Case Report

Two cases of severe COVID-19 in gestational week 27 and 28 respectively, after which both pregnancies proceeded to term

H. Östling [a], M. Ugarph-Edfeldt [b], K. Hildén [a,*]

[a] Department of Obstetrics and Gynaecology, School of Medical Sciences, Örebro University, Örebro, Sweden
[b] Department of Anaesthesia and Intensive Care, School of Medical Sciences, Örebro University, Örebro, Sweden

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ABSTRACT

COVID-19 in pregnancy increases the risk of caesarean section. We present two cases of late gestation pregnant women with severe COVID-19. Both were successfully treated with mechanical ventilation without termination of pregnancy and, following recovery from COVID-19, had vaginal deliveries at term. These two cases demonstrate the possibility of treating pregnant women with severe COVID-19 with mechanical ventilation in the late second and early third trimesters without them having a pre-term delivery. With a multidisciplinary approach, such management could avoid the maternal risks of surgery during a severe infection and, at the same time, enable term birth with a lower risk of neonatal complications.

Introduction

The impact of COVID-19 on pregnancy and neonatal outcome has been a growing focus of research as the pandemic has evolved. Previous reviews have reported an increased risk of adverse pregnancy outcomes such as pre-eclampsia, thrombo-embolic complications, and in particular a higher frequency of caesarean section and preterm birth. [1–4] Pregnant women also appear to have an increased risk of requiring intensive care and mechanical ventilation due to severe COVID-19. [1,5] However, there is a lack of clarity around the timing of delivery in women with severe COVID-19 in pregnancy. [6–8] The majority of reported cases of severe COVID-19 in the second and third trimester of pregnancy have been delivered by caesarean section. There are very few reports of severe COVID-19 in which the pregnancy was not terminated prematurely. [9]

In these case reports we present two women with severe COVID-19, in the late second to early third trimester, both of whom were successfully treated with mechanical ventilation without termination of the pregnancy. Both women were able to continue the pregnancy and later delivered vaginally at term.

Case report one

The first case was a 26-year-old healthy woman with a body mass index (BMI) of 30 and two previous normal pregnancies. All routine tests and screening during pregnancy were normal. The patient presented with fever and respiratory symptoms at 27 + 0 weeks' gestation and tested positive for SARS-CoV-2 one week later. At 28 + 4 weeks, twelve days after the onset of symptoms, the patient required admission to a special COVID-19 ward due to worsening respiratory symptoms and respiratory rate (RR) 24 breaths/min, oxygen saturations (SpO_2) of 96% and a heart rate (HR) of 113 beats/min. The following day, the patient's condition deteriorated further, with severe breathlessness and oxy-haemoglobin desaturation to 89–90%. With the use of high-flow nasal oxygen (HFNO) at 40 L/min and an inspired oxygen fraction (FiO_2) of 0.45, the patient had a RR of 40 breaths/min and an SpO_2 of 92%. A pulmonary computed tomography (CT) scan revealed that all lobes were affected by confluent infiltrates, some with ground glass characteristics, but no pulmonary embolism. The patient was transferred to the intensive care unit (ICU), where she was intubated and ventilated with positive end-expiratory pressure (PEEP) of 12 cm H_2O and a plateau pressure of 24 cm H_2O, resulting in tidal volumes around 500 mL. On days 2–8 following ICU admission the patient required PEEP 12–15 cm H_2O and FiO_2 between 0.45–0.6, resulting in a pO_2/FiO_2 ratio of 112–150 mmHg. Due to dis-synchronisation with the ventilator settings during the first week, the patient was heavily sedated with propofol, remifentanil, clonidine and midazolam. To optimise ventilation the patient was paralysed with an atracurium infusion for 48 h. From ICU day 8, the patient was weaned from ventilation. A low-dose noradrenaline infusion was used during the first five days of admission to achieve a median blood pressure >65 mmHg. The patient was persistently tachycardic (HR 110–130 beats/min)

throughout her ICU stay. She also had persistent pyrexia (temperature 39 °C), refractory to paracetamol, which was treated with a cooling device.

The patient was mobilised from side to side every four hours to avoid supine hypotensive syndrome due to pregnancy. Nursing procedures and attempts to mobilise often resulted in desaturation, which was managed with intermittent increases in the FiO_2. The patient received thromboprophylaxis with dalteparin from ICU day 1. Cefuroxime treatment was initiated on the first day in ICU, this being standard management at the time. Due to raised levels of procalcitonin, supra-added bacterial infection was suspected, and antibiotic treatment was changed to tazobactam/piperacillin on ICU day 3. Cultures from blood, urine and airways showed no significant bacterial growth that could explain the increase in procalcitonin, but both C-reactive protein and procalcitonin decreased after the change in antibiotic regimen. The patient was weaned from mechanical ventilation after twelve days. At the time of extubation, PEEP was 6 cm H_2O and FiO_2 0.25. After extubation she received an FiO_2 of 0.3 on HFNO 30 L/min, which yielded a pO_2/FiO_2 ratio of 300 mmHg and a RR of 20–25 breaths/min. The patient was re-admitted to the COVID-19 ward, where treatment with HFNO continued for another five days. Persistently high blood glucose was recorded during hospitalisation, and the patient was diagnosed with gestational diabetes. Fetal assessment with regular cardiotocography during the recovery period was normal. The patient was discharged on day 21 of hospital care after a negative SARS-CoV-2 test. At follow-up, the blood glucose levels were normalised with insulin. Estimated fetal growth with ultrasound three and six weeks after discharge was normal. The patient had a spontaneous vaginal delivery at 40 + 4 weeks' gestation. Throughout labour, there were no signs of fetal distress, and the infant was born with Apgar scores of 9 at 1 min and 10 at 5 min. The infant's birth weight, height and head circumference were within normal range. The infant's development at two months follow-up was normal.

Case report two

The patient was a 21-year-old, healthy, primipara with a BMI of 27.3. All routine tests and screening during pregnancy were normal. At 25 + 6 weeks' gestation, she developed fever, dyspnoea and dry cough. Seven days later, at 26 + 6 weeks' gestation, the patient presented with severe respiratory symptoms and signs of RR 28 breaths/min, SpO_2 95% and a HR 122 beats/min. She was admitted to the COVID-19 ward and tested positive for SARS-CoV-2. A pulmonary CT scan showed diffuse multiple round consolidations in all lung lobes but no ground glass infiltrations and no pulmonary embolism. Three days after admission, her condition deteriorated with increasing RR and decreasing SpO_2. The patient received respiratory support by a HFNO, with some initial improvement. She soon became more anxious and tachypnoeic and was transferred to the ICU. At the time of arrival there, her RR was 50/min and the HFNO settings were increased to 40 L/min and an FiO_2 of 0.5, resulting in SpO_2 of 93%. Within another hour, she required intubation and ventilation. The initial ventilator settings were PEEP 8 cm H_2O, plateau pressure 23 cm H_2O and FiO_2 0.45–0.5, resulting in a minute volume of 9–10 L/min and pO_2/FiO_2 ratio of 150-165 mmHg. During ICU days 1–6 the FiO_2 was adjusted between 0.25–0.45. with the higher values required during mobilisation. The PEEP was increased to 12 cm H_2O during ICU days 3–6 in order to reduce the FiO_2. Dexmedetomidine was added to propofol and opioid sedation on day 3. The patient was nursed in the lateral position, and was turned from side to side every four hours to avoid supine positioning. Thromboprophylaxis was given from ICU day 1. The patient was successfully extubated to HFNO, 35 L/min with FiO_2 0.25 after seven days in ICU, and transferred to the COVID-19 ward later that day. Two days later (seven days after admission to hospital) she was discharged. Thromboprophylaxis was continued for four

weeks and subsequent antenatal checks were normal, showing good fetal growth. The patient had an assisted vaginal birth at 41 + 1 weeks' gestation. There were no signs of fetal distress during labour, and the infant was born with Apgar scores of 6 at 1 min and 10 at 5 min. The umbilical cord venous pH was 7.33. The infant's birth weight, height and head circumference were within the normal range and the infant's development at two months was normal.

Discussion

The cases presented occurred in the early phase of the COVID-19 pandemic. To our knowledge, they were the first two cases of severe COVID-19 in late pregnancy in Sweden. There were no national recommendations or international guidelines at that time, and the scientific reporting was very sparse. Both patients required intubation shortly after arrival in the ICU. According to the Berlin definition, both women's symptoms were classified as moderate acute respiratory disease syndrome (ARDS) caused by SARS-CoV-2,[10] although there were some differences in disease severity between the two. The first patient had a higher oxygen demand (lowest pO_2/FiO_2 ratio 112 mmHg compared with 150 mmHg), a longer period of mechanical ventilation and more characteristic opacities on the CT scan than the second patient. These differences and intervals are consistent with population data from the Swedish Intensive Care Register (SIR).[11] The decision to allow the pregnancies to continue, despite the need for ventilation, was discussed at multidisciplinary rounds between obstetricians, anaesthesiologists and specialists in infectious disease medicine. There were concerns that acute surgery was a high-risk procedure in critically ill patients; the COVID Surgical Collaborative has recently shown an increased risk of pulmonary complications after surgery during COVID-19.[12] We considered the risk of maternal complications associated with caesarean section in the presence of severe viral infectious disease to be high and were also concerned about the significant impact of iatrogenic prematurity on the neonate. We also took into account the burden of pregnancy itself on the maternal capacity to tolerate severe viral infection. However, the multidisciplinary view was that as long as the patient could be treated satisfactorily with mechanical ventilation and there was no other organ failure, the balance of risks favoured continuing with the pregnancy. During the ICU stay, the clinical situation was re-evaluated twice daily, including changes in ventilator settings and infectious status as well as cardiovascular parameters, renal function or signs of coagulopathy. In early 2020, it was still unclear whether steroids were beneficial or harmful in severe COVID-19 and the infectious disease specialists recommended avoiding this drug. We thereby abstained from giving betamethasone either as a treatment for COVID-19 or to reduce the risk of fetal respiratory complications in case of premature birth.

We assessed the risk of fetal asphyxia due to viral infection to be low. Premature birth is one of the significant burdens of disease in early childhood, and the risk of fetal complications due to premature delivery should always be considered and ideally avoided, without endangering the mother's health.[13] On this basis, we believed that conservative treatment, if possible, would prove beneficial to the fetus. With respect to fetal surveillance, there was a risk of misinterpreting the cardiotocograph due to the impact of fever, sedatives and prematurity, and it was feared that frequent cardiotocograph monitoring might lead to unnecessary caesarean delivery. Therefore, we decided to evaluate fetal viability by examining the fetal heart rate using Doppler ultrasound in the ICU. Our conservative management of these two cases may be controversial, as most similar cases reported have been delivered by caesarean section. However, our management was based on practical experience of similar situations and a thorough evaluation of different aspects of risk for the mother and the fetus. It is possible that the ICU stay may have been shorter if the women had undergone caesarean section at the time of respiratory failure instead of receiving

expectant management. However, previous case reports have not shown a clear picture of improvement, even after caesarean delivery.[6,7] Furthermore, the time in ICU for our two patients was not prolonged compared with COVID-19 patients in general.[14] Neither of our patients had any known risk factors for severe COVID-19 disease. We observed that the first patient developed gestational diabetes at the end of the infectious episode. Since corticosteroids had not been administered, the impaired glucose tolerance was not a result of these drugs. This raises the question of whether this diagnosis was latent before the infection or triggered by the infection itself.

In conclusion, these two cases indicate the possibility of treating pregnant women with severe COVID-19, in the late second and early third trimester, with critical care including mechanical ventilation, without delivering the baby prematurely. This approach avoids the maternal risks of surgery during an ongoing severe infection and the neonatal complications associated with preterm delivery.

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