Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Comment on evidence for and against vertical transmission of severe acute respiratory syndrome coronavirus 2 (coronavirus disease 2019)

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TO THE EDITORS: We read with great interest Lamouroux's discussion of vertical transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1] They report a low frequency (1%) of serum SARS-CoV-2 ribonucleic acid (RNA) viral load (RNAemia) and a low expression of the angiotensin-converting enzyme 2 (ACE2) receptor in the maternal-fetal interface between 6 and 14 weeks' gestation as arguments against biologic plausibility of vertical transmission in the first trimester of pregnancy. We would like to expand the discussion regarding vertical transmission.

Vertical transmission of maternal pathogens may occur transplacentally via amniotic fluid infection or as an ascending infection. Presumably, for hematogenous or transplacental transmission, maternal viremia would be required. A study by Huang et al[2] showed a 15% frequency of RNAemia among adults with symptomatic coronavirus disease 2019.

Consistent with Lamouroux's statement that ACE2 is low in the first trimester of pregnancy, ACE2 RNA expression is developmentally regulated with extremely low expression at 6 to 14 weeks' gestation, although there is high expression at 24 weeks' gestation.[3] ACE2 RNA is highly expressed in human villous trophoblast, extravillous trophoblast, and syncytiotrophoblast as well as in several fetal organ cells (such as the heart, liver, and lung but not the kidneys) at 24 weeks' gestation.[3] Interestingly, another study demonstrated ACE2 protein expression in human syncytiotrophoblast by immunocytochemistry at 6 to 16 weeks' gestation and at term.[4] In placental villi, the main sites of immunocytochemical expression of ACE2 are the syncytiotrophoblast, cytotrophoblast, endothelium, and vascular smooth muscle of primary and secondary villi.[5] The presence of an ACE2 receptor in gestational tissue raises the possibility of vertical transmission.

In utero or congenital infection of SARS-CoV-2 via amniotic fluid has been suggested, with positive polymerase chain reaction (PCR) results in amniotic fluid obtained by needle aspiration after uterine incision but before amniotomy during a cesarean delivery at 32 weeks' gestation, with precautions taken to prevent environmental contamination of specimens.[6] The PCR test for SARS-CoV-2 was negative in vaginal secretions, umbilical cord blood, and neonatal nasopharynx samples at birth but was positive in nasopharyngeal samples at 24 hours.[6]

Placental infection (PCR test that is positive for SARS-CoV-2 in placental submembrane and cotyledon samples) has also been demonstrated in a pregnancy with miscarriage in the second trimester.[7] Placental histology demonstrated mixed inflammatory infiltrates composed of neutrophils and monocytes in the subchorial space and nonspecific increased intervillous fibrin deposition and funisitis in the absence of bacterial or fungal infection.

Whether in utero (hematogenous or transamniotic) infection or placental infection is possible is not clear yet, but it certainly appears plausible. We would advocate that translational, systematic evaluation demonstrating an infectious virus in paired maternal and infant tissue samples is required to better address this question of vertical transmission. ■

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