

# Quantification of Specific Antibodies Against SARS-CoV-2 in Breast Milk of Lactating Women Vaccinated With an mRNA Vaccine

Erika Esteve-Palau, MD, PhD; Araceli Gonzalez-Cuevas, MD; M. Eugenia Guerrero, MLS; Clara Garcia-Terol, RM, MS; M. Carmen Alvarez, RN, MS; David Casadevall, MD, PhD; Vicens Diaz-Brito, MD, PhD

# Introduction

The COVID-19 pandemic has raised questions among individuals who are breastfeeding, both because of the possibility of viral transmission to infants during breastfeeding and, more recently, of the potential risks and benefits of vaccination in this specific population. Previous studies have reported the presence of anti-SARS-CoV-2 antibodies in breast milk of COVID-19-infected lactating women,<sup>1</sup> and recently several studies have demonstrated the passage of postvaccine antibodies through breast milk in women vaccinated with novel mRNA-based vaccines.<sup>1,2</sup> In the present study, conducted between February and March 2021 at Parc Sanitari Sant Joan de Déu, an urban hospital in Spain, we sought to characterize the levels of specific SARS-CoV-2 antibodies in the breast milk of mRNA-vaccinated women across time, as well as their correlation with serum antibody levels.

# **Methods**

This prospective cohort study, carried out according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline, included lactating women older than 18 years who were vaccinated against SARS-CoV2 with the Pfizer-BioNTech COVID-19 vaccine. The ethics committee of the Sant Joan de Déu Research Foundation approved this study, and all participants signed for informed consent.

Serum and breast milk samples were simultaneously taken from each participant at 3 time points: 2 weeks after receiving the first dose of the vaccine (time point 1), 2 weeks after receiving the second dose (time point 2), and 4 weeks after the second dose (time point 3). All participants underwent nasopharyngeal SARS-CoV-2 rapid antigen testing (Ag-RDT) (Architect, Abbott). Levels of immunoglobin (Ig) G antibodies against the spike protein (S1 subunit) and against the nucleocapsid (NC) of SARS-CoV-2 were determined for each sample. Because vaccination does not induce nucleocapsid antibodies response, any IgG-NC positive result was considered as a prior infection. Statistical analyses were performed with R version 4.0.3 (R Project for Statistical Computing), and figures created using ggplot2 R package.

## Results

This study included 33 participants; mean (SD) age and postpartum time were 37.4 (3.3) years and 17.5 (10.1) months, respectively. No participants had confirmed SARS-CoV-2 infection prior to vaccination, nor during the study period (ie, tests for IgG-NC and Ag-RDT were all negative). We collected and analyzed 93 serum and milk samples from the 33 participants. Samples from time point 1 were taken at a median (range) of 14 (12-17) days after the first dose, while samples of time points 2 and 3 were taken at 14 (14-15) days and 28 (28-30) days after the second vaccine dose, respectively.

Median (interquartile range) IgG(S1) levels for serum-milk pairs at each time point were 519 (234-937) to 1 (0-2.9) arbitrary units (AU) per mL for time point 1, 18 644 (9923-29 264) to 78 (33.7-128) AU/mL for time point 2, and 12 478 (6870-20 801) to 50.4 (24.3-104) AU/mL for time point 3

**Open Access.** This is an open access article distributed under the terms of the CC-BY License.

JAMA Network Open. 2021;4(8):e2120575. doi:10.1001/jamanetworkopen.2021.20575

Author affiliations and article information are listed at the end of this article.

(Figure 1). The Pearson correlation coefficient between breast milk and serum IgG(S1) levels was 0.7 (Figure 2).

### Discussion

Our results suggest that breast milk from women vaccinated with the novel mRNA-based Pfizer-BioNTech vaccine contains specific anti-SARS-CoV-2 IgG(S1) antibodies. Furthermore, we found that after the second dose, breast milk IgG(S1) levels increased and were positively associated with corresponding serum levels.

The main limitation of this study is its small sample size. It remains to be determined if breast milk antibody levels decrease or plateau after vaccination, or whether these findings can be reproduced for other mRNA and non-mRNA-based vaccines. The kinetics of IgG and other specific immunoglobulins against SARS-CoV-2, such as IgA and IgM, have been well studied after the disease<sup>5</sup> (mainly in serum but also in breast milk<sup>6</sup>), although their dynamics after vaccination are not fully known. Larger prospective studies examining these issues are needed to confirm the safety of SARS-CoV-2 vaccination in individuals who are breastfeeding and further assess the association of vaccination with infants' health and SARS-CoV-2-specific immunity.

Figure 1. Evolution of Immunoglobulin (Ig) G S1 Subunit (S1) Levels in Breast Milk and Serum of Vaccinated Participants Across Time



AU indicates arbitrary units.

Figure 2. Correlation Between Immunoglobulin (Ig) G S1 Subunit (S1) Levels in Serum and Breast Milk of Vaccinated Participants



AU indicates arbitrary units.

JAMA Network Open. 2021;4(8):e2120575. doi:10.1001/jamanetworkopen.2021.20575

#### **ARTICLE INFORMATION**

Accepted for Publication: June 8, 2021.

Published: August 11, 2021. doi:10.1001/jamanetworkopen.2021.20575

**Open Access:** This is an open access article distributed under the terms of the CC-BY License. © 2021 Esteve-Palau E et al. *JAMA Network Open*.

**Corresponding Author:** Vicens Diaz-Brito, MD, PhD, Department of Infectious Diseases, Parc Sanitari Sant Joan de Déu, 08830 Sant Boi, Barcelona, Spain (vicente.diaz@pssjd.org).

Author Affiliations: Department of Infectious Diseases, Parc Sanitari Sant Joan de Déu, Sant Boi, Barcelona, Spain (Esteve-Palau, Alvarez, Diaz-Brito); Department of Microbiology, Parc Sanitari Sant Joan de Déu, Sant Boi, Barcelona, Spain (Gonzalez-Cuevas, Guerrero); Department of Obstetrics and Gynecology, Parc Sanitari Sant Joan de Déu, Sant Boi, Barcelona, Spain (Garcia-Terol); Cancer Research Program, Hospital del Mar Research Institute, Barcelona, Spain (Casadevall).

Author Contributions: Drs Diaz-Brito and Esteve-Palau had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Esteve-Palau, Diaz-Brito.

Acquisition, analysis, or interpretation of data: All authors.

Drafting of the manuscript: Esteve-Palau, Casadevall, Diaz-Brito.

Critical revision of the manuscript for important intellectual content: All authors.

Statistical analysis: Esteve-Palau, Casadevall, Diaz-Brito.

Obtained funding: Esteve-Palau.

Administrative, technical, or material support: Esteve-Palau, Casadevall.

Supervision: Esteve-Palau, Gonzalez-Cuevas, Guerrero, Garcia-Terol, Alvarez, Diaz-Brito.

Conflict of Interest Disclosures: None reported.

Additional Contributions: We acknowledge the samples collection effort of Geneva Garcia, RN, from the Department of Infectious Diseases at Parc Sanitari Sant Joan de Déu. No additional compensation was provided.

#### REFERENCES

1. Pace RM, Williams JE, Järvinen KM, et al. Characterization of SARS-CoV-2 RNA, antibodies, and neutralizing capacity in milk produced by women with COVID-19. *mBio*. 2021;12(1):e03192-e20. doi:10.1128/mBio.03192-20

2. Perl SH, Uzan-Yulzari A, Klainer H, et al. SARS-CoV-2-specific antibodies in breast milk after COVID-19 vaccination of breastfeeding women. *JAMA*. 2021;325(19):2013-2014. doi:10.1001/jama.2021.5782

3. Collier AY, McMahan K, Yu J, et al. Immunogenicity of COVID-19 mRNA vaccines in pregnant and lactating women. JAMA. 2021;325(23):2370-2380. doi:10.1001/jama.2021.7563

4. Pace RM, Williams JE, Järvinen KM, et al. Characterization of SARS-CoV-2 RNA, antibodies, and neutralizing capacity in milk produced by women with COVID-19. *mBio*. 2021;12(1):e03192-20. doi:10.1128/mBio.03192-20

**5**. Deeks JJ, Dinnes J, Takwoingi Y, et al; Cochrane COVID-19 Diagnostic Test Accuracy Group. Antibody tests for identification of current and past infection with SARS-CoV-2. *Cochrane Database Syst Rev.* 2020;6:CD013652. doi:10.1002/14651858.CD013652

**6**. Demers-Mathieu V, Do DM, Mathijssen GB, et al. Difference in levels of SARS-CoV-2 S1 and S2 subunits- and nucleocapsid protein-reactive SIgM/IgM, IgG and SIgA/IgA antibodies in human milk. *J Perinatol*. 2020;41(4): 850-859. doi:10.1038/s41372-020-00805-w