Maternal Transmission of SARS-CoV-2-specific Antibodies, but not Cytokines/Chemokines to Neonates Following Infection and Vaccination During Pregnancy

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Abstract

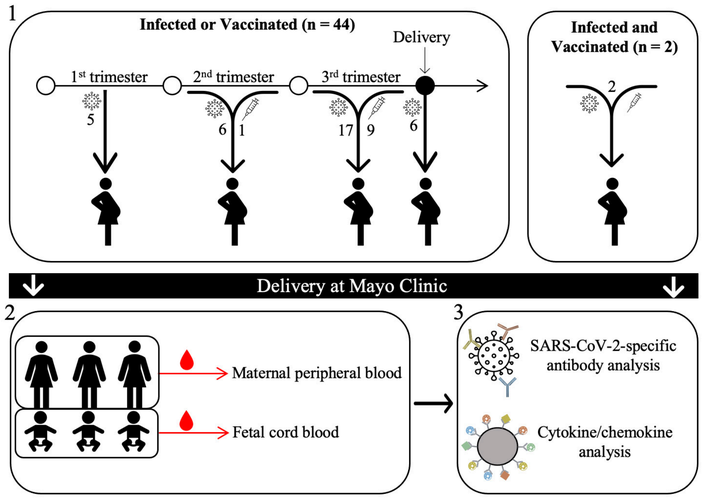
Background: Despite extensive studies of human immune responses to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection and coronavirus disease 2019 (COVID-19) vaccination, research examining protective correlates of vertical transmission following maternal exposure in pregnancy remain limited. Here, we characterized antibody and cytokine responses in maternal and cord blood following infection or vaccination at various timepoints during gestation.

Methods: Spike S1 protein-specific binding antibodies and antibodies capable of blocking the interaction between the receptor binding domain (RBD) and the angiotensin converting enzyme 2 (ACE2) were measured in maternal and cord blood by ELISA. Serum concentrations of 74 cytokines/chemokines were measured by multiplex assay. Humoral responses and cytokine levels from matched maternal and fetal cord sera were compared and examined for potential correlations.

Results: We observed a highly significant correlation between Spike S1-specific antibody titer and RBD-ACE2 blocking antibody activity between maternal and fetal cord serum ($p < 2.2e-16$, $R > 0.90$). Blocking antibody activity was significantly higher for mothers infected during the 3rd trimester compared to earlier trimesters; however, vaccinated mothers developed and transferred higher antibody titers with greater RBD-ACE2 blocking antibody activity to their neonates than infected mothers. Furthermore, vaccine-induced Spike S1 IgG transfer ratios (fetal cord/maternal) were significantly higher than those induced by infection ($p = 0.002$). Multiplex assay showed significantly elevated levels of 33 cytokines/chemokines, mainly pro-inflammatory in infected maternal serum samples, while the paired fetal cord samples exhibited an anti-inflammatory cytokine predominance.

Conclusions: Our data support selective vertical transmission of potentially protective humoral responses against SARS-CoV-2, especially following vaccination in the 3rd trimester. The anti-inflammatory cytokine predominance in cord blood that persists despite maternal SARS-CoV-2 infection may offset the adverse outcomes of inflammation in pregnancy for the neonate.

Study Design



Mother-Neonate Dyad Antibody Correlations

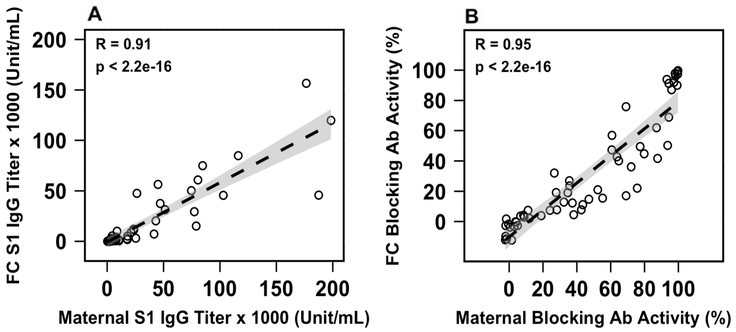


Figure 1. Mother-Neonate Dyad Antibody Response Correlations. Correlations between maternal and fetal cord plasma (**A**) anti-S1 IgG concentrations and (**B**) RBD-ACE2 blocking antibody activity at time of delivery. Quantitative (**A**) and functional (**B**) antibody characteristics were strongly correlated among mother dyads ($R>0.90$, $p<2.2e-16$).

Infection/Vaccine Timing Impacts Transplacental Antibody Transmission

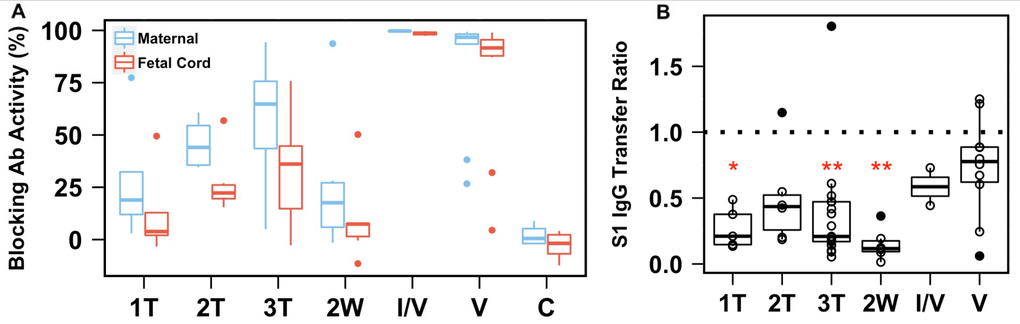


Figure 2. Functional and Transplacental Antibody Responses. (**A**) Maternal and fetal cord plasma RBD-ACE2 blocking antibody activity of those infected during different trimesters (T), infected 2 weeks prior to delivery (2W), infected and vaccinated (IV), vaccinated (V), and unexposed pregnant controls (C). (**B**) Anti-Spike S1 IgG transfer ratios (fetal cord plasma/maternal plasma) among the same groups in plot **A**.

Differing Mother-Neonate Cytokine/Chemokine Responses

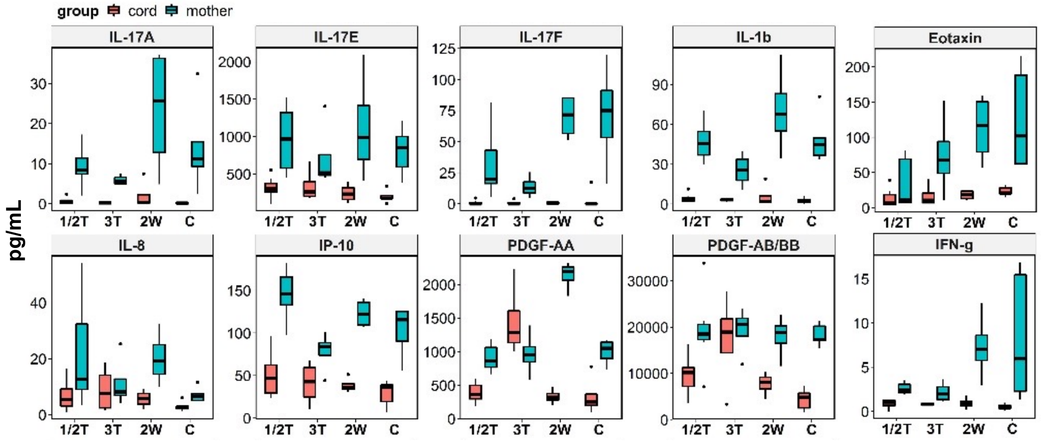


Figure 3. Cytokine/Chemokine Responses in Maternal and Fetal Cord Plasma. Cytokine and chemokine concentrations in maternal and fetal cord plasma after delivery from subjects infected during the 1st/2nd trimester (1/2T), infected during the 3rd trimester (3T), infected 2 weeks prior to delivery (2W), and unexposed pregnant controls (C). Pro-inflammatory predominance observed in maternal plasma samples compared to paired fetal cord samples.