Anti-SARS-CoV-2 antibodies induced in breast milk after Pfizer-BioNTech/BNT162b2 vaccination

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TITLE

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OBJECTIVE

After trials demonstrated 94-95% efficacy in preventing coronavirus disease 2019 (COVID-19), two lipid nanoparticle-formulated, nucleoside-modified messenger RNA-based vaccines received emergency use authorization by the U.S. Food and Drug Administration in December 2020.[1] Although no lactating people were included in vaccine trials, national organizations support vaccination of this population, suggesting potential infant protection by passive transfer of maternal antibodies.[1,2] However, there are no published data to support this theoretic benefit. We sought to characterize breast milk levels of anti-SARS-CoV-2 antibodies in lactating people undergoing COVID-19 vaccination.

STUDY DESIGN

Participants were prospectively recruited during Phase IA rollout of the COVID-19 vaccine at a tertiary care center, after IRB approval. Inclusion criteria included lactation and planned vaccination with the Pfizer-BioNTech/BNT162b2 vaccine. After obtaining informed consent, participants provided frozen breast milk samples at the following timepoints of vaccination: prior to, within the first 24 hours of, and weekly following. Samples were assessed for SARS-CoV-2 RNA by quantitative real-time PCR and anti-spike immunoglobulin (Ig) G and IgA by an enzyme-linked immunosorbent assay.

RESULTS

Five subjects and 29 human milk samples were included in the analysis. Subject characteristics are reported in Figure 1A. All pre-vaccine milk samples tested negative for SARS-CoV-2 RNA, as defined by C_t>40 for the N1 target (Figure 1B). Anti-spike IgG and IgA levels were significantly elevated relative to pre-vaccine baseline at all time points. Anti-spike protein IgG remained sustained at a significant elevation beginning at 20 days after the first dose compared with the pre-vaccine baseline ($P<0.01$) through the final milk sample (Figure 1C). Levels of anti-spike protein IgA were significantly elevated from baseline starting two weeks after first dose through the final sample; however, individual-level data suggest a possible gradual decline in anti-spike IgA in human milk over time following the second dose (Figure 1D).

CONCLUSION

We characterize longitudinal breast milk levels of anti-spike IgG/A following Pfizer-BioNTech/BNT162b2 vaccination, demonstrating sustained elevation of IgG/IgA levels. This response is similar to prior studies on maternal vaccination, which have shown high levels of breast milk IgA/G production for up to six months following vaccination for influenza and pertussis.[3,4] A concurrent decrease in infant respiratory illness rates suggest that maternal vaccination confers protection against infection in breastfed infants.[3] Thus, the Pfizer-BioNTech/BNT162b2 vaccination may also confer protection against COVID-19 to breastfed infants as well.

Although vaccination remains one of the most crucial interventions to control infection spread, vaccine hesitancy remains a barrier to widespread uptake.[5] Our study is limited by a small number of participants, but we report data that suggest potential immune benefit to infants of lactating people up to 80 days following COVID-19 vaccination. Further studies are needed to characterize the length of antibody production in breast milk, and the effect on infant infection rates after maternal COVID-19 vaccination.

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References

1. Centers for Disease Control and Prevention. Interim Clinical Considerations for Use of mRNA COVID-19 Vaccines. Available at: https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html. Accessed March 18, 2021.
2. American College of Obstetricians and Gynecologists. Vaccinating Pregnant and Lactating Patients Against COVID-19. Available at: https://www.acog.org/en/Clinical/Clinical%20Guidance/Practice%20Advisory/Articles/2020/12/Vaccinating%20Pregnant%20and%20Lactating%20Patients%20Against%20COVID%2019. Retrieved March 18, 2021.
3. Schlaudecker EP, Steinhoff MC, Omer SB, et al. IgA and Neutralizing Antibodies to Influenza A Virus in Human Milk: A Randomized Trial of Antenatal Influenza Immunization. PLoS One. 2013;8(8). doi:10.1371/journal.pone.0070867
4. Demers-Mathieu V, Huston RK, Markell AM, McCulley EA, Martin RL, Dallas DC. Impact of pertussis-specific IgA, IgM, and IgG antibodies in mother's own breast milk and donor breast milk during preterm infant digestion. Pediatr Res. 2020 Jun 29:10.1038/s41390-020-1031-2. doi: 10.1038/s41390-020-1031-2. Epub ahead of print. PMID: 32599609; PMCID: PMC7769915.
5. McAteer J, Yildirim I, Chahroudi A. The VACCINES Act, Deciphering Vaccine Hesitancy in the Time of COVID19. Clin Infect Dis. Published online April 13, 2020. doi:10.1093/cid/ciaa433

Figure Legend

Figure 1. Breast milk levels of anti-SARS-CoV-2 antibodies after vaccination with Pfizer-BioNTech/BNT162b2.

A total of 5 lactating women who received two doses of the Pfizer-BioNTech BNT162b2 vaccine were included in the analysis. (A) Self-reported clinical data of the study subjects are shown, with subject 2 identifying as immunocompromised. (B) Pre-vaccine baseline milk samples were analyzed for SARS-CoV-2 RNA using the N1 target compared with RNAse P, with undetectable viral RNA defined as Ct>40. Anti-spike protein IgG (C) and IgA (D) antibody levels in human milk were analyzed at serial time points following the first and second vaccine doses. Delipidated human milk samples were diluted at a 1:1 ratio with sample diluent and tested in duplicate for IgG and IgA against SARS-CoV-2 full length spike protein using ELISA Kits from Cell Signaling Technology (Catalog #20154C for IgG and Catalog #58873C for IgA). Antibody signal detections were analyzed by spectrophotometric absorbance at 450 nm. Gray vertical lines represent the timing of the administration of the second dose. Of note, the first sample from Subject 1 was obtained 17 days following the first vaccine. Data are displayed as mean ± SEM and were analyzed using Mann-Whitney U test. *P<0.05, **P<0.01.

Figure 1

A. Self-reported characteristics of study participants.

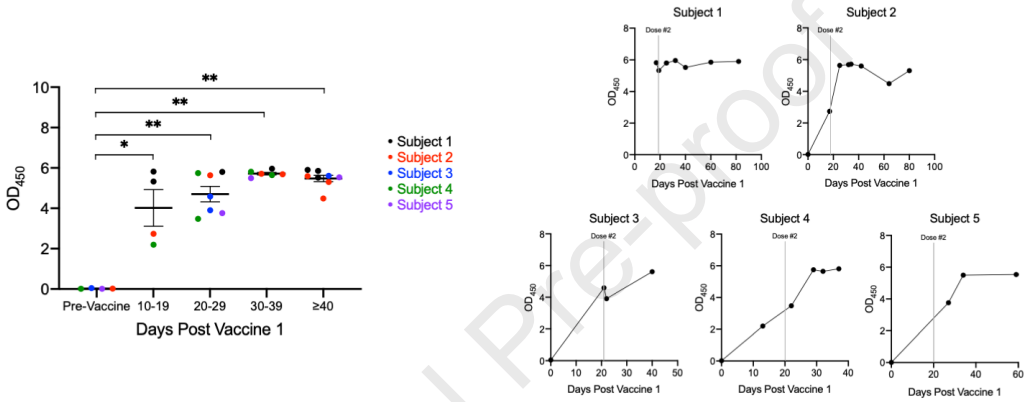
Subject	Age (years)	Race	Medical conditions	Medications	Immuno-suppressed condition or medication	Prior test-confirmed COVID-19 infection	Gestational age at delivery (weeks)	Current age of infant (months)
1	31	White	Depression, obesity	Escitalopram	No	No	39	10
2	43	Black	Colitis, eczema	Adalimumab	Yes	No	39	24
3	34	Asian	None	Birth control	No	No	38	5
4	26	White	Depression	Fluoxetine	No	No	34	9
5	31	White	Anxiety	Anti-anxiety medication, birth control	No	No	38	1

B. SARS-CoV-2 *N1* mRNA expression prior to vaccination.

Subject	C_t Value*
1⁺	>40
2	>40
3	>40
4	>40
5	>40

*C_t value greater than 40 denotes no detection of SARS-CoV-2 in breast milk sample.
⁺Sample obtained after vaccine dose 1, but prior to dose 2.

C. Human Milk SARS-CoV-2 Anti-Spike Protein IgG



D. Human Milk SARS-CoV-2 Anti-Spike Protein IgA