

## **Covid 19 & vertical transmission**

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## **1 INTRODUCTION**

The current coronavirus pandemic is a serious public health emergency and has led to widespread damage globally. Although there are many coronaviruses, the particular that is responsible for this pandemic is the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It has incubation period of around 2 to 7 days and most symptomatic patients can have fever, malaise, cough, or loss of taste or smell, with some cases developing into life threatening pneumonia and acute respiratory distress syndrome with case fatality rates range from 1% to 2%. Pregnancy is considered as a vulnerable group for any infection and knowledge regarding the possible risk of vertical transmission of this virus is very limited but is important for counseling regarding COVID-19 related pregnancy risks and for further management. COVID 19 infection in mothers basically leads to hypoxia, inflammatory response & cytokine storm. It appears around 10% of SARS- Cov-2 infected pregnant women require hospitalization with respiratory support COVID-19 can infect the placenta as confirmed by the presence of SARSCoV-2 viral RNA in the placenta and evidence of virions found within the syncytiotrophoblast. The possible neonatal outcomes are increased risk of

- Miscarriage, Still birth, Preterm labour
- Fetal growth restriction
- FIRS(Fetal Inflammatory Response Syndrome)
- Long term- Neuro sensorial development delay

### **1.1 VERTICAL TRANSMISSION**

Of COVID-19 is a serious concern. Approximately 5% of infant delivered tested positive for SARS-Cov-2-RNA and half of them within 12hrs after birth. The possible mechanisms of Vertical transmission are:

- Transplacental transmission after the virus infects the placenta
- Intrapartum transmission via ingestion or aspiration of cervical vaginal secretions during delivery
- Postpartum transmission by direct contact during breastfeeding

## 1.2 MULTIPLE INFECTIOUS VECTORS

have been shown to be capable of vertical transmission. Researchers have identified the potential role of angiotensin-converting enzyme 2 (ACE2), Transmembrane serine protease 2 (TMRRSS2) and ENDOU- a placental endoribonuclease homologous to Nsp15 in the vertical transmission of SARS-CoV-2.

## 2 CORONA VIRUS MAY CROSS PLACENTA:

Hypothetically, **two conditions are necessary** for transplacental transmission to be possible:

- (a) the virus must reach the placenta; and
- (b) the receptor for the virus, must be present in the placenta

### 2.1 GENGLER ET AL. (SEP 2020)

By testing placental tissues at various gestational ages in both COVID- 19-positive and -negative mothers, confirmed that ACE expression is present consistently throughout pregnancy regardless of COVID-19 status (1). The angiotensin-converting enzyme 2 (ACE2) receptor is expressed in the placenta and is found in the syncytiotrophoblast, cytotrophoblast, endothelium, and vascular smooth muscle from both primary and secondary villi. Transmembrane serine protease 2 (TMPRSS2) is also a key enzyme of the SARS CoV-2 viral entry machinery.

### 2.2 JING ET AL., ( NOV 2020)

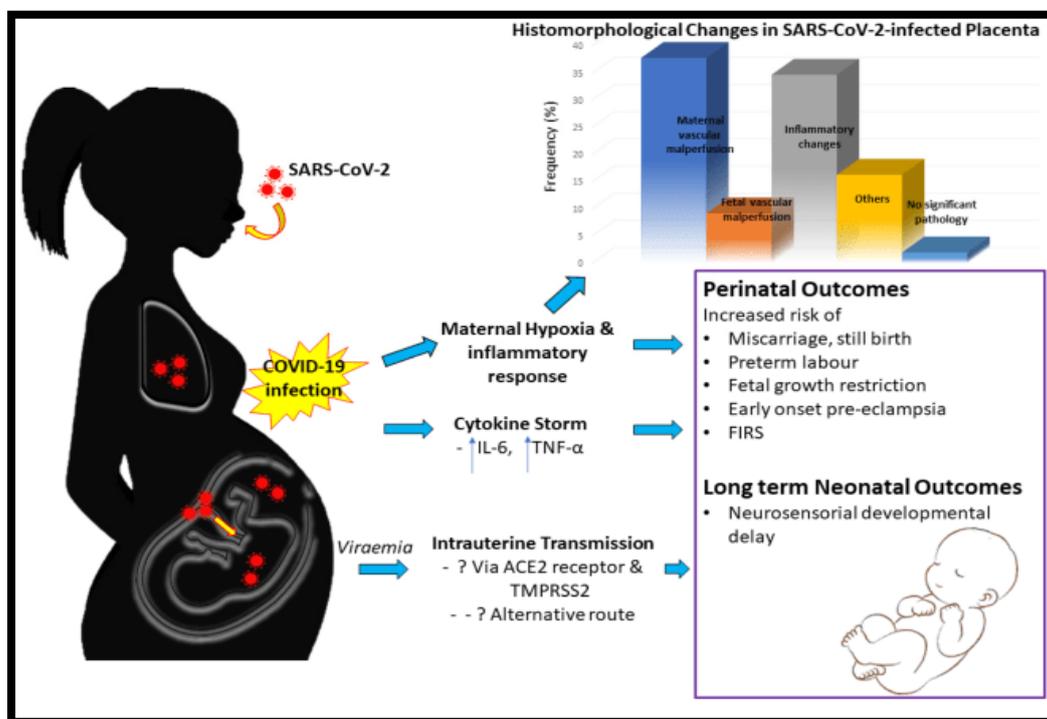
Conducted a protein-protein interaction (PPI) network study searching for proteins relevant to pregnancy-associated COVID-19 in pregnancy complicated with severe preeclampsia (sPE) and intra-amniotic infection and/or inflammation. Common proteins included the SARS-CoV-2 entry receptor ACE2 and ENDOU, a placental endoribonuclease homologous to Nsp15, a protein produced by the virus to escape host immunity. Remarkably, placental ENDOU mRNA expression far exceeded that of ACE2(2).

## 3 PLACENTAL PATHOLOGY :

Early publications did not show evidence for placental infection by the virus but the recent studies confirm the **presence of virus induced changes within the placenta**. COVID-19 placenta shows various histopathological findings. **Komini –Aizawa et al (sept 2020)** reported **Vascular malperfusion** as the most common finding in the placental pathology among COVID-19-positive mothers (3).

**Sharps et al.,(Nov. 2020)** showed that in 20 studies that reported placental histopathology findings in third trimester placentas following maternal SARS-CoV-2 infection, evidence of both fetal vascular malperfusion (35.3% of cases) and maternal vascular malperfusion (46% of cases) were

reported, along with evidence of inflammation in the placentas (villitis 8.7% cases, intervillitis 5.3% of cases, chorioamnionitis 6% of cases) (4)



#### 4 EVIDENCE FOR FOETAL INFECTION :

Whereas a systematic review by **Fomari et al. (Apr 2020)** found neonatal infection in 5 cases (7.1%) of neonates. Nine papers reported original data about delivery to mothers infected by Sars-Cov-2, involving a total of 70 neonates born to mothers with proved Sars-Cov-2 infection. 65 newborns (92.9% of cases) from seven independent studies was negative for a transplacental infection according to oropharyngeal or nasopharyngeal swab performed in the first hours or days of life. Four neonates from two different studies reported early-onset infection detected at second days of life. The elevated IgM antibody level suggests that the neonate was infected in utero, since IgM antibodies are not transferred to the fetus via the placenta (6).

It is not correct to state that the possibility of vertical transmission of Covid-19 has been definitely confirmed or excluded.

#### 4.1 DANA PM ET AL (JUNE 2020)

Concluded that there is no evidence of vertical transmission in pregnant women with COVID-19. Placenta from pregnant COVID-19 women demonstrated different degrees of fibrin depositions both around and inside the villi, as well as increased local syncytial nodules. One of the placentas had severe

infarction and another one presented a concurrent chorionic hemangioma morphology. The records of 15 pregnant women with COVID-19 indicated that there were no neonatal death, neonatal asphyxia and still birth (5)

#### 4.2 ALZAMORA MC ET AL. ( JUNE 2020)

Reported a case of severe COVID-19 during pregnancy and possible vertical transmission , the neonatal nasopharyngeal swab was positive for severe acute respiratory syndrome– coronavirus 2 (SARS-CoV-2) through RT-PCR 16 hrs after caesarean delivery in the COVID positive mother. This is the earliest reported positive PCR in the neonate raising the concern for vertical transmission as the neonatal Isolation was implemented immediately after birth without delayed cord clamping or skin to skin contact. COVID-19 serology was negative in the new born, the Maternal IgM & IgG became positive on post partum day 4 (day 9 after symptoms onset).(7)

However, some questions remain unanswered. In the studies described above, most pregnant women had mild to moderate COVID-19 symptoms, and in all cases, symptoms manifested during the third trimester of pregnancy, therefore, the time interval from clinical manifestation of SARS-CoV-2 to delivery was short. Since the placental barrier may temporarily delay the transfer of the virus from the mother to the fetus it is uncertain whether there could be a risk of vertical transmission.

#### 4.3 RCOG GUIDELINES OCTOBER 2020

Evidence suggests that intrauterine vertical transmission to foetus do occur though it is uncommon. If it does occur, it appears to not be affected by mode of birth, method of feeding or whether the woman and baby stay together (rooming in).

#### 4.4 EVIDENCE OF VERTICAL TRANSMISSION

of COVID-19/SARS-CoV-2 is still unclear but possible, although data should be interpreted with caution. Further extensive and high quality research in this field is warranted. Although there is currently no concrete evidence of intrauterine vertical transmission of SARS-CoV-2, but the virological and serological evidence is valuable to clarify this issue, The need for optimal sampling , reliable assays and longitudinal follow-up of infants after birth is essential to draw reliable conclusions.

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