

# Obstetrical and intensive care strategies in a high-risk pregnancy with critical respiratory failure due to COVID-19: a case report

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## Case Report

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# Abstract

## Background

With the disease burden increasing daily, there is a lack of evidence regarding the impact of COVID-19 in pregnancy. Healthy pregnant women are still not regarded as a susceptible group despite physiological changes that make pregnant women more vulnerable to severe infection. However, high-risk pregnancies may be associated with severe COVID-19 disease with respiratory failure, as outlined in this report. We discuss the importance of timely delivery and antenatal steroid administration in a critically ill patient.

## Case

A 27-year-old pregnant woman (1-para) with type I diabetes, morbid obesity, hypothyroidism and a previous Caesarean section, presented with critical respiratory failure secondary to COVID-19 at 32 weeks of gestation. A preterm emergency Caesarean section was performed, after steroid treatment for foetal lung maturation. The patient benefited from prone positioning however, transient acute renal injury, rhabdomyolysis and sepsis led to prolonged intensive care and mechanical ventilation for 26 days post-Caesarean. The baby had an uncomplicated recovery.

## Conclusion

COVID-19 infection in high-risk pregnancies may result in severe maternal-neonatal outcomes such as critical respiratory failure requiring mechanical ventilation and premature termination of the pregnancy. Antenatal steroids may be of benefit for foetal lung maturation but should not delay delivery in severe cases.

## 1. Introduction

With a case morbidity of up to 3% [1] and mortality 1.2% [2] in pregnant women, the SARS-CoV-2 virus has exposed vulnerable groups in the society to an unprecedented global health crisis. Despite being more prone to viral infections, health agencies have struggled to identify pregnant women as a susceptible group in the general population [3, 4]. We present a case of severe COVID-19 in pregnancy leading to preterm Caesarean delivery and critical respiratory failure with intensive-care treatment of both mother and newborn.

## 2. Case Presentation

A 27-year old (Gravida 2, Para 1) was transferred from her local county hospital to Skåne University Hospital at gestational week (GW) 32+1 due to a positive throat swab for SARS-CoV-2 (quantitative real time polymerase chain reaction), increasing oxygen demand and a lack of intensive care beds for COVID-19.

The patient, a pre-school teacher of Middle Eastern descent, had a seven-day history of fever, lower abdominal pain, malaise, headache, cough, dyspnoea and polyuria (Figure 1). The patient suffered from extreme obesity (BMI 57 kg/m<sup>2</sup>), poorly regulated type-1 diabetes mellitus and hypothyroidism. She had been prescribed acetylsalicylic acid (160 mg daily) due to preeclampsia in her previous pregnancy, in which she was delivered with Caesarean section at GW 36. During the current pregnancy, an obstetric ultrasound showed a foetal weight deviation of + 32% (LGA: large for gestational age) at GW 29+6. Thromboprophylaxis (8000 IE Tinzaparin), with an initial dose of betamethasone (12 mg intra-muscular) for foetal lung maturation was given at the local hospital. A chest computed tomography (CT) revealed bilateral diffuse ground-glass opacities with no signs of pulmonary embolism (Figure 2).

At the University hospital, a multidisciplinary team of obstetricians, anaesthesiologists and neonatologists started to prepare for Caesarean delivery. The Tinzaparin dose was doubled to 16000 IE divided in two doses daily and a normal cardiotocograph (CTG) were registered. The respiratory condition of the patient deteriorated during the night and despite

oxygen at 100% (high flow nasal cannula HFNC) and gas flow at 60–80 L/minute, the oxygen saturation fell below 90% and critical respiratory failure with metabolic acidosis ensued (Figure 1). The patient was subsequently intubated and put on mechanical ventilation at the COVID intensive care unit (ICU). The second 12 mg dose of Betamethasone for foetal lung maturation was administered, with the plan to perform an emergency Caesarean section. After stabilisation, the CTG showed reduced variability and recurring episodes of foetal bradycardia associated with the patient's positioning. An emergency Caesarean was performed at GW 32+2, 8 days after the onset of the respiratory symptoms and 4 hours after intubation. The operation was technically challenging due to extreme obesity and intraabdominal adhesions. Piperacillin/Tazobactam was administered preoperatively and the total blood loss was 200 ml.

Oxygenation was critically impaired during the first two days in the ICU. During day 1–9 of the intensive care period, the patient required prone positioning and intermittent muscle relaxation to optimise respiration and to provide lung-protective ventilation (Table 2). To treat muco-purulent secretions interfering with ventilation, aerosolized dornase-alfa was used. No antiviral treatment was administered. In addition to the respiratory failure, the patient developed acute renal injury. Due to persistent high fever, continuous renal replacement therapy was used for invasive cooling in order to maintain adequate temperature control. A nosocomial superinfection with *Klebsiella aerogenes* was detected in tracheal secretions, urine cultures and later on in blood (Figure 1). Treatment with Meropenem (1 g x 3 daily) was initiated. Due to a prolonged ICU-course and palpable stress, cough, high fever, and a lack of contact during wake-up tests, a tracheostomy was performed on day 17, to facilitate weaning from mechanical ventilation. Rhabdomyolysis ensued on day 18–20, which further complicated the recovery period (Table 1). Tracheal swabs for SARS-CoV-2 returned repeatedly negative and the patient was transferred to the non-COVID ICU. The patient was successfully weaned off mechanical ventilation 26 days post Caesarean.

The neonate, a boy weighing 3100 grams (99<sup>th</sup> percentile), had absent tone and lack of spontaneous breathing (Table 3). Manual ventilation was initiated after which the heart rate and oxygen saturation stabilised promptly. After 6 minutes, spontaneous breathing was established. Nasal continuous positive airway pressure (nCPAP) with positive end expiratory pressure (PEEP) at 5 cmH<sub>2</sub>O and 30% oxygen was applied. Upon arrival to the neonatal ICU, umbilical artery and vein catheters were inserted. Arterial cord blood gas analysis showed mild respiratory acidosis (pH 7.21, pCO<sub>2</sub> 8.9 kPa) at birth. During the catheterisation procedure, the need for oxygen increased from fraction of inspired oxygen (FiO<sub>2</sub>) 0.3 to 0.6, presenting with deep intercostal retractions. A chest X-ray showed atelectasis of the inferior right lung lobe. Nasal intubation was performed, and a volume targeted conventional mechanical ventilation initiated. Surfactant (Poractant alfa®) 200 mg/kg was given intratracheally. The FiO<sub>2</sub> decreased incrementally over the following 12 hours and the neonate was extubated after 24 hours. No further breathing support was needed. Nasal swabs for SARS-CoV-2 were negative at 48 and 96 hours postpartum.

### 3. Discussion

We report a case of critical COVID-19 in a high-risk pregnancy, with acute respiratory failure requiring mechanical ventilation and premature termination of the pregnancy. Although pregnant women are not recognised as a vulnerable group for COVID-19, there is a growing body of evidence linking late pregnancy and prior maternal risk factors such as high BMI, diabetes and hypertension to adverse pregnancy outcomes including maternal and neonatal deaths [1, 2, 5, 6, 7].

The patient presented with several risk factors that have been linked to an increased likelihood for severe COVID-19 course including morbid obesity (BMI 57 kg/m<sup>2</sup>), diabetes mellitus [7] and Asian origin [8]. Ethnicity has been implicated due to a general higher prevalence of medical problems such as cardiovascular disease, diabetes and higher deprivation in such societies. In a cohort of hospitalised cases in the United States, peak respiratory support for severe COVID-19 in pregnancy has been reported to occur on day 8 and intubation on day 9 [7]. Co-morbidities like previous pulmonary/cardiac disease and high BMI were again associated with severe disease.

A multidisciplinary team opted to complete antenatal steroid therapy for foetal lung maturation since the foetus was at risk for respiratory distress (GW 32, LGA and poorly regulated maternal diabetes). Some reports have warned against the use of corticosteroids in critically ill patients, due to risk of delivery postponement and worsening of the clinical course [9], including delayed viral clearance. The International Society of Ultrasound in Obstetrics and Gynaecology advises against antenatal steroid treatment in preterm COVID-19 cases (GW 34-36) and recommends caution at earlier gestations [10]. In contrast, the Swedish Federation of Obstetricians and Gynaecologists supports the use of antenatal steroids before GW 34 in COVID-19 cases [11]. The RECOVERY trial [12] reported a reduction in ICU deaths by one-third in ventilated COVID-19 patients receiving dexamethasone therapy. These findings were supported by another recent study where early administration of dexamethasone was found to reduce the duration of mechanical ventilation and overall mortality in patients with moderate-to-severe respiratory failure [13]. Further investigation into the potential risks and benefits of antenatal steroid treatment in severe COVID-19 cases in pregnancy is therefore warranted.

The patient was mechanically ventilated for about 4 hours prior to the Caesarean section and put in prone position 2 hours after surgery. Swedish guidelines recommend delivery within 24 hours in cases where the mother requires more than 5 litres oxygen [11]. In this case, a multidisciplinary team decided to postpone delivery in order to temporarily stabilise the respiratory condition of the patient and complete steroid treatment for foetal lung maturity. It remains unclear whether an earlier Caesarean section could have prevented the patient from critical respiratory failure.

Serum interleukin-6 (IL-6) levels peaked on day 1 of the ICU period (2378 ng/L) and remained below 90 ng/L from day 3 onwards. Other acute phase proteins (APPs) such as fibrinogen, ferritin and C-reactive protein levels were also elevated, although no clear dynamics were seen during the first 19 days of intensive care. Hyperactive immune responses characteristic for severe COVID-19, have been shown to cause stress induced tissue injury and multiorgan impairment [14]. Elevated levels of IL-6 have been associated with an increased risk of mortality [15]. The APP and liver enzyme levels improved drastically after delivery, suggesting that severe COVID-19 infection during pregnancy may improve after delivery [16].

Prior poor health, nosocomial infection followed by acute renal failure, rhabdomyolysis and sepsis led to prolonged ICU care. Rhabdomyolysis has been presented as a possible late complication of COVID-19 although other infections, drug interactions, hypoxemia, extremes of body temperature etc may also have been implicated [17]. To the best of our knowledge, this is the first report on COVID-19 with subsequent rhabdomyolysis postpartum.

In summary, this case-report describes the obstetric and intensive care management of a critical case of COVID-19 in the third trimester. We discuss the timing of delivery and the role of antenatal steroid treatment for foetal lung maturation, which may be factors important for future recommendations regarding severe COVID-19 in pregnancy.

## Declarations

### CONTRIBUTORS

ZK: conception, planning, data collection, analysing and writing the manuscript.

MB: planning, data collection, writing the manuscript.

JKL: planning, data collection, writing the manuscript.

ES: planning and revising the manuscript.

MAH: planning and revising the manuscript.

SRH: conception, planning and revising the manuscript.

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MZ: conception, planning, data collection, writing, analysing and revising the manuscript.

All authors have read and approved the manuscript.

## CONFLICTS OF INTEREST

The authors declare that they have no conflict of interest.

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collection and analysis, decision to publish, or preparation of the manuscript.

## PATIENT CONSENT

Obtained from patient's legal guardian (Husband) since patient was unable to give consent (induced coma).

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## Tables

### Table 1.

Maternal laboratory results during admission and readmission.

Variable	Reference Range	Day of Emergency Caesarean Section (24/5/2020)	Day after Caesarean Section (25/5/2020)	At the time of writing-Day 19 of intensive care (13/6/2020)
Haemoglobin (Hb) g/L	117-153	93	86	80
Platelet count x10 <sup>9</sup> /L	165-387	190	152	314
White cell count x10 <sup>9</sup> /L	3.5-8.8	10.1	9.0	10.1
Neutrophil count x10 <sup>9</sup> /L	1.8 - 7.5	9.0	7.8	7.4
Lymphocyte count x10 <sup>9</sup> /L	1.0 - 4.0	0.5	0.2	2.0
Ferritin µmol/L	13-148	666	366	254
C-reactive protein (CRP) mg/L	<5	157	222	29
Procalcitonin µg/L	< 0.05	1.3	5.2	1.4
Troponin-T ng/L	<5	5	7	141
Myoglobin µg/L	25-58	26	-	13732
Glucose mmol/L	4.2-6.0	7.9	10.7	5.8
Aspartate aminotransferase (ASAT) µkat/L	0.25-0.6	16	12	2.8
Alanine aminotransferase (ALAT) µkat/L	0.15-0.75	3.6	3.5	4.4
Alkaline phosphatase (ALP) µkat/L	0.70-1.9	1.9	1.3	1.3
Gamma-glutamyl transferase (GGT) µkat/L	0.15-0.75	1.5	1.2	3.8
Bilirubin µmol/L	5-25	9	15	6
Lactate Dehydrogenase (LDH) µkat/L	1.8-3.4	19	14	11
Pancreatic amylase µkat/L	0.15-1.1	0.67	0.79	0.35
Plasma Albumin g/L	36-48	21	-	25
Estimated Glomerular Filtration Rate (eGFR)	80-125	38	24	14
Creatinine µmol/L	45-90	116	119	338
Urea mmol/L	2.6-6.4	5.1	6.4	39.4
Sodium mmol/L	137-145	141	143	145
Potassium mmol/L	3.5-4.4	4.8	4.1	5.0
Chloride mmol/L	98-110	114	111	98
Calcium ion mmol/L	1.15-1.33	1.20	1.21	1.27
Magnesium mmol/L	0.70-0.95	0.69	0.94	0.94
Prothrombin-complex International Normalized Ratio (P-INR)	0.9-1.2	1.0	1.0	0.9

Activated Partial Thromboplastin Time (APTT) in seconds (s)	26-33	45	40	31
D-Dimer				2.6
Fibrinogen g/L	2.0-4.0	5.4	5.8	6.0
pH	7.35-7.45	7.18	7.36	7.46
Partial pressure of carbon dioxide pCO <sub>2</sub> in kPa	4.6-6.0	5.4	5.9	6.2
Partial pressure of oxygen pO <sub>2</sub> in kPa	10.0-13.0	6.7	9.3	9.1
Base Excess mmol/l	22-27	14	23	32
Bicarbonate HCO <sub>3</sub> <sup>-</sup> mmol/l	-3.0-3.0	-12.2	-0.9	+8.4
Lactate mmol/L	0.5-1.6	2.9	3.8	1.9
Saturation of oxygen %	97-100	77	93	93

**Table 2.**

Mechanical ventilation respiratory parameters during the first two weeks of intensive care

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14
<b>Prone Ventilation</b>	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	No	No
<b>Muscle relaxation</b>	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	No	No	No	No
<b>FiO<sub>2</sub></b>	0.65-0.1	0.5-0.8	0.45-0.8	0.5-0.8	0.5-0.7	0.4-0.8	0.35-0.6	0.35-0.45	0.45-0.55	0.35-0.5	0.3-0.5	0.3-0.45	0.4-0.45	0.4-0.6
<b>PEEP</b>	14-15	14-15	12-15	12-14	14-16	14-16	16	11-16	10-14	11-12	10-12	8-10	8-10	8-10
<b>PF-ratio</b>	8-15	13-20	15-21	10-20	12-22	16-25	22-31	19-32	15-24	19-27	23-27	21-26	19-24	20-26

Abbreviations: D = day, FiO<sub>2</sub> = fraction of inspired oxygen, PEEP = positive end-expiratory pressure, P/F = arterial oxygen partial pressure (kPa) / FiO<sub>2</sub>.

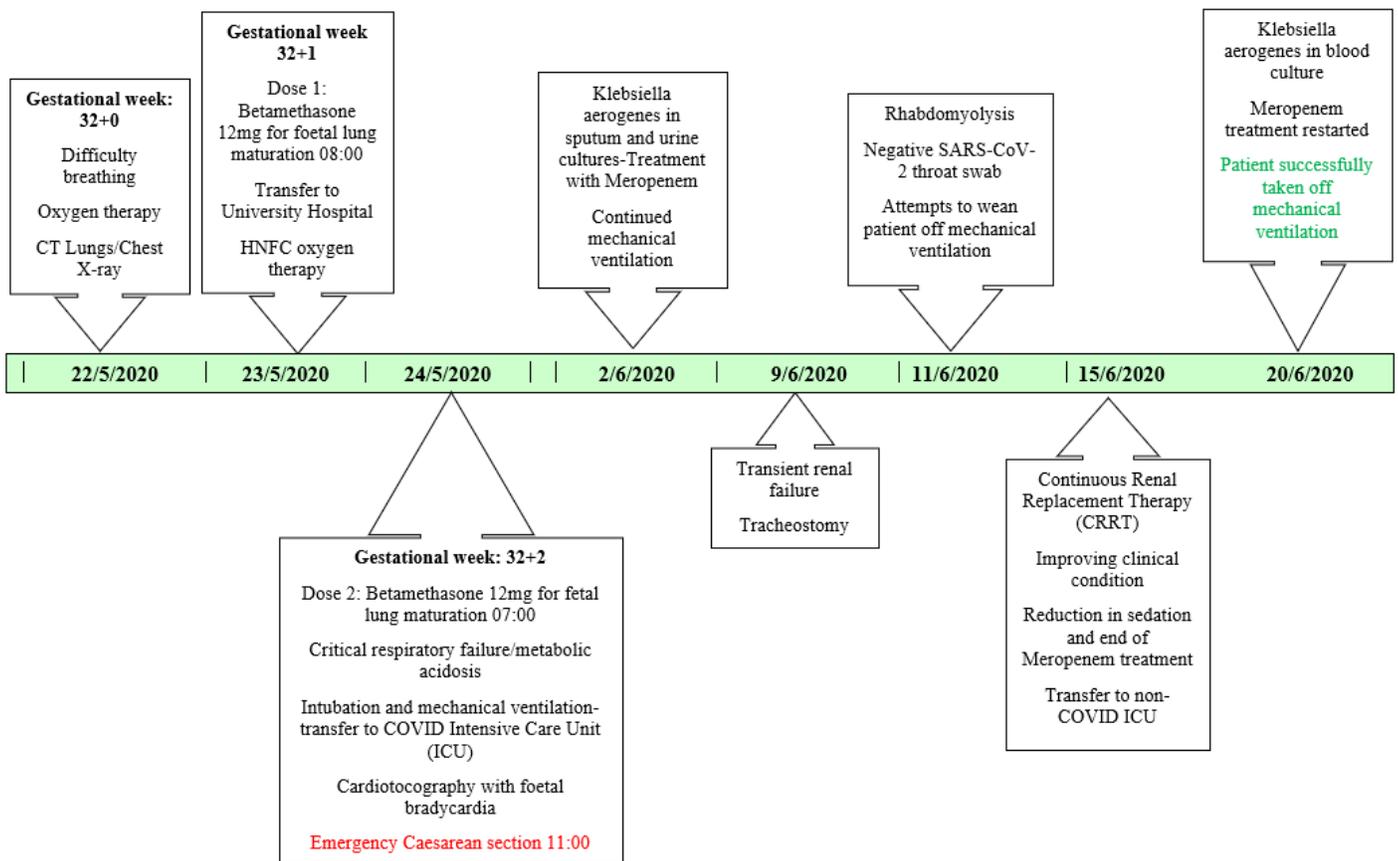
P/F ratio: ≤39.9 = mild acute respiratory distress syndrome (ARDS), ≤26.6 = moderate ARDS, ≤13.3 = severe ARDS.

**Table 3.**

Neonatal Apgar Score at 1, 5 and 10 minutes

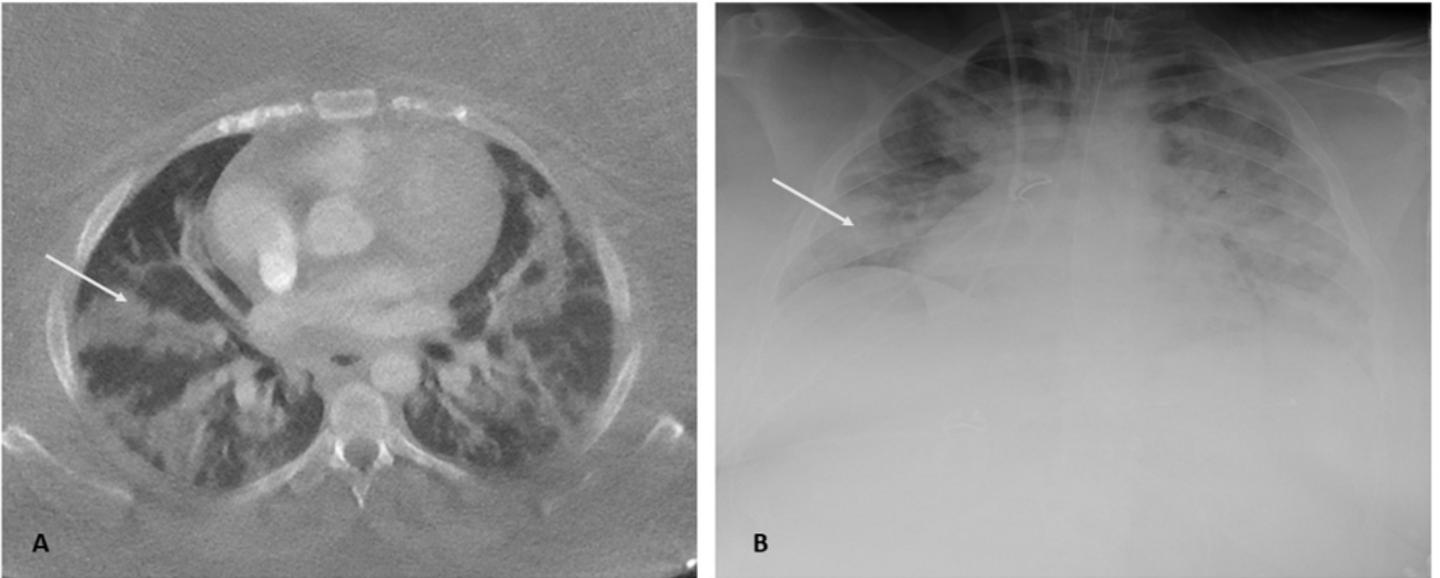
	1 minute	5 minutes	10 minutes
Activity	0	0	1
Pulse	2	2	2
Grimace	0	1	1
Appearance	1	1	2
Respiration	0	1	2
<b>Total Apgar score</b>	<b>3</b>	<b>5</b>	<b>8</b>

## Figures



**Figure 1**

Timeline of course of disease in patient.



**Figure 2**

A. Low-dose computed tomography axial scan from May 23 showing bilateral multifocal ground-glass opacities, with both peripheral and perihilar distribution, corresponding to COVID-19 pneumonia B. Chest radiograph from May 24 with opacities progression as well as signs of congestion