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PII: S0002-9378(22)00570-1
DOI: https://doi.org/10.1016/j.ajog.2022.07.016
Reference: YMOB 14615


Received Date: 8 April 2022
Revised Date: 3 July 2022
Accepted Date: 13 July 2022


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Disclosure Statement
The authors report no conflicts of interest.

Source of Funding
No funding was received.

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Word count: 500
Objective: Infants are at risk for developing a severe COVID-19 illness\(^1\) and are a source of virus spread.\(^2\) Recent studies have demonstrated reduction of SARS-CoV-2 positive tests in infants\(^3\) and COVID-19 infant hospitalizations following maternal COVID-19 vaccination.\(^4\) BNT162b2 messenger RNA (mRNA) COVID-19 vaccination during the second trimester of pregnancy was associated with high neonatal SARS-CoV-2 immunoglobulin G (IgG) levels at birth.\(^5\) Our aim was to evaluate SARS-CoV-2 IgG levels in infants up to six months of age following maternal vaccination during the second trimester of pregnancy.

Study Design: This prospective cohort study, performed between September 2021 and January 2022, included infants at the age of 3-6 months, of mothers vaccinated with the second BNT162b2 (Pfizer/BioNTech) mRNA COVID-19 vaccine. The second dose was received 3 weeks following the first dose according to the standard established for Israel at the time, during the second trimester of pregnancy, and women were not previously diagnosed with COVID-19 (based on self-reported information). All infants had a SARS-CoV-2 IgG antibody level measurement at birth collected by umbilical cord sampling. None of the infants were reported to have a COVID-19 infection during the study period. Following recruitment, we obtained venous blood from each infant which was assessed by SARS-CoV-2 IgG II Quant Abbott@, a two-step chemiluminescent microparticle immunoassay used for the quantitative determination of IgG antibodies. Correlations between infant antibody titers, feto-maternal and infant characteristics, and the time interval from maternal vaccination to the infant follow-up antibody test were analyzed.

Results: Antibody levels were measured for 40 infants. The median (range) level of IgG antibodies at birth was 2790.3 (350.1-13405.0) AU/ml and declined to a median (range) of 199 (18.4-904.3) AU/ml at a median (range) age of 19.2 (14.6-27.6) weeks. Three of 40 (7.5%) infants had a negative (<50 AU/ml) antibody test at a median (range) age of 26.1 (21.5-26.1) weeks. No differences were found between the different clinical and demographic characteristics of breastfed and non-breastfed infants. The median (range) level of SARS-CoV-2 IgG levels at follow-up was higher in the 28 breastfed infants (232.0 [105.7-904.3] AU/ml) than in the 12 non-breastfed infants (145.3 [18.4 to 575.5] AU/ml) (p=0.02).
Multivariable analysis revealed that infant SARS-CoV-2 IgG antibody titers at follow-up were positively correlated with SARS-CoV-2 IgG levels at birth and breastfeeding, yet negatively correlated with time passed from maternal second vaccine dose. For each week that passed since maternal second vaccine dose, SARS-CoV-2 IgG antibody levels decreased by 5.8% (95% CI, -8.6 to -3.9%, p<0.001). Breastfeeding was significantly and independently associated with higher levels of SARS-CoV-2 IgG levels (absolute difference, 75.1%; 95% CI, 28.4% to 138.7%, P=0.001). Moreover, the median (IQR) remaining percentage of SARS-CoV-2 IgG antibodies from birth to follow-up was significantly higher in breastfed infants compared to non-breastfed infants (8% (6.5; 11.8) vs 5.3% (2.9; 9.1), p=0.021) (Figure 1).

Conclusions: Our findings suggest that maternal COVID-19 vaccination during pregnancy may possibly provide protection from COVID-19 in early infancy, with SARS-CoV-2 IgG antibody levels enhanced by breastfeeding and sustained at least until six months of age.
REFERENCES


Figure Legends:

**Figure 1.** Correlation between the remaining percentage of the SARS-CoV-2 IgG antibodies at follow-up and duration from birth for breastfed and non-breastfed infants: A- From 100% SARS-CoV-2 IgG antibodies at birth to remaining percentage at follow-up, B- Focus on relevant time period of infant follow-up tests; breastfed infants: r=-0.62; 95% CI, -0.80 to -0.31; P<0.001, non-breastfed infants r=-0.84; 95% CI, -0.95 to -0.50; P=0.001
Figure 1. Correlation between the remaining percentage of the SARS-CoV-2 IgG antibodies at follow-up and duration from birth for breastfed and non-breastfed infants.