

Inflammation markers associated with COVID-19 during pregnancy may signal adverse impacts to long-term infant health

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New research results demonstrate how inflammation from a COVID-19 infection during pregnancy could potentially impact long-term infant health, including infant growth and brain development. Published in the



Journal of Perinatology, a new study from Boston Medical Center describes how infants of mothers who had a COVID-19 infection during pregnancy had significant elevations in inflammatory blood markers, also known as cytokines, at the time of delivery.

COVID-19 has impacted a growing number of pregnant patients throughout the pandemic, affecting an estimated 14 per 1,000 births in the U.S. in 2020. Typically, there are low rates of viral transmission to an infant after a COVID-19 infection during pregnancy, and no other apparent adverse effects on the infant at birth. In this new study however, researchers discovered elevated levels of markers, interleukin (IL)-6 and interferon gamma-induced protein (IP)-10, well-characterized inflammatory mediators central in the COVID-19 cytokine response, in both mothers and infants who experienced a COVID-19 infection during pregnancy. Marker IL-8 was also uniquely elevated in infants following maternal COVID-19 infection.

In pregnancy, the elevated levels of IL-6 and IL-8 have been associated with gestational pathologies including miscarriage, preeclampsia and preterm delivery. Perinatal exposure to these <u>cytokines</u> has also been associated with altered fetal development. In pregnancy, elevated maternal IP-10 has been implicated in miscarriage and preeclampsia, but the long-term infant effects of IP-10 exposure in the perinatal period are currently undefined. The results of this study indicate that there are unidentified effects of COVID-19 infection during pregnancy on infants, specifically the evidence of in-utero inflammation persisting weeks to months after initial maternal infection.

"This inflammation has the potential to significantly impact infant growth and development, highlighting the importance of continuing to follow children with COVID-19 exposure during pregnancy for unknown long-term consequences on their health," says Elizabeth Taglauer, MD, Ph.D., a neonatologist at Boston Medical Center, an



assistant professor of pediatrics at Boston University School of Medicine and first author on this study. "This study also importantly provides additional reasons to encourage pregnant women to pursue vaccination against COVID-19 to avoid any long-term adverse consequences for their infant."

Between July 2020 and June 2021, mother-infant dyads in early and late gestational stages of pregnancy were enrolled and categorized as a group of participants with a known COVID-19 infection during pregnancy. A control group was then enrolled between January and April 2021 for participants with no evidence of COVID-19 infection during pregnancy and a negative SARS-COV-2 testing at time of delivery. For this particular analysis, anyone who had received a COVID-19 vaccination was excluded. In this prospective cohort study, a maternal blood sample and an infant blood sample were collected from 31 COVID and 29 control dyads at the time of delivery and analyzed with a panel of 13 cytokines, which are soluble markers of immune responses. The cytokine levels for these 13 immune response markers were then compared between the COVID-19 and control groups to identify any differences. This study was completed as a multi-disciplinary effort from the Mothers and Infants Affected by Signs and Symptoms of COVID-19 (MASC) study team at Boston Medical Center.

"The results of our study indicate that a COVID-19 infection during pregnancy creates an inflammatory in-utero environment, with evidence of prolonged inflammation in infant blood markers at the time of delivery," says Elisha Wachman, MD, a neonatologist at Boston Medical Center, an associate professor of pediatrics at Boston University School of Medicine and senior author on this study. "This could lead to alterations in infant growth and development as an unforeseen complication from COVID-19 infection during pregnancy."

Researchers are focusing future research on mother-infant dyads who



received the COVID-19 vaccination during pregnancy who did not experience a COVID-19 infection. In an ongoing study, cytokine profiles of this group look very similar to the control group, meaning that they do not have evidence of elevated inflammatory markers in the infant. These results will soon be submitted for publication and provide additional evidence that vaccination rather than COVID-19 infection during pregnancy provides protection for the infant against any adverse effects.

More information: Elizabeth S. Taglauer et al, Evaluation of maternal-infant dyad inflammatory cytokines in pregnancies affected by maternal SARS-CoV-2 infection in early and late gestation, *Journal of Perinatology* (2022). DOI: 10.1038/s41372-022-01391-9

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