COVID-19 VACCINATED MATERNL/CORD BLOOD DON'T HAVE NEUTRALIZATION FOR OMICRON VARIANTS

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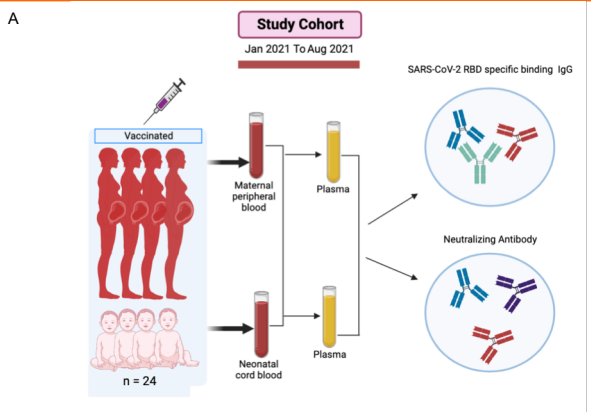
BACKGROUND: Maternally derived antibodies are crucial for neonatal immunity. Understanding the binding and cross-neutralization capacity of maternal/cord antibody responses to COVID-19 vaccination during pregnancy can inform neonatal immunity.

METHODS: Here we characterized the binding and neutralizing antibody profile at delivery in 24 pregnant individuals following two doses of Moderna mRNA-1273 or Pfizer BNT162b2 vaccination. We evaluated the transplacental antibody transfer by profiling maternal and umbilical cord blood. We analyzed for SARS-CoV-2 multivariant cross-neutralizing antibody levels for wildtype Wuhan, Delta, Omicron BA1, BA2, and BA4/BA5 variants by enzyme-linked immunosorbent assay.

RESULTS: Our results reveal that current vaccination induced significantly higher (p=0.003) RBD-specific binding IgG titers in cord blood compared to maternal blood for both Wuhan and Omicron BA1 strain. Interestingly, binding IgG antibody levels for the Omicron BA1 strain were significantly lower (P< 0.0001) when compared to the Wuhan strain in both maternal and cord blood. In contrast to the binding, the Omicron BA1, BA2, and BA4/5 specific neutralizing antibody levels were significantly lower (P< 0.0001) compared to the Wuhan and Delta variants. It is interesting to note that the BA4/5 neutralizing capacity was not at all detected in both maternal and cord blood.

CONCLUSION: Our data suggest that the initial series of COVID-19 mRNA vaccines were immunogenic in pregnant women, and vaccine-elicited binding antibodies were detectable in cord blood at significantly higher levels for Wuhan and Delta variants but not for Omicron variants. Interestingly, the vaccination did not induce neutralizing antibodies for Omicron variants. These results provide novel insight into the impact of vaccination on maternal humoral immune response and transplacental antibody transfer for SARS-CoV-2 variants and support the need for boosters as new variants emerge.

COVID-19 Vaccination in Pregnant Women Experimental Design



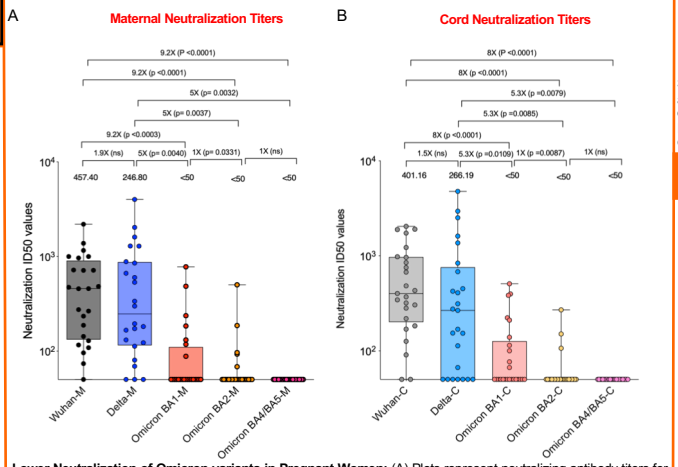
Recruitment of COVID-19 vaccinated Pregnant Women: (A) Pregnant women who received COVID-19 vaccination 14 days prior the delivery were enrolled in the study. Maternal and cord blood were collected at the time of delivery and analyzed for anti-SARS-CoV-2 specific binding antibodies using enzyme-linked immunosorbent assay (ELISA). SARS-CoV-2 neutralizing antibodies against wild type Wuhan and variants delta, omicron BA1, omicron BA2, and omicron BA4/BA5 ere measured by luciferase-based pseudovirus neutralization assay.

Maternal Demographic and Clinical Characteristics of COVID-19 Vaccinated Pregnant Women

COVID-19 vaccination during pregnancy (study cohort)	
Demographic	N = 24
Maternal age at delivery, year	34 ± 3.8
Race/Ethnicity	
Non-Hispanic white	17 (71)
Non-Hispanic Black	3 (12.5)
Asian	3 (12.5)
Hispanic any race	1 (4)
mRNA vaccination	
Gestational age at vaccination, week	26 (19-30)
Vaccine type	
Moderna	8 (33)
Pfizer	16 (67)
Obstetric data	
Gestational age at delivery, week	39 ± 1
Mode of delivery	
Vaginal	16 (67)
Cesarean	8 (33)

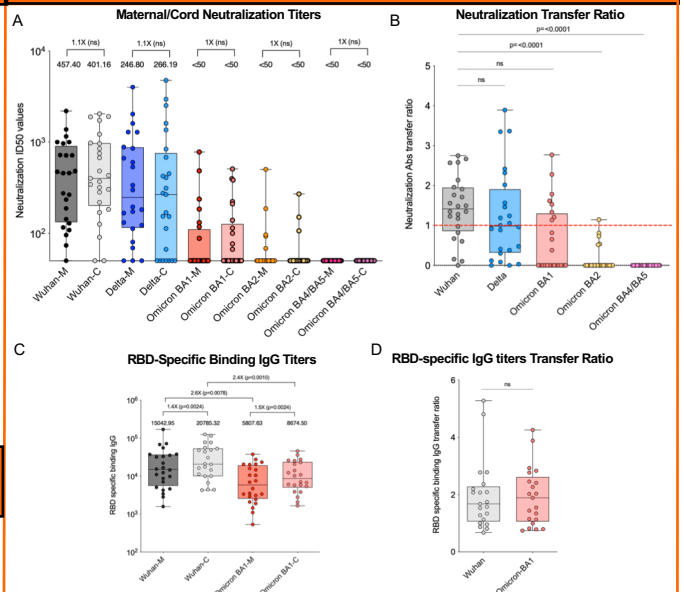
Maternal demographic and clinical characteristics of COVID-19 vaccinated women in pregnancy: COVID-19 Vaccinated pregnant women meeting the criteria for this study were enrolled and delivered from January 2021 through August 2021 (Data are presented as mean ± standard deviation, median, or number (percentage))

Vaccination did not Induce Neutralizing Antibodies for Omicron Variants in Pregnant Women



Lower Neutralization of Omicron variants in Pregnant Women: (A) Plots represent neutralizing antibody titers for maternal and Cord blood, different colors indicates different variants; Wuhan (Black), Delta (Blue), Omicron BA1 (Red), Omicron BA2 (Orange), and Omicron BA4/BA5 (Pink) variants. (B). Plots shows neutralizing antibody titers for cord blood; Wuhan (Gray), Delta (light Blue), Omicron BA1 (light Red), Omicron BA2 (light Orange), & Omicron BA4/BA5 (light pink).

Poor Neutralization Antibody Transfer Ratio for Omicron Variants in pregnant women



Significant Loss of antibody Transfer Ratio for Omicron Variants. (A) Box plot shows maternal/cord neutralizing antibody titers comparison. (B) Shows the neutralization transfer ratio for Wuhan (dark/gray), delta (blue/light blue), omicron BA1 (red/light red), omicron BA2 (orange/light orange), and omicron BA4/BA5 (pink/light pink) variants. (C) Represents RBD-specific binding IgG titers for Wuhan (black/gray) and, omicron BA1 (red/light red) in the maternal and cord blood. (D) Box plot indicates the RBD-specific IgG titers transfer ratio for Wuhan (gray) and omicron BA1(light red)

Conclusions

- COVID-19 mRNA vaccines were immunogenic in pregnant women for early variants (Detla).
- Vaccine-elicited RBD-binding antibodies higher in the cord blood compared to maternal blood. This was evident in both Wuhan and Omicron BA-1.
- Interestingly, the vaccination did not induce neutralizing antibodies for Omicron variants in both maternal and cord blood irrespective of higher binding antibodies.
- Most importantly, COVID-19 vaccination elicited lower neutralization antibody transfer efficiency for omicron subvariants
- These results provide novel insight into the impact of vaccination on maternal humoral immune response and transplacental antibody transfer for SARS-CoV-2 variants and support the need for more boosters with bivalent vaccines to fight against new SARS-CoV-2 variants.

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