 infection due to the suppression of different humoral and cell-mediated immunological functions associated with pregnancy.[4]

Moreover, pregnant women with comorbidities such as obesity and diabetes may be at an even greater risk of severe illness, similar to the general population with these comorbidities.

Studies have shown a high frequency of preterm births and an increased rate of cesarean deliveries, but perinatal outcomes were generally good and not associated with a severe clinical course. There is also no clear evidence of vertical transmission of COVID-19.[6] A study done at the Philippine General Hospital involving 209 obstetric patients showed an all-cause neonatal mortality rate of 1.04/100 neonates with almost all neonates being born term and stable (median age of gestation of 38 weeks).[7]

For our index case, she initially experienced mild respiratory symptoms such as sore throat, cough, and fever and then presented at the emergency room with desaturations and difficulty breathing with a rapidly deteriorating clinical picture during the initial course of her hospital stay prompting ICU admission. Clinical suspicion for COVID-19 was high as this disease initially presents with new-onset fever and respiratory symptoms and was eventually confirmed by a positive RT-PCR of the nasopharyngeal swab.

The management of COVID-19 is advancing, with treatment during the initial course of the disease based on the pathogenesis of COVID-19. Most treatments target the SARS-CoV-2 virus itself (antiviral therapies, passive immunity, and interferon) or involve the use of drugs that reduce systemic inflammation (immunosuppressive and immunomodulatory drugs). Studies showed a mortality benefit with dexamethasone, tocilizumab and baricitinib, and remdesivir.[8]

Our index case was initially stabilized by oxygen supplementation, early administration of corticosteroids, and initiation of prophylactic antibiotics for pneumonia. The following were also done: workup for COVID-19, completion of prenatal diagnostics, and fetal well-being studies. Early on, the patient was referred to other services for a multidisciplinary team approach to management: general medicine, pulmonary medicine,

infectious disease, and perinatology. Investigational drugs were initiated but were eventually discontinued: remdesivir and baricitinib due to progressively elevated liver enzymes and tocilizumab due to an adverse drug reaction (chills, dyspnea, and desaturation).

With the worsening clinical picture and limited options for therapy, the idea of using extracorporeal blood purification in the form of hemoperfusion for addressing cytokine storm was entertained.

Sometimes referred to as hemadsorption, hemoperfusion is an extracorporeal form of treatment that is used for the removal of cytokines from infection or inflammation by the use of a cartridge containing hemoadsorbent particles where anticoagulated whole blood passes through and adsorbed by the adsorbent. These devices can also be used to remove drugs, poisons, immunopathogenic agents, and so on.[9]

There is insufficient data regarding the safety of this treatment modality in the pregnant population, and concerns include the lack of experience in its use during pregnancy, the risk of maternal and fetal bleeding, uteroplacental insufficiency during the procedure, hemolysis, and thrombotic complications associated with mechanical pump trauma and the use of systemic anticoagulation.[10]

Acute respiratory distress syndrome (ARDS) is the most common cause of intubation in patients with COVID-19 and cytokine storm is pinpointed as one of the main factors in developing ARDS. Applying extracorporeal treatment like hemoperfusion, which uses adsorption, appears to filter cytokines from the blood and prevent them from seeding on the walls of the alveoli and pulmonary arteries, thereby potentially preventing ARDS and/or its progression.[11]

A case in Taiwan reported the use of an extracorporeal treatment in a 22-year-old pregnant woman at 32 weeks of gestation infected with COVID-19, who had respiratory failure and ARDS. The case demonstrated that this mode of treatment may improve outcomes and provide time for hemodynamic and metabolic stabilization. Unfortunately, early termination of pregnancy was done and the patient underwent a cesarean section for neonatal distress. The mother eventually succumbed to death due to sepsis and pulmonary embolism.[12]

A local study at the Philippine General Hospital involving 66 patients (the majority of whom were male and none of whom were pregnant) with COVID-19 showed that the majority of patients who underwent hemoperfusion died (62.1%, or 41 patients), while 36.4% (25 patients) survived to discharge.[13]

Our index case underwent hemoperfusion on her 14th hospital day at 27 weeks and 4 days age of gestation and tolerated the procedure well. Fetal monitoring was done before, during, and after the procedure with no noted fetal distress. The patient was stable throughout the procedure with no noted desaturations, fever, hypotensive episodes, bloody or watery vaginal discharge, and contractions.

Conclusion

Pregnant patients with COVID-19 are more likely to develop severe pneumonia with limited data available regarding the clinical course and management of this disease in pregnancy. It is assumed that the severity of this disease is linked to the virus-induced cytopathic effects and escape of the virus from the host immune system that may cause a cytokine storm.

COVID-19 protocols for the pregnant population are still unclear. The successful outcome of this case may open possibilities for future management of pregnant patients with severe COVID-19 infection, with hemoperfusion or other extracorporeal blood purification modalities considered during the early course of the disease to prevent disease progression.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Authorship contributions

Jean Michael L. Castillo - Involved in the conceptualization, writing- original draft, visualization.

Lara Marie D. Bustamante - Involved in writing- review and editing and supervision.

Bianca K. de la Vega - Involved in writing- review and editing.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Mohan BS, Nambiar V. COVID-19: An Insight into SARS-CoV-2 Pandemic Originated at Wuhan City in Hubei Province of China. J Infect Dis Epidemiol 2020;6:146. doi.org/10.23937/2474-

3658/1510146.
2. Villar J, Ariff S, Gunier RB, Thiruvengadam R, Rauch S, Kholin A, *et al.* Maternal and neonatal morbidity and mortality among pregnant women with and without COVID-19 infection: The INTERCOVID multinational cohort study. JAMA Pediatr 2021;175:817-26.
3. Nana M, Nelson-Piercy C. COVID-19 in pregnancy. Clin Med (Lond) 2021;21:e446-50.
4. Ragab D, Salah Eldin H, Taeimah M, Khattab R, Salem R. The COVID-19 cytokine storm; what we know so far. Front Immunol 2020;11:1446.
5. Soleimani A, Taba SM, Hasibi Taheri S, Loghman AH, Shayestehpour M. The effect of hemoperfusion on the outcome, clinical and laboratory findings of patients with severe COVID-19: A retrospective study. New Microbes New Infect 2021;44:100937.
6. Di Toro F, Gjoka M, Di Lorenzo G, De Santo D, De Seta F, Maso G, *et al.* Impact of COVID-19 on maternal and neonatal outcomes: A systematic review and meta-analysis. Clin Microbiol Infect 2021;27:36-46.
7. Clemente MJ, Amosco M, Octavio MBR, Bravo SL, Villanueva-Uy E. Maternal and Neonatal Outcomes of Pregnant Women with Clinically Confirmed COVID-19 Admitted at the Philippine General Hospital. Acta Med Philipp [Internet] 2021;55.
8. Montazersaheb S, Hosseiniyan Khatibi SM, Hejazi MS, Tarhriz V, Farjami A, Ghasemian Sorbeni F, *et al.* COVID-19 infection: An overview on cytokine storm and related interventions. Virol J 2022;19:92.
9. Ricci Z, Romagnoli S, Reis T, Bellomo R, Ronco C. Hemoperfusion in the intensive care unit. Intensive Care Med 2022;48:1397-408.
10. Sharma NS, Wille KM, Bellot SC, Diaz-Guzman E. Modern use of extracorporeal life support in pregnancy and postpartum. ASAIO J 2015;61:110-4.
11. Ronco C, Reis T, De Rosa S. Coronavirus epidemic and extracorporeal therapies in intensive care: Si Vis Pacem Para Bellum. Blood Purif 2020;49:255-8.
12. Karabulut Keklik ES, Dal H, Bozok Ş. Cytokine hemoadsorption in the management of a pregnant woman with COVID-19 pneumonia: Case report. SN Compr Clin Med 2020;2:2376-80.
13. Manalili SAR, Montemayor JAS, Montemayor JAS, Montemayor ES, Uy CFC. Clinical Profile and Outcomes of Coronavirus Disease 19 (COVID-19) Patients who Underwent Hemoperfusion (HP) in a Tertiary COVID-19 Referral Hospital: A Descriptive Study. Acta Med Philipp [Internet] 2022.