Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

be beneficial, CL surveillance of these patients may identify those who require closer monitoring, transfer to higher level of care, or potentially progesterone supplementation.[4,5] Further work is needed to determine optimal management strategies in patients with a prophylactic cerclage and short cervix.

Sunitha Suresh, MD
Caitlin MacGregor, MD
Division of Maternal-Fetal Medicine
Department of Obstetrics and Gynecology
NorthShore University HealthSystem
2650 Ridge Avenue,
Evanston, IL 60201
sunitha.c.suresh@gmail.com

Annie Dude, MD, PhD
The University of North Carolina at Chapel Hill
Chapel Hill, NC

Emmet Hirsch, MD
Department of Obstetrics and Gynecology
NorthShore University HealthSystem
The University of Chicago
Chicago, IL

The authors report no conflict of interest.

These findings were presented as an oral presentation at the 69th annual meeting of the Society for Reproductive Investigation, Denver, CO, March 15–19, 2022.

REFERENCES

1. Suhag A, Berghella V. Cervical cerclage. Clin Obstet Gynecol 2014;57:557–67.
2. Dijkstra K, Funai EF, O'Neill L, Rebarber A, Paidas MJ, Young BK. Change in cervical length after cerclage as a predictor of preterm delivery. Obstet Gynecol 2000;96:346–50.
3. American College of Obstetricians and Gynecologists' Committee on Practice Bulletins—Obstetrics. Prediction and prevention of spontaneous preterm birth: ACOG Practice Bulletin, Number 234. Obstet Gynecol 2021;138:e65–90.
4. Baxter JK, Airoldi J, Berghella V. Short cervical length after history-indicated cerclage: is a reinforcing cerclage beneficial? Am J Obstet Gynecol 2005;193:1204–7.
5. Hassan SS, Romero R, Vidyadhari D, et al. Vaginal progesterone reduces the rate of preterm birth in women with a sonographic short cervix: a multicenter, randomized, double-blind, placebo-controlled trial. Ultrasound Obstet Gynecol 2011;38:18–31.

 https://doi.org/10.1016/j.ajog.2022.07.018

SARS-CoV-2 immunoglobulin G antibody levels in infants following messenger RNA COVID-19 vaccination during pregnancy

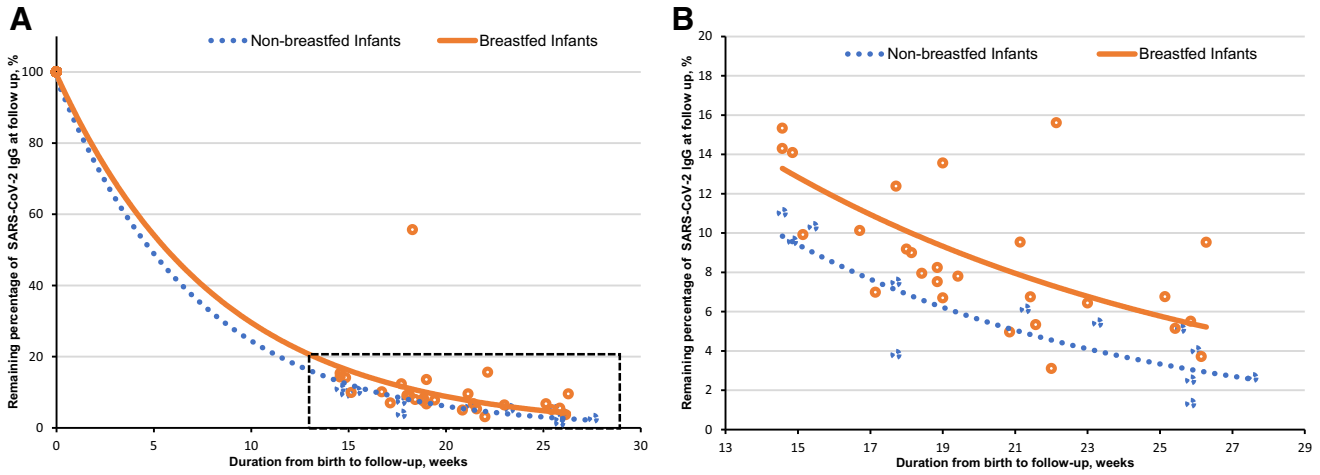
Check for updates

OBJECTIVE: Infants are at risk for developing 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 (Pfizer/BioNTech) 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 of up to 6 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 to 6 months of mothers vaccinated with the second BNT162b2 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 Laboratories, Chicago, IL), a 2-step chemiluminescent microparticle immunoassay used for the quantitative determination of IgG antibodies. Correlations between infant antibody titers, fetomaternal 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 (350.1−13,405.0) 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 nonbreastfed 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 nonbreastfed infants (145.3 [18.4−575.5] AU/mL) (P=.02). Multivariable analysis revealed that infant SARS-CoV-2 IgG

FIGURE
Remaining percentage of SARS-CoV-2 IgG antibodies at follow-up in infants



Correlation between the remaining percentage of SARS-CoV-2 IgG antibodies at follow-up and duration from birth for breastfed and nonbreastfed 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; $P<.001$; nonbreastfed infants: $r=-0.84$; 95% CI, −0.95 to −0.50; $P=.001$.

CI, confidence interval; *Ig*, immunoglobulin.

Kugelman. SARS-CoV-2 immunoglobulin G antibody levels in infants following messenger RNA COVID-19 vaccination during pregnancy. Am J Obstet Gynecol 2022.

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% confidence interval [CI], −8.6 to −3.9; $P<.001$). Breastfeeding was significantly and independently associated with higher SARS-CoV-2 IgG levels (absolute difference, 75.1%; 95% CI, 28.4−138.7; $P=.001$). Moreover, the median (interquartile range) remaining percentage of SARS-CoV-2 IgG antibodies from birth to follow-up was significantly higher in breastfed infants than in nonbreastfed infants (8% [6.5−11.8] vs 5.3% [2.9−9.1]; $P=.021$) (Figure).

CONCLUSION: 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 6 months of age. ■

Nir Kugelman, MD
Chen Nahshon, MD
Department of Obstetrics and Gynecology
Carmel Medical Center
Haifa, Israel
Ruth and Bruce Rappaport Faculty of Medicine
Technion − Israel Institute of Technology
Haifa, Israel
nirkug@gmail.com

Pninit Shaked-Mishan, PhD
Clinical Serology and Virology Laboratory
Carmel Medical Center
Haifa, Israel

Ofer Lavie, MD
Department of Obstetrics and Gynecology
Carmel Medical Center
Haifa, Israel
Ruth and Bruce Rappaport Faculty of Medicine
Technion − Israel Institute of Technology
Haifa, Israel

Nili Stein, MPH
Community Medicine and Epidemiology
Lady Davis Carmel Medical Center
Haifa, Israel

Reuven Kedar, MD
Department of Obstetrics and Gynecology
Carmel Medical Center
Haifa, Israel
Ruth and Bruce Rappaport Faculty of Medicine
Technion − Israel Institute of Technology
Haifa, Israel

Dan Waisman, MD
Department of Neonatology
Carmel Medical Center
Haifa, Israel
Ruth and Bruce Rappaport Faculty of Medicine
Technion − Israel Institute of Technology
Haifa, Israel

The authors report no conflicts of interest.

No funding was received for this study.

REFERENCES

1. Dong Y, Mo X, Hu Y, et al. Epidemiology of COVID-19 among children in China. Pediatrics 2020;145.

2. Alsohime F, Temsah MH, Al-Nemri AM, Somily AM, Al-Subaie S. COVID-19 infection prevalence in pediatric population: etiology, clinical presentation, and outcome. J Infect Public Health 2020;13:1791–6.

3. Carlsen EØ, Magnus MC, Oakley L, et al. Association of COVID-19 vaccination during pregnancy with incidence of SARS-CoV-2 infection in infants. JAMA Intern Med 2022. [Epub ahead of print].

4. Halasa NB, Olson SM, Staat MA, et al. Effectiveness of maternal vaccination with mRNA COVID-19 vaccine during pregnancy against COVID-19-associated hospitalization in infants aged <6 months - 17 states, July 2021–January 2022. MMWR Morb Mortal Wkly Rep 2022;71:264–70.

5. Kugelman N, Nahshon C, Shaked-Mishan P, et al. Maternal and neonatal SARS-CoV-2 immunoglobulin G antibody levels at delivery after receipt of the BNT162b2 messenger RNA COVID-19 vaccine during the second trimester of pregnancy. JAMA Pediatr 2022;176:290–5.

 https://doi.org/10.1016/j.ajog.2022.07.016

Is the phase of the menstrual cycle relevant when getting the covid-19 vaccine?

OBJECTIVE: Stability of the menstrual cycle is a key indicator of health, and its alteration can affect the physical, emotional, sexual, and social aspects of menstruating individuals' lives.[1] A recently published study showed a statistically significant increase in cycle length after vaccination against COVID-19 and no significant changes in the menses length.[2]However, there is no information about the potential association between vaccination time and change in cycle length. This study aims at assessing the association between the phase of the menstrual cycle at vaccination time and change in cycle length.

STUDY DESIGN: We analyzed data collected by the menstrual cycle tracking smartphone application Lunar App.[3] This application allows users to track their menstrual cycle and menses, recording the beginning and end dates, pain intensity, blood loss quantity during menses (more, equal, or less than usual), and their COVID-19 vaccination status.

The database contained 28,876 users and 162,529 cycles. The distribution of the percentages of the users' age ranges (years) was as follows: 18 to 24, 11.85%; 25−34, 49.15%; 35 to 44, 28.56%; 45 to 54, 8.31%; other, 2.13%. We filtered the database, keeping only users who had reported their vaccination status and at least 5 consecutive cycles. We considered the first doses or monodoses of the vaccine for the analysis and removed incomplete and/or wrong data. After this filtering process, we ended up with 371 users and 1855 cycles registered between September 2020 and February 2022. The relatively small size of the final sample is caused by the imposed restrictive inclusion and exclusion criteria to ensure the maximum attainable data quality.

For analysis, we employed the self-controlled case series method.[4] Each participant in our cohort was a control and a case before and after getting the COVID-19 vaccine, respectively. Our primary outcome was menstrual cycle length change in days. The secondary outcomes were menses length change in days and variations in the usual blood quantity and pain intensity during the menses. We stratified the analysis of all outcomes by the phase of the menstrual cycle of the user at vaccination time. We considered the luteal phase, ie, the period between menstruation and the 14 days before it[5] owing to the relative robustness of this phase. We considered the rest of the cycle as the follicular phase. The distribution of the medians (over each user) of cycle lengths before the vaccine had a median value of 28 days, with a (5−95) interpercentile range of (22−34) days.

For calculating the menstrual cycle length change, we computed the difference between the median length of the 3 cycles before the vaccine and the length of the cycle in which the vaccine was given (4th cycle) for each user. We then computed the median over all the users and the 95% confidence intervals of the point estimate. We used medians, because the data was not normally distributed. We proceeded similarly for the menses length but employed data from the fifth cycle. For the blood loss quantity and pain intensity, we computed the differences in the percentages of cycles with abnormalities in each endpoint before and after the vaccine and the 95% confidence intervals of the point estimates. Users reported abnormalities when they had more or less blood loss quantity or pain intensity than usual during menses. We employed the Wilcoxon signed-rank and chi-square tests for statistical hypothesis testing of medians and proportions, respectively. Statistical significance was set at $P<.005$. The participants of this study provided their consent for the analysis of their data for menstrual or reproductive health research purposes on registration in the app, and the study obtained the approval of an ethics committee. The app does not gather information about the usage of contraception or cycle control methods, and this is a potential limitation of our study, as it could affect the outcomes.

RESULTS: We observed an increase in the median cycle length of 0.5 (0.0−1.0) days (P value <0.005) for all