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## Letter to the editor

## Re: Vertical transmission and humoral immune response following maternal infection with SARS-CoV-2 by Massalha et al.

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## To the Editor,

Pregnant individuals, as a special group, are hesitant and reluctant to be vaccinated due to concerns about vaccine safety, so the proportion of pregnant individuals receiving COVID-19 vaccine lags behind other groups. However, studies have shown that SARS-CoV-2 infection during pregnancy is associated with an increased risk of maternal morbidity and adverse birth outcomes [1]. It is of clinical significance to explore the humoral immune response and vertical transmission of SARS-CoV-2 infection in pregnant people to understand the immune protection of pregnant people after infection and the risk of neonatal infection and to provide evidence for the vaccination of pregnant people.

Recently, Massalha et al. investigated vertical transmission and humoral immune response after maternal SARS-CoV-2-A infection [2]. In their study, among 36 neonates in which nasopharyngeal swabs were taken, one neonate (3%) had a positive PCR result. Based on these results, they concluded that the vertical transmission rate of SARS-CoV-2 was at least 3%, which is not rigorous. Babies who test positive in this way don't necessarily get the infection in utero, as they may get it through horizontal transmission shortly after birth. To more accurately identify newborns with vertically transmitted infections, some studies have chosen to examine IgM antibodies in umbilical cord blood [3]. IgG and IgM antibodies are produced after maternal infection; however, only IgG can pass through the placenta, so only the presence of IgM signals fetal exposure to antigens. Nevertheless, IgM antibodies in

cord blood were not detected near delivery in the neonates who were PCR positive in this study. Of course, this may also be determined by the specific immune system of the fetus. Since adaptive immunity relies on existing memory cells, the fetal immune system lacks antigenic stimulation and training and does not necessarily detect IgM antibodies during initial infection. In their study, it was also observed that 22% of pregnant individuals were undetectable for IgM 8 to 12 weeks after infection with the highest serum antibody positive rate. It could also be that the immune system changes during pregnancy to adapt to the growth of the half-allogeneic fetus. This makes it difficult to determine vertical transmission rates by detecting IgM in cord blood.

In addition, the placenta provides a protective barrier for the fetus. In fact, angiotensin converting enzyme 2 receptors and transmembrane serine protease 2 are rarely co-expressed in the placenta [4], which is typically required for SARS-CoV-2 to enter cells. But different variants may have different invasiveness. Studies have shown that omicron's ability to use transmembrane serine protease 2 is reduced when it invades cells [5], suggesting that the risk of vertical transmission may differ between variants of infection. In short, SARS-CoV-2 is not easy to transmit across the placenta to the fetus.

## Transparency declaration

The author declares no competing interests.

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