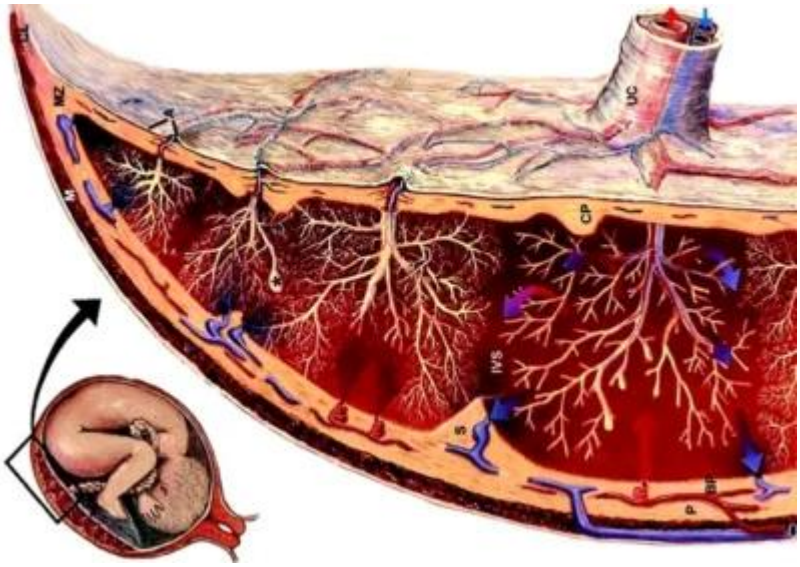
Severe vascular remodeling (including severe thickening and fibrosis of the vessel walls, smooth muscle cell proliferation, and vessel lumen occlusion) was found in the placental arteries of women infected with SARS-CoV-2 during pregnancy | 1

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) can infect the human placenta. Since the infection with SARS-CoV-2 seriously affects the vasculature of multiple organs, including the lungs, heart, and brain, the authors from Ukraine and the United States investigated whether and how SARS-CoV-2 affects placental arteries in women who were infected during pregnancy and gave birth to live full-term newborns.

The normal vascular pattern of the placenta includes vasculogenesis and angiogenesis, which are associated with the physiological expression of vascular endothelial growth factor (VEGF). A recent study of markers involved in vascular damage of the placental tissue in unvaccinated women infected with SARS-CoV-2 demonstrated increased expression of VEGF and the endothelial cell marker CD34 in the placental samples of SARS-CoV-2-positive women. According to the authors, these findings indicate alterations, disarrangements, or remodeling of normal vasculature, associated with vascular endothelial injury and inflammation, presumably endothelitis.
https://discovermednews.com/colocalization-of-sars-cov-2-spike-protein-with-markers-of-vascular-damage-and-autophagy-in-placentas/

Notably, a recent study that used computational methodology to predict human-SARS-CoV-2 protein interactions revealed that SARS-CoV-2 proteins mimic 30 proteins linked to the VEGF signaling pathway. The SARS-COV-2 proteins that possibly interact with VEGF-A are NSP7 and nucleocapsid, whereas spike protein, NSP8, and NSP7 possibly interact with vascular endothelial growth factor receptor 2. (Yapici-Eser H et al. Neuropsychiatric Symptoms of COVID-19 Explained by SARS-CoV-2 Proteins' Mimicry of Human Protein Interactions. Front. Hum. Neurosci, 23 March 2021.)
https://www.frontiersin.org/journals/human-neuroscience/articles/10.3389/fnhum.2021.656313/full



About the study

This study enrolled 85 women who were infected with SARS-CoV-2 and had symptoms of COVID-19 between 28 and 36 weeks of pregnancy. In all participants, infection with SARS-CoV-2 was diagnosed by reverse transcription polymerase chain reaction of nasopharyngeal swabs. The majority (68%) of women who tested positive for SARS-CoV-2 had mild COVID-19, whereas 32% experienced a severe disease with pneumonia. The exclusion criteria were the following: preeclampsia, hypertension, diabetes, large fetus (>5kg), smoking during pregnancy, and human immunodeficiency virus infection. The archived placental tissues from 28 women who gave birth to live full-term newborns in 2018, before the COVID-19 pandemic, were used as controls.

The authors performed immunohistochemistry using the antibodies against α-smooth muscle actin, a marker of pericytes and myofibroblastic cells. They also performed a morphometric analysis of the thickness of the placental arterial wall and lumen index (the ratio of the internal vessel area to the external vessel area). All sample preparations were randomized, and the data analysis was performed in a blinded manner.

Results

The morphometric analysis of the placental arterial walls revealed significant differences between women who had COVID-19 during pregnancy and healthy controls. In women with COVID-19, the median arterial wall thickness was approximately 30 μm, while in controls it was approximately 15 μm. This shows that arterial wall thickness in placentas of women with COVID-19 was twice as high as that of women without COVID-19. In thickened placental vessels, the immunohistochemistry with the antibodies against α-smooth muscle actin demonstrated a dramatic increase in smooth muscle mass. According to the authors, the placental arteries of women who had COVID-19 during pregnancy likely underwent smooth muscle cell proliferation.

The morphometric analysis also demonstrated a significantly smaller (5-fold) arterial lumen in placentas of women with COVID-19 than in healthy controls. Importantly, Masson’s trichrome staining demonstrated not only a quantitative thickening of placental vessels in those who had COVID-19 during pregnancy but also a fibrosis of the vessel walls.

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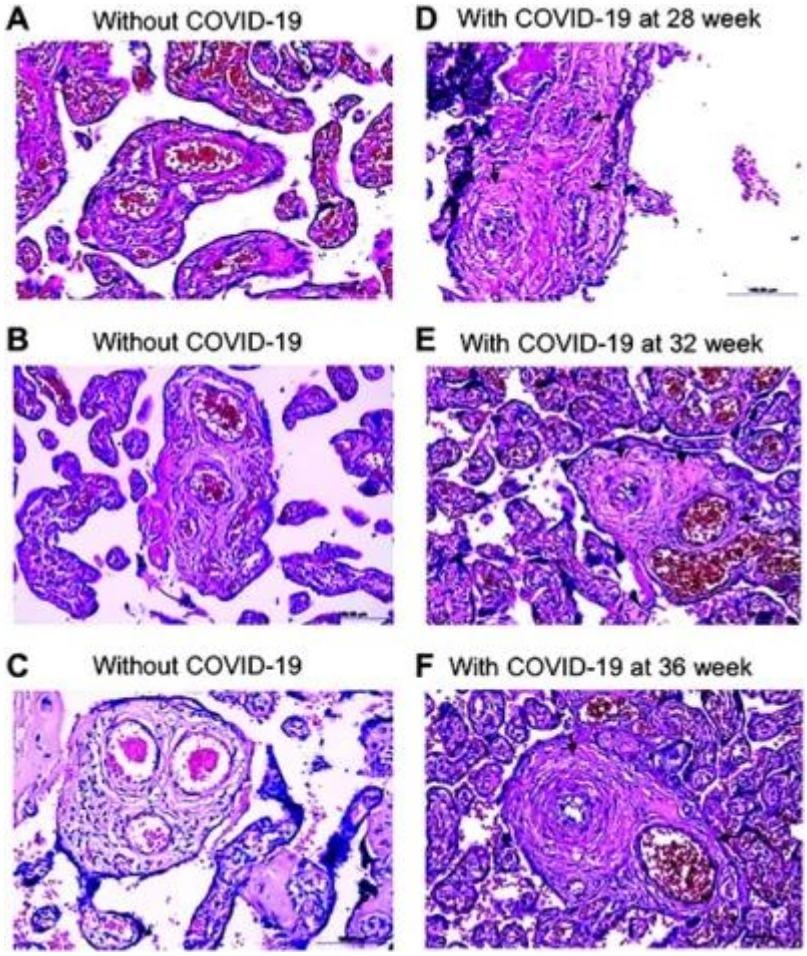
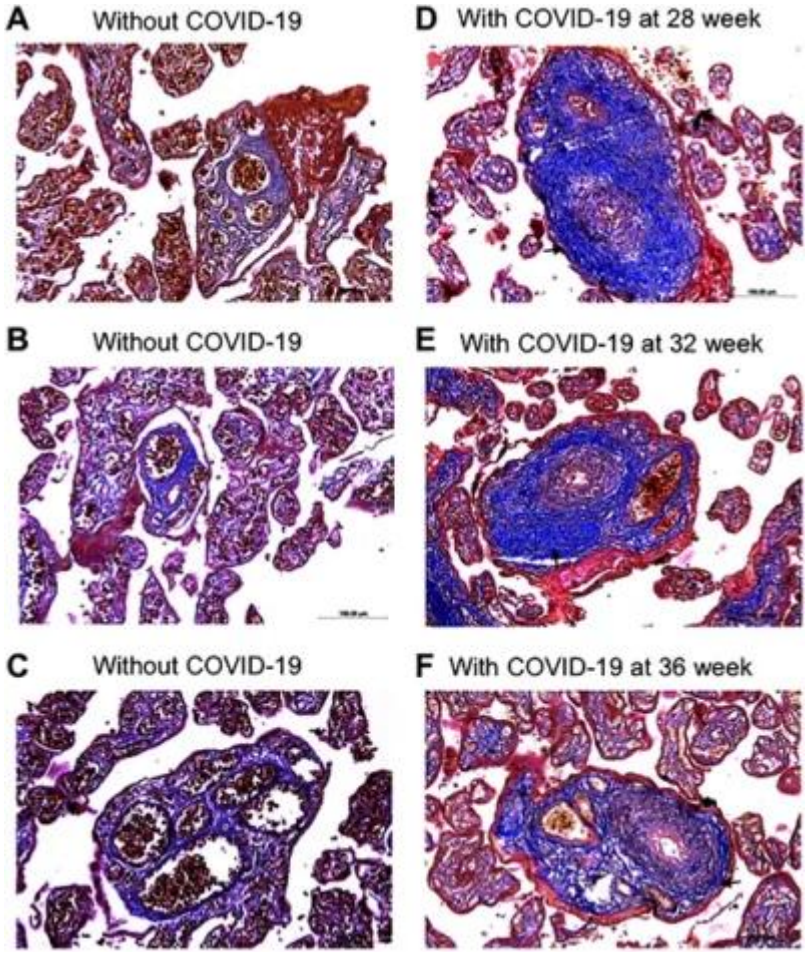


The original figure from the article by Gychka SG, Brelidze TI, Kuchyn IL, et al. PLoS ONE, 2022. Vascular wall thickening in the placentas of women who contracted COVID-19 during pregnancy



The original figure from the article by Gychka SG, Brelidze TI, Kuchyn IL, et al. PLoS ONE, 2022. Masson's trichrome staining.

Conclusion

This study demonstrated severe vascular remodeling found in the placental arteries of all women who tested positive for SARS-CoV-2 during pregnancy. Although the narrowing of the placental arterial lumen alters blood flow between the mother and the fetus, the newborns' health in this study cohort was not significantly affected.

The same research group previously reported 20 cases of prenatal fetal death in the group of 414 women infected with SARS-CoV-2 during pregnancy. This corresponds to a rate of almost 5%, which is significantly higher than the population average. Therefore, the authors emphasized that further studies are needed to determine the effects of placental vascular remodeling on neonatal well-being and development.

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Journal Reference

Gychka SG, Brelidze TI, Kuchyn IL, et al. (2022) Placental vascular remodeling in pregnant women with COVID-19. PLoS ONE 17(7): e0268591. (Open Access) https://doi.org/10.1371/journal.pone.0268591