Case report

No evidence of vertical transmission of SARS-CoV-2 after induction of labour in an immune-suppressed SARS-CoV-2-positive patient

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SUMMARY
We present a case of a 38±1 weeks pregnant patient (G1P0) with a proven COVID-19 infection, who was planned for induction of labour because of pre-existent hypertension, systemic lupus erythematosus, respiratory problem of coughing and mild dyspnoea without fever during the COVID-19 pandemic in March 2020. To estimate the risk of vertical transmission of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) during labour and delivery, we collected oropharyngeal, vaginal, urinary, placental and neonatal PCRs for SARS-CoV-2 during the period of admission. All PCRs, except for the oropharyngeal, were negative and vertical transmission was not observed. Labour and delivery were uncomplicated and the patient and neonate were discharged the next day. We give a short overview of the known literature about SARS-CoV-2-related infection during pregnancy, delivery and outcome of the neonate.

BACKGROUND
The pandemic, COVID-19, caused by the novel coronavirus SARS-CoV-2, originating from the Wuhan region of China, has spread rapidly throughout the world, including the Netherlands. COVID-19 pneumonia is a highly infectious disease and the ongoing outbreak has been declared a global public health emergency. In the Netherlands, the first COVID-19 patient was confirmed on the 27 February 2020. By the end of March 2020 in the Netherlands, 10 866 infected persons have been identified, of whom 3483 have been admitted to a hospital, more than 800 are currently admitted to an Intensive Care Unit (ICU) and 771 people died after COVID-19 confirmed infection.

Due to the adaptive physiological and anatomical changes combined with the immunosuppressive state of pregnancy, pregnant women, in general, are prone for airway pathogens and pneumonia.

Little is known about COVID-19 and pregnancy. So far, worldwide results have shown that clinical characteristics as well as CT imaging results of COVID-19 infection in pregnant women seem to be similar to non-pregnant adults. With the recent outbreak of the Zika virus in mind, we should be aware that new viruses can cross the placenta and cause congenital disease. So far, there seems to be limited evidence for vertical transmission of SARS-CoV-2 in pregnant patients. Schwartz et al described no vertical transmission in 38 pregnant women with COVID-19 and their neonates using PCR analyses. Unlike previous Middle East Respiratory Syndrome (MERS) and SARS infections in pregnant women, limited maternal deaths have been ascribed to COVID-19.

With this case report, we aim to contribute to the evidence of the absence of transplacental and intrauterine transmission of SARS-CoV-2. We hereby report the outcome, management and investigation into the vertical transmission of a COVID-19 infection in a pregnant woman with pre-existent hypertension and systemic lupus erythematosus (SLE).

CASE PRESENTATION
In March 2020, a 31-year-old patient, G1P0, amenorrhea of 38±1 weeks, was scheduled for induction of labour because of pre-existent hypertension combined with a stable SLE with normal kidney function. Tests for Sjogrens Syndrome antibodies (SSA and SSB) were negative. The patient used methyldopa, prednisolone and azathioprine as prescribed medication. To reduce the risk of pre-eclampsia, acetylsalicylic acid was prescribed according to local protocol until 36 weeks of pregnancy. Fetal biometry was within normal range throughout pregnancy (antenatal ultrasounds for fetal biometrical parameters were performed at 28, 30, 34 and 36 weeks of gestation) with a continuous estimated fetal weight around the 16th percentile.

Due to the development of the progressive problem of coughing, the patient contacted our outpatient clinic before the scheduled induction of labour. Her history mentioned the daily use of prednisolone for SLE, did not reveal recent fever or having visited a known high-risk COVID-19 region or came in contact with people with a confirmed SARS-CoV-2 infection. After consulting the microbiologist, a PCR for SARS-CoV-2 was performed following the national protocol by collecting an oropharyngeal sample. The following day the result of the test was positive. To prevent further potential maternal respiratory distress, we decided to proceed with the scheduled induction of labour.

After a multidisciplinary consultation, the patient was admitted into an isolated zone on the delivery ward, following national and local COVID-19 guidelines.


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On admission, physical examination revealed a temperature of 37.2°C, heart rate of 82 beats/min, blood pressure of 141/88 mm Hg, transcutaneous saturation of 99% by a FiO₂ 0.21, with a respiratory rate of 12 breaths/min. Lung auscultation revealed no abnormal breath sounds. Laboratory findings were normal with a C-reactive protein of 14 mg/L, leucocytes of 6.5×10⁹/L, haemoglobin of 119.2 g/L, thrombocytes of 192×10⁹/L, neutrophils of 5.63×10⁹/L, lymphocytes of 0.22×10⁹/L, monocytes of 0.59×10⁹/L, creatinine of 38 μmol/L, estimated Glomerular Filtration Rate (eGFR) of >90 mL/min, uric acid of 0.18 mmol/L, Alanine aminotransferase (ALT) of 20 U/L and Lactate dehydrogenase (LDH) of 203 U/L. After vaginal examination, a Foley catheter with 50 cc of sterile water was placed intravaginally to induce labour after which the patient went into labour. The patient received epidural analgesia to prevent maternal respiratory insufficiency because of her immunocompromised state and the concomitant SARS-CoV-2 infection. Because of the detection of elevated neonatal IgM and IgG antibodies, there were no signs of neonatal infection with SARS-CoV-2. Four-week post partum, all maternal COVID-19-related symptoms were gone and there were no signs of a neonatal COVID-19 infection.

**Table 1** PCR sampling for COVID-19 during different stages of labour

<table>
<thead>
<tr>
<th>Sample Type</th>
<th>Swab Date</th>
<th>Time</th>
<th>COVID-19</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal oropharyngeal</td>
<td>19-03-2020</td>
<td>09:00, at the outpatient clinic</td>
<td>Positive</td>
</tr>
<tr>
<td>Vaginal swab before rupture of membranes</td>
<td>20-03-2020</td>
<td>18:00</td>
<td>Negative</td>
</tr>
<tr>
<td>Vaginal swab after rupture of membranes</td>
<td>20-03-2020</td>
<td>22:30</td>
<td>Negative</td>
</tr>
<tr>
<td>Maternal urinary swab of catheter urine</td>
<td>20-03-2020</td>
<td>23:00</td>
<td>Negative</td>
</tr>
<tr>
<td>Placental swab maternal side</td>
<td>20-03-2020</td>
<td>23:45</td>
<td>Negative</td>
</tr>
<tr>
<td>Placental swab fetal side</td>
<td>20-03-2020</td>
<td>23:45</td>
<td>Negative</td>
</tr>
<tr>
<td>Neonatal oropharyngeal swab</td>
<td>21-03-2020</td>
<td>00:30</td>
<td>Negative</td>
</tr>
</tbody>
</table>

**OUTCOME AND FOLLOW-UP**

By using PCR samples for SARS-CoV-2 at different times and from different anatomical regions during delivery, we demonstrate no evidence of vertical transmission of SARS-CoV-2 after vaginal birth in an immune-suppressed SARS-CoV-2 positive patient with pre-existing hypertension and SLE. All PCR samples which could indicate vertical transmission (vaginal, maternal urine, maternal and fetal side of the placenta, oropharynx of the neonate) were tested negative. One week after delivery the patient still reported coughing and episodes of mild dyspnoea. There were no signs of neonatal infection with SARS-CoV-2.

**DISCUSSION**

We report a term, prelabour, immuno-suppressed pregnant women with pre-existent hypertension and SLE who tested positive for SARS-CoV-2 and gave birth to a healthy female neonate. There was no evidence of transplacental or intrapartum transmission of SARS-CoV-2 following induction of labour in combination with administration of high doses of corticosteroids. An uneventful induction of labour, delivery, postpartum and postnatal course was observed.

During the course of the COVID-19 infection, several decisions had to be made based on the, at that moment, sparse available literature about COVID-19 and delivery. First, we decided to continue with the scheduled induction of labour, since she was at term with only mild respiratory symptoms, but at risk for respiratory insufficiency because of her immunocompromised state and the concomitant SARS-CoV-2 infection. Because of a lack of evidence of contra-indication for corticosteroids in patients with COVID-19 without respiratory insufficiency balanced against the known risk of an adrenal crisis without supportive therapy, we decided to provide our patient with a stress scheme of corticosteroids during the induction of labour. Due to the immunosuppressive medication during pregnancy and delivery, we argued for a possible higher risk of vertical transmission. The transplacental viral transmission was suggested by Dong et al because of the detection of elevated neonatal IgM and IgG antibodies directly post partum. This suggests vertical transmission and fetal infection since IgM antibodies cannot be transferred across the placenta. However, the reliability of IgM assays has been questioned. Depending on the routes and mechanism of intrauterine infection, further risk assessment can be made. If the transplacental transmission can occur, follow-up of fetal development after infection should be recommended. Viral shedding in diverse anatomical compartments (vaginal discharge, faeces, urine, amniotic fluid and haematogenous/placenta) could lead to fetal or neonatal infection during pregnancy, labour or delivery with possible consequences for the mode of delivery.
The limited evidence of vertical transmission is comforting, but it is important to determine if and how, at which moments and in which situations, vertical transmission can occur. This will allow adequate advice for patients at risk and shared decision-making concerning delivery mode, antenatal and postnatal follow-up.

Royal College of Obstetricians and Gynaecologists (RCOG) guidelines recommend not to separate mother and child, with a maternal confirmed COVID-19 infection but to make use of adequate personal protective measures to prevent transmission.5,15 Mother and child were discharged the next day to minimise the risk of spreading SARS-CoV-2 by shortening the hospital time. We provided strict instructions about COVID-19—clinically, acquisition of data, reporting. PLAF: supervised, reporting, interpretation. FCS: patient care, in lead of crisis management during delivery, supervised. KG: patient care, reporting, data acquisition, analysis and indication of whether changes were made. See: https://creativecommons.org/licenses/by/4.0/.

Learning points

► Our case shows an uncomplicated vaginal birth in a patient with pre-existent hypertension and systemic lupus erythematosus (SLE) using long-term corticosteroids without signs of vertical transmission of SARS-CoV-2.

► The physical stress of vaginal birth did not influence dyspnoea and/or saturation levels in an immune-suppressed patient with pre-existent hypertension and SLE.

► In the absence of an obstetric or maternal contraindication, vaginal birth in COVID-19 patient’s mild/moderate respiratory symptoms can and should be considered.

► With personal protection measurements in place, COVID-19-positive mother and child should not be separated during the postpartum period. These measures may be sufficient to avoid horizontal transmission of the newborn as seen in our case.

► To interpret the vertical transmission of SARS-CoV-2, PCR samples for and immunoglobulins against SARS-CoV-2 should be included in the medical workup of pregnant women suspected for or with a confirmed COVID-19 infection. The same workup should be done for the newborn within the first few hours after birth.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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REFERENCES
