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## Original Research Article

## Is vertical transmission that dreadful in COVID 19 pregnancy

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## ABSTRACT

**Introduction:** Since the emergence of coronavirus illness in 2019 (COVID-19), there has been discussion on whether pregnant women are more vulnerable to COVID-19 and whether there is any vertical transmission through the placenta.

**Methodology:** We describe a collection of thirty placentae collected from pregnant women who were tested at our hospital for SARS cov-2 infection by RT-PCR and turned to be positive. They were divided based on clinical symptoms into asymptomatic, mild and moderate groups before giving birth. We performed a thorough histopathological examination of placental tissue, RTPCR of amniotic fluid and placentae, between April 2021 and July 2021.

**Results:** All were term deliveries (between 37 and 39 gestational weeks). Sixty percent were asymptomatic and 23% had mild symptoms, 17% had moderate symptoms. On histopathological examination, signs of maternal and/or foetal malperfusion were present in 36.6% of cases, which can be explained by the presence of altered coagulative or microangiopathic state induced by SARS-CoV-2.

**Conclusion:** In spite of the fact that most of the neonates born to mothers with COVID 19 positive status, were tested negative for SARS CoV 2 by RTPCR, we observed that COVID 19 in term patients admitted for delivery is associated with increased rates of placental histopathological abnormalities particularly fetal vascular malperfusion and villitis of unknown cause. These findings seem to occur even among asymptomatic term patients.

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## 1. Introduction

The 2019 coronavirus disease (COVID-19), a novel zoonotic illness was initially found in late December 2019 in Wuhan, Hubei Province, China, following an outbreak of severe pneumonia of unknown aetiology.<sup>1</sup>

The etiological culprit was successfully isolated and identified as a previously unknown beta-coronavirus, termed 2019 novel coronavirus (2019-nCoV) provisionally.<sup>2</sup>

On the basis of phylogenetic study, it was later officially classified as Severe Acute Respiratory Syndrome Virus 2 (SARS-CoV-2) by the International Committee on

Taxonomy of Viruses.<sup>3</sup>

SARS-emergence CoV-2's and rapid spread via prolonged human-to-human transmission pose a serious pandemic threat to humanity worldwide. After the 2009 Influenza A (H1N1) swine flu, the World Health Organization (WHO) named COVID-19 as the fifth documented pandemic on March 11, 2020.<sup>4</sup>

As of November 9, 2020, there were an estimated 50.4 million confirmed cases worldwide, with 1.26 million deaths, resulting in a global death toll of 1.26 million.

The SARS-CoV-2 illness has caught healthcare providers off guard since it behaves differently than any other "respiratory" infection, and it affects more than just the lungs. In addition to the characteristic respiratory symptoms

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and fever, a number of individuals with severe COVID-19 had extrapulmonary clinical signs relating to heart, renal, liver, digestive tract, and neurological diseases. Placentas are no different. COVID-19 infection creates tell-tale symptoms of damage in the placenta, according to increasing amounts of data.<sup>5</sup>

In spite of increasing molecular and ultrastructural evidence of SARS-CoV-2 in the placentas of COVID-19-positive mothers, no virus-induced illnesses have been observed in neonates.<sup>6</sup>

Vertical transmission occurs when an infectious pathogen is passed from the mother to the foetus during the antepartum and intrapartum periods, or from the mother to the neonate during the postpartum period, via the placenta in utero, body fluid contact during birthing, or direct touch. A single-cell RNA sequencing investigation of the coexpression of ACE2 and transmembrane serine protease 2 (TMPRSS2), a transmembrane serine protein for viral spike (S) protein priming, revealed that only a small fraction of placental cells express both proteins in each trimester. Furthermore, this group discovered that coexpression of these proteins is modest in chorioamniotic membranes from the third trimester.<sup>7–10</sup>

In addition to maintaining immune tolerance to foetal cells, the human placenta possesses an immunological barrier that prevents infections from entering the body. The innate immune system is thought to play a critical role in protecting foetuses and newborns from SARS-CoV-2 infection.<sup>11</sup>

Natural killer (NK) cells (70 percent), decidual macrophages (15 percent), and CD4 T cells (15 percent) are among the immune cells found in the decidua basalis, which is the maternal component of the maternofetal interface.<sup>12</sup>

Furthermore, the syncytiotrophoblast cells, which make up the outermost layer of chorionic villi and are in direct touch with the maternal blood, lack an intercellular gap connection, which prevents pathogens from entering the maternal blood. Physical barriers, such as trophoblastic basement membranes, provide an extra layer of protection against pathogens. The innate immune system, the structural barrier, and the interaction between decidual immune cells and invading foetal extravillous trophoblasts may all work together to protect the foetus.<sup>13</sup>

Placental examination can provide useful information that can help us better understand illness aetiology and identify the underlying causes of poor pregnancy outcomes.<sup>14</sup>

The histomorphological and ultrastructural abnormalities documented on placentas from SARS-CoV-2-positive women are confined to solitary case reports and a few case series due to the novelty of COVID-19. The information gap between COVID-19's effects on the placenta and pregnancy outcomes must be investigated.

## 2. Aims and Objectives

1. To describe morphology and histopathological features in placentae of women with SARS-CoV-2 infection during term pregnancy and
2. To determine presence of vertical transmission from mothers infected with sars covid 2 in third trimester.

## 3. Materials and Methods

This is a prospective observational study conducted at our Hospital, A Nodal centre exclusively for covid positive patients.

### 3.1. Inclusion criteria

1. All pregnant women who tested positive for covid 19 and delivered at our hospital
2. Women whose placentae and amniotic fluid could be tested for RTPCR and histopathological examination.

### 3.2. Exclusion criteria

Pregnant women who tested positive for COVID 19 but

1. Didn't give consent
2. With incomplete medical records
3. With hypertensive disorders
4. With diabetes complicating pregnancy
5. Whose placental examination could not be performed

## 4. Results

COVID-19 infection has not been linked to teratogenic effects in newborns. Only 24 (8 percent) of 313 neonates born to mothers with COVID-19 were positive for SARS-CoV-2, according to Gajbhiye et al. (2020), raising a crucial concern about the success rate of transplacental viral infection (intrauterine transmission) to the foetus. It is worth noting that maternal infection is not the same as placental infection. Similarly, evidence of placental viral infection does not imply intrauterine vertical transfer of the virus to the foetus. It is expected that the virus will be actively replicated in the placenta. If this is true, however, the mechanism for keeping this highly contagious virus from reaching the foetus remains unknown. One possibility is that the placenta's maternal–fetal interface acts as a strong barrier

In our study, we included thirty women who had been tested positive antenatally for SARS-CoV-2 by nasal swabs because of symptoms in 12 (40%) and 18(60%) asymptomatic pregnant women when entering for delivery, detected by universal screening.

The severity of symptoms are classified as

**Asymptomatic:** no symptoms (with negative imaging when performed);

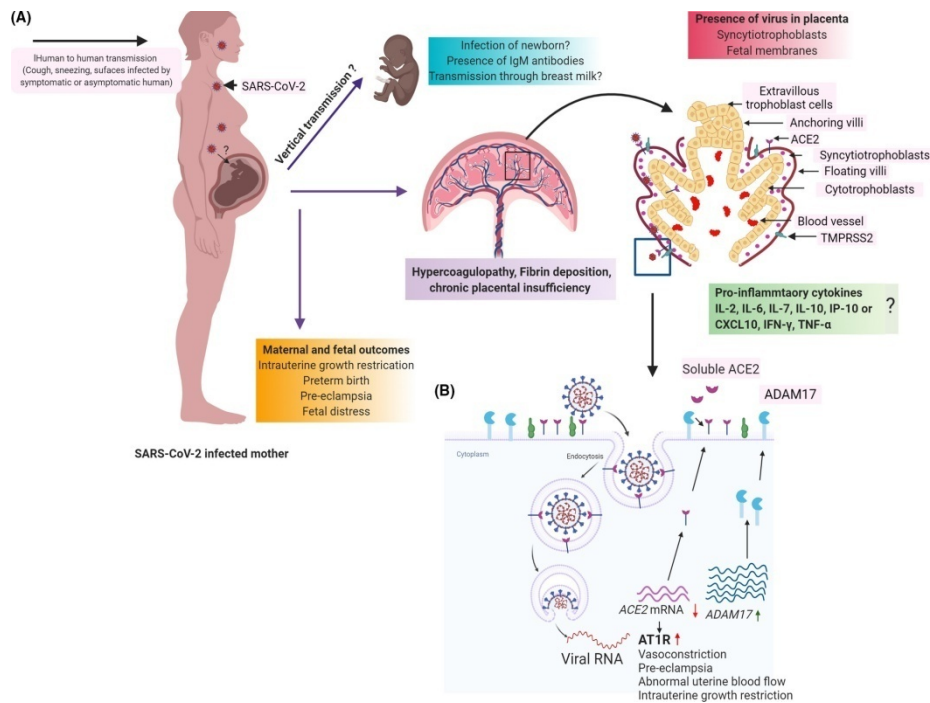


Fig. 1:

**Mild:** one or more symptoms among fever, cough, pharyngeal pain, headache, myalgia, nausea, emesis, diarrhea, anosmia, ageusia, but no dyspnea (abnormal imaging when performed);

**Moderate:** evidence of lower respiratory disease by clinical assessment or imaging and Oxygen saturation ( $\text{SaO}_2$ )  $\geq 94\%$  on room air;

**Severe:** one or more symptoms among  $\text{SaO}_2 \leq 94\%$  in ambient air,  $\text{PaO}_2/\text{FiO}_2 < 300$  mmHg (i.e. arterial oxygen partial pressure/fraction of inspired oxygen), respiratory rate  $> 30$ /minute or pneumonia involving more than 50% of the lungs' volume at X-ray scan.

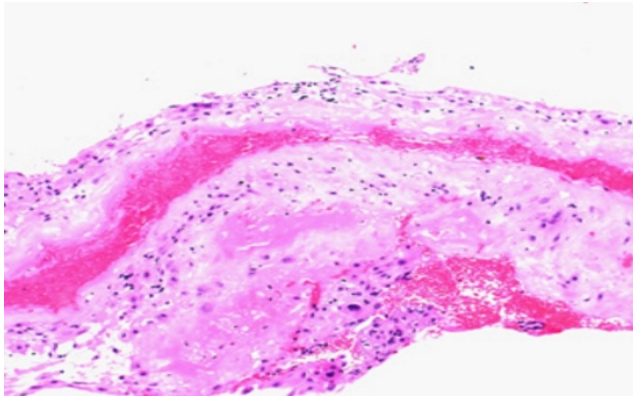
Altogether, thirty placenta specimens have been sent to our institute for histopathologic testing. Placentae were treated according to conventional methods, which included histopathologic analysis of one block of the umbilical cord, one block of the chorionic membranes, and three blocks of placenta tissue after being fixed for at least 48 hours to minimise infectiousness.<sup>14</sup> In addition, macroscopically visible alterations such as hematoma infarctions were embedded. Haematoxylin and eosin were used to stain all of the slides. The present Amsterdam Placental Workshop Group Consensus Statement was used to classify pathological findings.

They categorised the histological features into six classes based on the primary placental patterns observed:

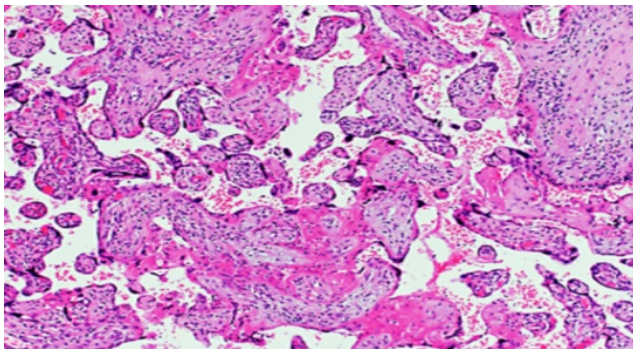
1. Normal, when placentas did not show any specific alteration;

2. Delayed Villous Maturation, according to the Amsterdam consensus definition (a monotonous villous population with centrally placed capillaries and decreased vasculosyncytial membranes, in at least 30% of one full-thickness parenchymal slide);
3. Fetal vascular malperfusion (FVM) is a symptom of decreased vascular supply in placentas.<sup>15–18</sup> It has been observed in four investigations with COVID-19-affected placentas. FVM is related with foetal vascular thrombosis, aberrant cord insertion, umbilical cord hypercoiling, and maternal hypercoagulable state.<sup>19,20</sup> SARS-endotheliotropic CoV-2's behaviour via the ACE2 receptor on endothelial cells makes it sensitive to vascular endothelial dysfunction, resulting in complement-induced coagulopathy in COVID-19-infected patients and making them susceptible to microthrombi formation.
4. Chorioamnionitis, considering acute forms;
5. Maternal Vascular Malperfusion, including placental hypoplasia, infarction (considered when larger than 5% in non-peripheral placental zones), retroplacental hemorrhage, distal villous hypoplasia and accelerated villous maturation;
6. Chronic inflammation, when placentas showed features attributable to chronic deciduitis or high and low grade chronic villitis of unknown etiology.

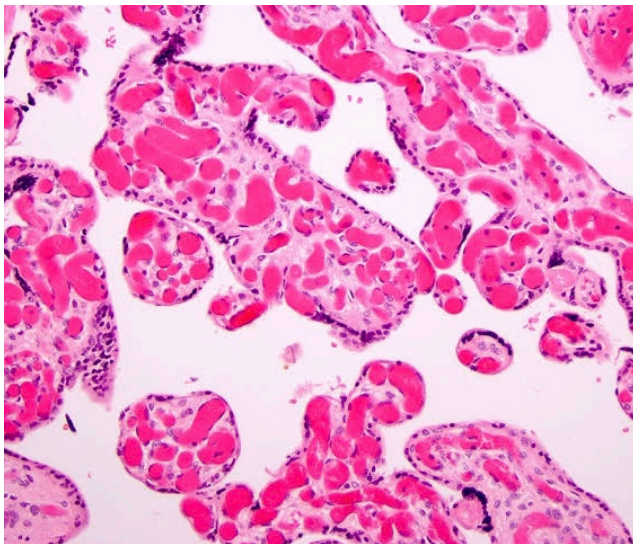
In our study, all placentas were term deliveries with (between 37 weeks and 39 weeks ) and mode of delivery being vaginal delivery in 14 cases( 46.6%) and



**Fig. 2:** Decidual arteriopathy-decidual artery showing complete necrosis of arterial wall and intraluminal fibrosis



**Fig. 3:** Subtle chronic villitis



**Fig. 4:** Chorangiomas

caesarean delivery in 16 cases (53.3%). Mothers age ranged between 20-29 years and BMI ranged between 21-25 at the time of birth. Twelve patients were symptomatic(40%) for SARS-COV2 (fever, cold, cough). The other pregnant women (60%) were asymptomatic at the time of delivery. Eleven out of thirty patients had covid placental changes like increase of intervillous fibrin, acute congestion, extensive infarction, decidual vasculopathy, intervillous thrombosis and signs of fetal malperfusion like chorangiomas, karyorrhexis, thrombi in fetal circulation and these placentae showed inflammatory changes like chorionic villitis, chorioamnionitis, subchorionitis.

**Table 1:**

		Percentage	P value
No of women with COVID-19 in the study	30		
NO of placentae having histopathological changes	11	36.6%	0.0003
No of placentae positive for COVID 19 by RTPCR	7	23.33%	0.0006
No of amniotic fluid samples positive for COVID 19 by RTPCR	4	13.33%	0.08
No of neonates positive for COVID 19 by RTPCR	3	10%	0.07

The statistical analysis was made using chi square test.

Number of placentae having histopathological changes were 11(36.6%) p value (0.0003). The number of placentae positive for COVID 19 by RTPCR were 7(23.3%) p value (0.0006). The number of amniotic fluid samples positive for COVID 19 RTPCR were 4(13,3%) p value (0.08). The number of neonates positive for COVID 19 by RTPCR were 3(10%) p value (0.07) which is statistically insignificant.

**Table 2:**

Intervillous fibrin deposition	8	72.7%
Extensive infarction	7	63.6%
Chorangiomas	5	45.4%
Acute congestion	2	18.1%

The most common histopathologic change noted in our study was Intervillous fibrin deposition (72.7%), followed by extensive infarction(63.6%), chorangiomas(45.4%), acute congestion(18.1%).

Out of 30 neonates born to these 30 covid positive women by cesarean section, 3 were tested RTPCR positive suggesting incidence of neonatal covid positivity to be 10%, which is statistically insignificant

Out of 3 neonates, 2 were admitted to NICU and were discharged healthy.1 neonate expired due to congenital heart disease after 2 days of life.

## 5. Conclusion

Eleven out of thirty (36%) placentas showed features of maternal vascular malperfusion that is acute congestion, extensive infarction, intervillous fibrin deposition, intervillous thrombi suggesting a common theme of abnormal maternal circulation, as well as an increased incidence of chorangiosis. These findings provide mechanistic insight into the observed epidemiologic associations between COVID 19 in pregnancy and adverse perinatal outcomes. Collectively these findings suggest that increased antenatal surveillance for women with diagnosed with SARS CoV 2 may be warranted.

There is no concrete evidence to suggest presence or absence of vertical transmission in COVID 19 infected mothers. Further studies are required to establish the correlation between placental changes, detection of COVID 19 in amniotic fluid and placenta and vertical transmission.

## 6. Source of Funding

None.

## 7. Conflict of Interest

None.

## References

- Mackenzie JS, Smith DW. COVID-19: a novel zoonotic disease caused by a coronavirus from China: what we know and what we don't. *Microbiol Aust.* 2020;p. MA20013. doi:10.1071/MA20013.
- Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature.* 2020;579(7798):7095418.
- Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. *Nat Microbiol.* 2020;5(4):536–44.
- Liu YC, Kuo RL, Shih SR. COVID-19: The first documented coronavirus pandemic in history. *Biomed J.* 2020;43(4):328–33.
- Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. *Lancet Infect Dis.* 2020;20(5):533–4.
- Zaim S, Chong JH, Sankaranarayanan V, Harky A. COVID-19 and Multiorgan Response. *Curr Probl Cardiol.* 2020;45(8):100618.
- Fan C, Lei D, Fang C, Li C, Wang M, Liu Y, et al. Perinatal Transmission of 2019 Coronavirus Disease-Associated Severe Acute Respiratory Syndrome Coronavirus 2: Should We Worry? *Clin Infect Dis.* 2021;72(5):862–4.
- Gatta AND, Rizzo R, Pilu G, Simonazzi G. Coronavirus disease 2019 during pregnancy: a systematic review of reported cases. *Am J Obstet Gynecol.* 2020;223(1):36–41.
- Yang Z, Wang M, Zhu Z, Liu Y. Coronavirus disease 2019 (COVID-19) and pregnancy: a systematic review. *J Matern Fetal Neonatal Med.* 2020;30:1–4. doi:0.1080/14767058.2020.1759541.
- Yang Z, Liu Y. Vertical Transmission of Severe Acute Respiratory Syndrome Coronavirus 2: A Systematic Review. *Am J Perinatol.* 2020;37(10):1055–60.
- Carsetti R, Quintarelli C, Quinti I, Mortari EP, Zumla A, Ippolito G, et al. The immune system of children: the key to understanding SARS-CoV-2 susceptibility? *Lancet Child Adolesc Health.* 2020;4(6):414–6.
- Pereira L. Congenital Viral Infection: Traversing the Uterine-Placental Interface. *Annu Rev Virol.* 2018;5(1):273–9.
- Robbins JR, Bakardjiev AI. Pathogens and the placental fortress. *Curr Opin Microbiol.* 2012;15(1):36–43.
- Khong TY, Mooney EE, Balmus AI, Boyd NC, Brundler TK, Derricott MA, et al. Sampling and Definitions of Placental Lesions: Amsterdam Placental Workshop Group Consensus Statement. *Arch Pathol Lab Med.* 2016;140(7):698–713.
- Facchetti F, Bugatti M, Drera E, Tripodo C, Sartori E, Cancila V, et al. SARS-CoV2 vertical transmission with adverse effects on the newborn revealed through integrated immunohistochemical, electron microscopy and molecular analyses of Placenta. *EBioMedicine.* 2020;59:102951. doi:10.1016/j.ebiom.2020.102951.
- Giroloamo D, Khalil R, Alameddine A, S, Angelo D, Galliani E, et al. Placental histopathology after SARS-CoV-2 infection in pregnancy: a systematic review and meta-analysis. *Am J Obstet Gynecol MFM.* 2021;3(6):8379009–8379009.
- Menter T, Mertz KD, Jiang S, Chen H, Monod C, Tzankov A, et al. Placental Pathology Findings during and after SARS-CoV-2 Infection: Features of Villitis and Malperfusion. *Pathobiology.* 2021;88(1):7573905–7573905.
- Amaral W, Moraes CL, Rodrigues A, Noll M, Arruda JT, Mendonça CR. PMID. 2020.
- Chew MX, Teoh PY, Wong YP, Tan GC. Multiple umbilical cord strictures in a case of intrauterine foetal demise. *Malays J Pathol.* 2019;41(3):31901924–31901924.
- Heider A. 2017.

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