Cord Blood Antibodies following Maternal COVID-19 Vaccination During Pregnancy

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Condensation: COVID-19 mRNA vaccination in pregnancy resulted in maternal humoral immune response and transplacental transfer of IgG to infant, more robust with longer latency to delivery.

Short title: Antibody Transfer after Maternal COVID-19 Vaccination

Objective:

Vaccination of pregnant women can be an important strategy to confer protection to neonates and young infants[1]. However, there are limited data on the immunologic response of pregnant women to mRNA COVID-19 vaccination[2] and the kinetics of transplacental antibody transfer[3,4]. Our objective was to investigate transfer of SARS-CoV-2 IgG to infants following maternal COVID-19 vaccination in pregnancy and factors associated with increased efficiency of transfer.

Study Design:

This is a prospective case series of pregnant women who delivered at Prentice Women's Hospital in Chicago, IL, USA (January-March 2021). Women who received COVID-19 vaccination during pregnancy were identified via review of the electronic health record (EHR). Demographic and clinical information, including the specific vaccine used and the latency from vaccination until delivery was obtained from the EHR. At the time of the study, two mRNA COVID-19 vaccines, Pfizer/BioNTech and Moderna/NIH, had received emergency use authorization, and healthcare workers were the initial qualifying group.

Maternal blood and umbilical cord blood (herein referred to as 'infant') were retrieved from specimens submitted for blood typing. SARS-CoV-2 IgM and IgG were measured from plasma using the Access SARS-CoV-2 IgG and IgM Antibody tests (DXI Platform, Beckman Coulter, Brea CA) in a CAP/CLIA certified clinical laboratory. The chemiluminescent assay reports quantitative antibodies to the SARS-CoV-2 receptor binding domain in arbitrary units [AU]/mL, with values

of ≥1 considered positive. Antibody transfer ratio was calculated as infant IgG divided by maternal IgG concentrations.

Descriptive statistics were calculated. Linear regressions were used to identify factors significantly associated with antibody transfer ratios as well as infant IgG values. This study was IRB approved prior to its initiation.

Results:

We collected matched maternal plasma and cord blood from 27 women that received a COVID-19 vaccine during pregnancy; they delivered 28 infants (1 twin). Maternal age was 33 ± 3 (mean ± SD) years; race/ethnicity was 75% non-Hispanic white, 11% Hispanic. Gestational age at first vaccine dose was 33 ± 2 weeks. Vaccine type was 18 (64%) Pfizer, 6(18%) Moderna, and 4 (14%) unknown. Twenty-two women (74%) received both vaccine doses prior to delivery with a mean latency of 6 ± 3 weeks.

About half of women (15/27) and no infants had positive IgM (>1) (**Figure 1A**). All but 1 woman (26/27) had positive SARS-CoV-2 IgG at time of delivery. Only 3 infants did not have positive IgG (1 set of twins); these 2 women had received their first vaccine less than 3 weeks prior to delivery.

The average maternal to infant IgG transfer ratio was 1.0 ± 0.6 (**Figure 1B**), however an increased latency from vaccination until delivery (weeks) was associated with an increased transfer ratio (β=0.2, 95% CI 0.1-0.2) (**Figure 1C**). Correspondingly, having received the second

vaccine dose prior to delivery was significantly associated with increased infant IgG (β=19.0, 95% CI 7.1-30.8). Similarly, latency from vaccination to delivery was associated with increased infant IgG (β=2.9, 95% CI 0.7-5.1).

Conclusion:

Most pregnant women who received the COVID-19 mRNA vaccine in the 3rd trimester had transplacental transfer of IgG to the infant. The observed mean IgG transfer ratio demonstrates about equal infant antibody level to maternal level. This is slightly lower than what has been reported in pertussis vaccination (1.19 to 1.36)[5], but greater than transfer ratio following SARS-CoV-2 infection (0.72 ± 0.57)[4]. A novel finding is that the transfer ratio appears to increase with latency from vaccination. These data suggest, at least among women in their third trimester, that earlier vaccination may produce greater infant immunity, the immunobiology of which requires further study.

Notably, due to vaccine eligibility and timing, most women included herein were healthcare workers in their 3rd trimester. Future research, including a more diverse cohort of women and women who received vaccination earlier in their pregnancy, is needed. Nevertheless, these results show promising evidence of passive immunity against SARS-CoV-2 in newborns after maternal receipt of COVID-19 mRNA vaccine.

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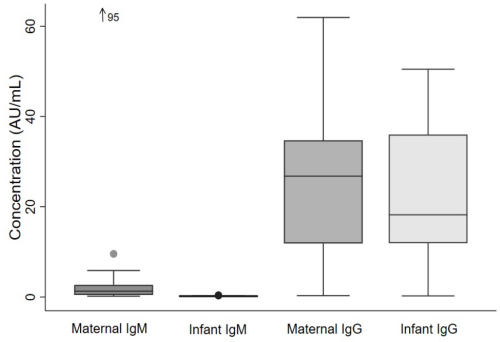
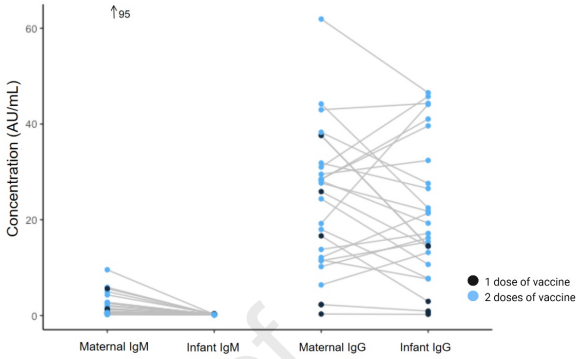
Figure legend: (A) Anti-SARS-CoV-2 antibody levels in maternal and umbilical cord (infant) blood following maternal COVID-19 vaccination (n=27 mothers, 28 infants); (B) Paired maternal and infant IgM and IgG levels of women with 1 dose (n=5) and 2 doses (n=22) of vaccine during pregnancy. Paired infant IgM was 0.2 for 1 outlier maternal IgM of 95 AU/ml.; (C) Association between latency (weeks) from first vaccine dose and antibody transfer ratio (infant IgG/maternal IgG).

Maternal and infant SARS-CoV-2 antibodies and IgG transfer

A Maternal and infant SARS-CoV-2 antibody levels



B Paired maternal and infant IgG and IgM levels



C Scatterplot of antibody transfer ratio and latency from vaccination to delivery