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**Complicated delivery in a patient with acute respiratory distress syndrome on  
Coronavirus disease 2019 infection**

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**Key Clinical Message**

The choice of anesthesia and route of delivery for severe COVID-19 infection should be determined by a multidisciplinary team on a case to case basis according to maternal and fetal status.

**Keywords :** ARDS, COVID-19, Critical care medicine, Anaesthesiology, Obstetrics

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## SUMMARY

We report the case of a 39-year-old parturient who contracted coronavirus disease 2019 (COVID-19) at 28 weeks of gestation. Her clinical state deteriorated even with supportive care and anti-retroviral therapy. At 32 weeks of gestation she developed acute respiratory distress syndrome (ARDS). An emergent caesarean section was performed; rapid clinical degradation required intubation and 11 days of invasive ventilation. She tested positive for Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) up to 3 weeks after the initial diagnosis. Further studies are needed to study maternal to fetus transmission rates and the duration of contagiousity of SARS-CoV-2 infected patients.

## INTRODUCTION

5% of patients infected by coronavirus disease 2019 (COVID-19) require intensive care and most patients develop acute respiratory distress syndrome (ARDS).[1] Morbidity and mortality remains high and early recognition is a vital step in providing appropriate care.[2] There are several reported cases of COVID-19 infections during pregnancy.[3] All these cases are mild infections with cough, fever and myalgia as the main symptoms, similar to infections in non-pregnant adults. Mothers with COVID-19 infections shows increased risks of preterm birth, miscarriage, preeclampsia and caesarean delivery. There were no cases of vertical transmission to neonates.[4] Currents recommendations do not provide any guidance regarding the optimal time of delivery or the safety of vaginal versus caesarean delivery.[5] Those decisions should be individualized and discussed in multidisciplinary teams. We describe the case of a parturient who develops ARDS on COVID-19 infection. The patient provided informed and written consent.

## **CASE PRESENTATION**

At 28 weeks of a gestation, a 39-year-old patient (gravida 1, para 0) presented a dry cough, chills, myalgia and loose stools. She was in previous good health and the singleton pregnancy was unremarkable.

Two weeks later, she complained of worsening cough, chest pain, dyspnea III NYHA, sudation and fever up to 38.4°C, which pushed her to consult the emergency department of a community hospital 4 days later. All staff caring for the patient wore appropriate personal protective equipment according to local protocols. Droplet and contact precautions were initiated immediately.

Upon first evaluation by the emergency staff the parturient presented a temperature of 38.1°C, the pulse was 130 beats per minute, the blood pressure 132/73 mmHg, the respiratory rate 22 breaths per minute, and oxygen saturation 96% while she was breathing ambient air. Breaths sounds were symmetrical. Chest X-ray showed right basal alveolar infiltrate. Laboratory tests and results (table 1) were unremarkable except for lymphopenia, mild hyponatremia and mild elevation of C-reactive protein. Recent studies have correlated lymphopenia with COVID-19 cases(1). Electrocardiogram showed sinus rhythm without any sign of myocarditis or ischemia. Nasopharyngeal and oropharyngeal swabs were obtained to test for respiratory syncytial virus, influenza A & B and SARS-CoV2. Sputum culture and urinary antigen for Legionella were also carried out. All the tests returned negative, except for SARS-CoV-2.

The patient was admitted in a regular room for surveillance. Whilst waiting for the results of SARS-Co-V 2, empirical Clarithromycin was initiated due to the clinical suspicion of atypical pneumonia. On hospital day 5, patient presented a persistence of fever at 38.7°C, worsening of dyspnea with oxygen saturation 86% at ambient air and diffuse crackles at auscultation of breath sounds. New laboratory tests showed elevation of the C-reactive protein and D-dimers. Arterial blood gas, performed while breathing 3 liters/minutes of oxygen, showed respiratory alkalosis with  $\text{PaO}_2/\text{FiO}_2$  ratio of 456mmHg. Due to the worsening clinical condition and pregnancy, the patient was transferred immediately to a primary care hospital.

On arrival, a nonstress test confirmed a reactive fetal heart. Fetus presented a tachycardia at 200 beats per minutes without decelerations. Clarithromycin was stopped and hydroxychloroquine at a dose of 200mg twice daily plus atazanavir 400mg once daily was started. Antenatal corticosteroid therapy using betamethasone was administered to hasten fetal pulmonary maturation. Patient was now breathing with 6 liters/minutes of oxygen to maintain 93% oxygen saturation. Due to the rapid decline in respiratory function, she was admitted to the intensive care unit (ICU).

The following day (32 weeks of gestation), a multi-disciplinary decision was made to perform an urgent cesarean section to improve respiratory function and decrease circulatory volume after a rapid clinical deterioration with a  $\text{PaO}_2/\text{FiO}_2$  ratio of 125mmHg and oxygen saturation 95% under 8 liters/minute of oxygen. Patient was equipped prior to operation with an invasive arterial line and two peripheral venous catheters. She received oxygen at 8 l/min during the whole intervention. An epidural catheter was threaded without complication;

continuous phenylephrine was administered according to local protocol. Apgar score were 6 and 6, blood loss was 300 milliliters. Delayed cord clamping was not performed as the baby was to be immediately admitted in neonatology. There was no evidence of neonatal or intraamniotic infection.

Post operatively, on arrival in ICU, the patient presented a rapid degradation in respiratory function with refractory hypoxemia breathing 15 liters/minutes of oxygen. She was intubated in rapid sequence induction uneventfully. Hydroxychloroquine and atazanavir were replaced by remdesivir for a total of 10 days.

Patient received protective ventilation defined by volume-controlled ventilation at 6 milliliters/kg of ideal body weight, plateau pressure inferior to 28 cmH<sub>2</sub>O and driving pressure inferior to 14 cmH<sub>2</sub>O. Curarisation with cisatracurium was initiated to achieve 0/4 on train of four scale, sedation was performed with propofol and fentanyl. At the time of intubation, laboratory tests showed worsening of the inflammatory syndrome; all other tests were unremarkable. Arterial blood gas showed respiratory acidosis with PaO<sub>2</sub>/FiO<sub>2</sub> of 194mmHg. Chest radiograph showed diffuse alveolar condensation (Figure 1). All the findings were consistent with acute respiratory distress syndrome (ARDS) on COVID-19. She received one session of prone positioning 3 days later due to worsening of PaO<sub>2</sub>/FiO<sub>2</sub> at 114mmHg. Later she developed septic shock, moxifloxacin and piperacillin/tazobactam were started; all the blood samples and cultures were sterile. Thoraco-abdominal CT scan was performed showing images compatible with SARS-CoV2 pneumonia without further findings or secondary infection (Figure 2). She evolved well and the antibiotics were stopped after 5 days. After 11 days of invasive ventilation patient respiration improved with PaO<sub>2</sub>/FiO<sub>2</sub> > 200mmHg and extubation was performed.

Post extubation she presented delirium with hallucinations. Metabolic and neurological causes were excluded; a further psychiatric evaluation discarded puerperal psychosis. The etiology of the hallucinations was attributed to the extended sedation. During this period, she was treated with low dose quetiapine. Within a few days, the evolution was favorable, and she was transferred to a regular room on day 14 of intensive care admission. The patient required further psychological support due to the development of posttraumatic syndrome.

Nasopharyngeal and oropharyngeal swabs were still positive for SARS-CoV-2 three weeks after the first positive swab. Another polymerase chain reaction (PCR) SARS-CoV-2 was performed two weeks later (five weeks after first positive test) and was negative.

The neonate was immediately admitted to neonatal intensive care unit where he developed hyaline membrane disease due to the incomplete pulmonary maturation. He received continuous positive airway pressure (CPAP) and further required intubation. Surfactant and caffeine citrate were given. He was extubated the day after and tested 4 times negative for SARS-CoV-2.

## **OUTCOME AND FOLLOW-UP**

The patient was seen on a regular basis by a psychiatric team for post-traumatic stress syndrome, it evolved well. Three weeks after discharge she was seen as outpatient in the obstetrics clinic, the examination was unremarkable. She was also seen 6 months after the hospitalization in the pneumology consultation, lung functions were normal and CT scan showed complete resolution of the COVID-19 pneumoniae.

## DISCUSSION

It is well known that physiological changes in respiratory, cardio-vascular and the immune system during pregnancy render this population to be particularly vulnerable to infections. Even if early reports on pregnancy and COVID-19 infection were reassuring suggesting that pregnant women are not at increased risk for this infection, neither a worse course of the disease and for the most part patients remain asymptomatic till after delivery.[6-8] Clinical characteristics and severity of COVID-19 in pregnant women appears to be similar to the non-pregnant population. In the severe cases the choice of anesthesia and route of delivery for this group still remains unclear and should be determined on a case to case basis according to maternal and fetal status.[5,9]

This case describes a pregnant woman who experienced severe COVID-19 with ARDS requiring emergent cesarean section at 32 weeks of gestation using epidural anesthesia. The choice of delivery was made in the hopes that premature delivery would allow an improvement on the respiratory status of the mother which was rapidly declining.[8-9] The choice of regional anesthesia with epidural top up was considered to minimize hemodynamic instability, aerosolization and cross infection during airway management.[10] The cesarean was uneventful but unfortunately rapid clinical respiratory degradation in postoperative period required intubation, 11 days of invasive ventilation and 14 days of intensive care unit.

A large cohort of 147 pregnant patients were evaluated by a joint mission World Health Organisation-China, published in february 2020 where only 1 % of patients were critically ill. [11] This was defined as having respiratory failure requiring mechanical ventilation, or other organ failure and shock. Regional anesthesia with epidural top up or single shot subarachnoid blockade was suggested in all parturients if oxygen saturation (94% and above) was present. This would then have to be considered in future pregnant patients with severe COVID-19 in the hopes that intubation can be avoided.

Chen et al. reported nine cases of women above 36 weeks of gestation with COVID-19 infection who underwent cesarean section with both maternal and fetal outcomes being good.[3] To our knowledge none of the patients in this study required post-operative intubation. The choice of the mode of delivery was based on the uncertainty of mother-to-child transmission; pre-eclampsia; fetal distress and a history of cesarean section.

Approximately 80% of COVID-19 infections are mild, 15% are considered severe requiring oxygen and 5% requiring mechanical ventilation. Pregnant women are more subject to severe infection by their physiological modifications in their immune and cardiovascular systems. Altered pulmonary volumes renders pregnant women susceptible to severe infections. It is well known that at term many pregnant women can present gestational rhinitis and slight thrombopenia. These features may mask the COVID-19 symptoms and lead to late diagnosis.[12]

In our case, fortunately, the mother and her neonate evolved well. Her baby was not infected by SARS-CoV-2, despite the mother being tested positive up to three weeks after the initial diagnosis. Further studies are needed to study maternal to fetus transmission rates and the duration of contagiousity of SARS-CoV-2 infected patients.

**Conflict of Interest Statement**

None for all authors

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None



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Figure 1. Chest X-ray after intubation

Figure 2. CT scan of the lung at day 9 of intensive care

Table 1. Clinical Laboratory results

Variable	Reference Range	Day 1	Day 6	Day 7 CS	Day 8 Intubation	Day 11	Day 17 Extubation	Day 20 Discharge ICU	Day 32
C-reactive protein	(< 10) mg/l	36	133	180	190	191	93	12	
D-dimer	(<500) ng/ml	936	1155		1704	1454	4285		
Sodium	(135 - 145) mmol/l	133	135	135	138	144	146	142	
Potassium	(3.5 - 4.6) mmol/l	4.1	3.2	4	5.2	4.4	4	3.8	
Urea nitrogen	(2.9 - 6.4) mmol/l		1	1	2.2	6.4	7.2		
Creatinine	(44 - 80) µmol/l	43	40	34	58	47	51	55	
Aspartate aminotransferase	(9 - 32) U/l	19	35	28		34	23	29	
Alanine aminotransferase	(9 - 36) U/l	12	11	10		6	7	11	
Alkaline phosphatase	(36 - 108) U/l	96	124	127	123	117			
White-cell count	(4.0 - 10.0) G/l	6	6.3	7	13.5	8.1	7.6	8.8	
Hemoglobin	(117 - 157) g/l	119	115	119	113	99	100	109	
Hematocrit	(35 - 47) %	36	34	36	36	33	33	35	
Platelet count	(150 - 350) G/l	197	161	154	196	238	344	396	
Absolute neutrophil count	(1.8 - 7.5) G/l		5.92				5.78		
Absolute lymphocyte count	(1.5 - 4.0) G/l		0.13				0.76		
Procalcitonine	(<0.25) µg/l		0.3	0.49	0.49	0.2	0.1	0.08	
SARS-CoV 2		+						+	-
Prothrombine time	80-120 %		120			140	90		
INR			1			1	1		
aPTT	26-37 sec		40			35	34		
PaO2/FiO2	>300 mmHg	457	456	125	87	133	244		
pH	7.35-7.45	7.47	7.48	7.46	7.42	7.27	7.42		
Carbon dioxide	35-45 mmHg	29	28.2	28	30.3	59.8	47.2		
Oxygen	73-103 mmHg	95.9	146	75	52.2	79.8	73.3		
Bicarbonate	22-26 mmmol/l	23.5	23.3	20.1	19.3	27.2	30.5		
Oxygen saturation	95-99%	96	86	95.2	86.6	93.3	93.7		
Base excess				-2.8	-4.2	-0.6	5.4		
Lactate	0.63-2.44 mmol/l	0.8	0.9	1.14	1.94	0.63	0.92		

CS: Cesarean section; + = positive test; - = negative test; SARS-CoV 2= Nasopharyngeal PCR  
SARS-CoV 2 test