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A case report on vertical transmission of Covid-19 presenting as gangrene of lower limb in neonate

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Abstract
Coronavirus pandemic, a global health crisis which has gripped the entire world, is now posing challenges to all fields of medicine including obstetricians and gynecologists. With the increasing panic in mothers regarding effects of covid-19 infection, its effects on maternal and fetal health, it has become more crucial for obstetricians worldwide to find solutions.
With over a million individuals infected, the global pandemic has been growing at an alarming rate exposing vulnerable populations to an unprecedented global health crisis suggesting that pregnant women and their fetuses are particularly susceptible to poor outcomes [1].

Keywords: Pregnancy, Covid-19, vertical transmission, perinatal outcome

1. Introduction
The novel coronavirus disease 2019 (Covid-19), caused by the severe acute respiratory syndrome–coronavirus-2 (SARS-CoV-2) is a highly infectious disease that was first described by Huang *et al*, whose report focused primarily on the main characteristics and outcomes of nonpregnant adults. The largest published series in pregnancy described 55 pregnant women infected with Covid-19, of whom only one had a severe presentation, and there were no deaths. There is still much unknown regarding the impact of the disease on pregnancy, differences in clinical course, and outcomes in this population, as well as the risk of vertical transmission [2]
The most common symptoms in affected women included fever, cough, and dyspnea. The main laboratory findings included leukocytosis, lymphopenia, thrombocytopenia, and elevated C-reactive protein. [2]
Based on the results of real-time polymerase chain reaction (RT-PCR) assays for the identification of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), primary reports from China suggested that intrauterine vertical transmission was unlikely. However, the introduction of serologic testing of cord and neonatal blood for SARS-CoV-2 has raised concerns [3]

2. Case Report
A 21yr old Primigravida at 32weeks gestational age reported to the labor room with complaint of PV leak, diagnosed as PPROM. She was regularly booked at us throughout her pregnancy. Her routine investigations were normal Hb 12.1g, WBC 13,600cells/cumm, Lymphocytes 26.9. She is a known case of hypothyroidism on treatment with Tab. Thyronorm 50mcg OD since first trimester. Scan done at 26weeks gestation was reported normal. She was examined and decision was to take up for emergency LSCS following steroid prophylaxis.
She underwent emergency LSCS, delivered a live male baby of weight 2.2 kg with apgar score 7, 8. Immediately post delivery baby was stable except for peripheral cyanosis of lower limbs which persisted even after 10-12hrs post-delivery only in the right lower limb and then developed respiratory distress for which baby was shifted to NICU. Right lower limb cyanosis progressed to gangrene. Right lower limb arterial doppler was done on 3rd day of life which was reported as, diffuse arterial wall thickening i.e intraluminal echogenic content showing no demonstrable flow in right femoral, superficial femoral, popliteal arteries, s/o thrombosis. Right anterior and posterior tibial and dorsalis pedis arteries showing trickle flow likely due to collaterals.

Fig. 1: Bluish discolouration of right lower limb

Baby was thoroughly investigated, found to be Covid Ig G positive, following which mother's Covid IgM and IgG and RT PCR was sent, reported as RT PCR and IgG positive which indicates that the lower limb gangrene is due to in utero transmission of SARS-CoV-2 infection. Mother's post operative period was uneventful. Treatment given to the baby in NICU was CPAP followed by ventilator (3days) treatment for respiratory distress, Inj. Enoxaparin, Inj. IVIG, Inj. Meropenem and fresh frozen plasma transfusion. 15days post delivery, the gangrene was limited to right forefoot, baby is stable and on spoon feeding.

Fig. 2: Gangrene limited to right fore foot

This case indicates vertical transmission of SARS-CoV-2 which can cause long term morbidity in neonates. Hence, all neonates born to mothers with PROM/PPROM shoul undergo complusory Covid testing, so that appropriate investigations are done to prevent long term morbidity.

3. Discussion

The physiological changes occurring during pregnancy make the mother more vulnerable to severe infections. Anatomical changes such as an increase in the transverse diameter of the thoracic cage and an elevated level of the diaphragm, decrease maternal tolerance to hypoxia.

Covid-19 infection has caused higher incidence of miscarriage, fetal growth restriction, fetal distress and premature labor in pregnant women [2].

With regard to the fetus and the newborn, the immaturity of the innate and adaptive immune systems makes them highly susceptible to infections. Dysregulation of factors such as cytokines and the complement cascade can have deleterious consequences for brain development and function [1].

Zhao *et al*. demonstrated that angiotensin-converting enzyme 2 (ACE2), which was recently identified as the putative surface receptor of sensitive cells for SARS-CoV-2, is expressed in the human placenta. This opens up the possibility of SARS-CoV-2 spreading transplacentally through ACE2. In addition, damage to the placental barrier caused by severe maternal hypoxemia in women with Covid-19 could potentially lead to vertical transmission of SARS-CoV-2 causing intrauterine infection

The common complications noted in Covid positive neonates included transient lymphocytopenia, pneumonia, deranged liver function tests, DIC, MODS. From these findings, we can say that the fetus and newborn baby might show a response, often sub-clinical, to the mother's infection and, thus, vertical maternal-fetal transmission cannot be ruled out [1].

Based on the results of real-time polymerase chain reaction (RT-PCR) assays for the identification of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), primary reports from China suggested that intrauterine vertical transmission was unlikely. However, the introduction of serologic testing of cord and neonatal blood for SARS-CoV-2 has raised concerns [3].

In addition to testing for SARS-CoV-2 RNA by qRT-PCR, serological tests could be an important supplement to help clarify the question of vertical transmission of SARS-CoV-2. For this, longitudinal follow-up of infants born to women with Covid-19 during pregnancy is required. For example, in a Covid positive mother at the time of delivery or few weeks before delivery, in addition to biological samples (cord blood, placental tissue, amniotic fluid, amnion-chorion interface swab) collected immediately after birth even if negative for SARS-CoV-2 RNA, newborn should be tested for serological tests, but if the newborn tests positive for antibodies as seen in this case where mother was RT PCR positive, IgG positive and baby was RT PCR negative but IgG positive manifested as lower limb gangrene immediately after delivery (APLA syndrome was ruled out in the mother) goes in favor of in utero vertical transmission of Covid 19.

If the IgG antibodies in the infant persist till the age of 18 months or beyond, the diagnosis of congenital infection can be confirmed [4].

4. Conclusion

Vertical transmission of Covid 19 is a possibility. It is also possible that mothers can be asymptomatic and still be RT PCR positive. Ideally all mothers nearing EDD or before induction should and must be tested, especially in symptomatic patients and cases of PROM/PPROM. If mothers are positive, all neonates should be tested, not only antigen test but also serological test for antibody so that infection is identified and appropriate treatment started if needed at the earliest to prevent and decrease long term morbidity and mortality.

Although the majority of mothers do not have any major complications, severe maternal morbidity as a result of Covid-19 and perinatal deaths are reported. Careful monitoring of pregnancies with Covid-19 infection so as to identify vertical transmission at the earliest and to prevent perinatal transmission are warranted [1].

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