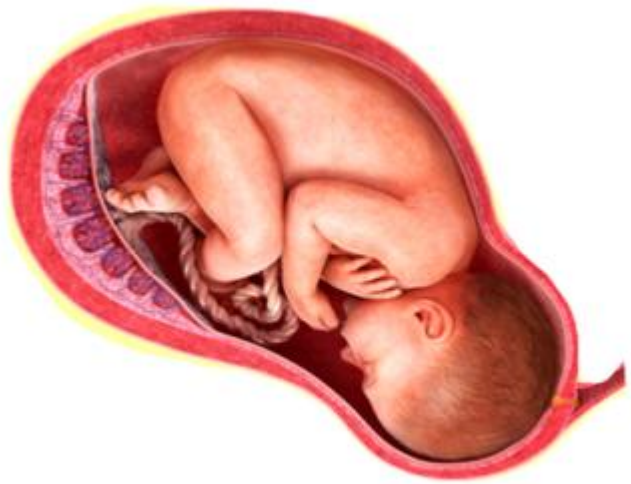
Some recent evidence suggests that maternal infection with severe acute respiratory syndrome coronavirus disease 2 (SARS-CoV-2) during pregnancy may be associated with a greater rate of numerous complications in infected mothers and their newborns. The complications observed in mothers include preeclampsia, preterm birth, and miscarriages, whereas complications observed in newborns exposed to maternal COVID-19 *in utero* include neurodevelopmental delay, motor deficits, seizures, and microcephaly. In this study, the authors from the United States investigated gender-specific differences in risk for neurodevelopmental disorders in fetuses *in utero* exposed to SARS-CoV-2.

Previous studies have identified that the effects of SARS-CoV-2 on the placental immune response are sexually dimorphic. Mothers infected with SARS-CoV-2 with male fetuses were found to have lower levels of anti-SARS-CoV-2 antibodies and significantly up-regulated interferon signaling pathways in their placentas compared to SARS-CoV-2-infected mothers with female fetuses. According to these findings, fetal gender may influence the maternal immune response to the virus. https://www.science.org/doi/10.1126/scitranslmed.abi7428 Of note, in a recent animal study that showed maternal-fetal transmission of SARS-CoV-2 at time points matching the second and third trimesters of human pregnancy, higher levels of viral infection were found in male fetuses than in female fetuses. https://discovermednews.com/experimental-evidence-of-maternal-fetal-transmission-of-sars-cov-2-and-viral-tropism-for-fetal-brain-cells/



About the study

The researchers utilized the hospital's electronic health records to compare the cohort born during the pandemic, with two other groups, one that included all live births in 2018, before the pandemic, and the second that included all live births in 2019, taking into account that part of the follow-up period would take place during the pandemic. The mean maternal age was 33.0 years (30.0–36.0).

The primary outcome was defined as any diagnosis of a neurodevelopmental disorder, based on the presence of at least one ICD10 code in the "developmental" category. The codes included F8x, which refers to pervasive and specific developmental disorders, such as developmental disorders of speech and language (F80), specific developmental disorders of scholastic skills (F81), specific developmental disorders of motor function (F82), pervasive developmental disorders (F84), other/unspecific disorder of psychological development (F88/89), and code F7x, which refers to intellectual disabilities.

Results

The pandemic cohort enrolled 18,323 live births, 877 of which were exposed to SARS-CoV-2 *in utero.* Of the 877 offspring exposed to SARS-CoV-2 *in utero*, 3.0% (26 infants) were diagnosed with neurodevelopmental disorder during the first 12 months of their life.

At the 12-month follow-up, the adjusted regression model accounting for race, ethnicity, insurance status, hospital type, maternal age, and preterm status demonstrated the association between SARS-CoV-2 positivity and significantly increased risk for neurodevelopmental disorder diagnosis only in male offspring.

At the 18-month follow-up, the results available for 551 offspring exposed to SARS-CoV-2 *in utero* were consistent with results observed at the 12-month follow-up. Significantly increased risk for diagnosis of neurodevelopmental disorder was found only in male offspring.

Conclusion

This study demonstrated that the risk of neurodevelopmental sequelae in fetuses exposed to maternal SARS-CoV-2 infection may be gender-specific. At the 12-month and 18-month follow-up, an increased risk for neurodevelopmental disorders was found in male offspring exposed to maternal COVID-19 *in utero*.

These results suggest that male fetuses may be more vulnerable to maternal SARS-CoV-2 infection, but, larger studies should more accurately assess and characterize this risk.

This study has been published on a preprint server and is currently being reviewed.

Journal Reference

Edlow AG, Castro VM, Shook LL. Sex-specific neurodevelopmental outcomes in offspring of mothers with SARS-CoV-2 in pregnancy: an electronic health records cohort. medRxiv preprint https://doi.org/10.1101/2022.11.18.22282448