LAMPIRAN

Lampiran 1

BIODATA PENELITI

A. Data Pribadi

Nama	: Risca Ainun Jariah
Tempat, Tanggal Lahir	: Sambera Jembatan, 06 November 2000
Email	: ainunjariah0611@gmail.com
Alamat Asal	: Sambera Jembatan, Kec. Muara Badak
Alamat di Samarinda	: Jl. D.I Panjaitan, Kec. Sungai Pinang

B. Riwayat Pendidikan

Tamat SD	: SDN 020 Muara Badak Tahun 2013
Tamat SMP	: SMP Al-Muhajirin Muara Badak Tahun 2016
Tamat SMA	: SMK Kesehatan Samarinda Tahun 2018

Lampiran 2

SURAT PERNYATAAN

Saya yang bertanda tangan dibawah ini

Nama : Risca Ainun Jariah

NIM : 1811102415117

Program Studi : S1 Farmasi

Judul Penelitian : Literatur Review : Vaksinasi COVID-19 untuk Ibu Hamil dan Menyusui

Dengan surat pernyataan ini saya menyatakan bahwa saya menggunakan metode penelitian "*Literature Review*". Demikian permohonan yang saya sampaikan, atas perhatiannya saya ucapkan terima kasih.

Samarinda, 12 Agustus 2022

Pemohon	**Pembimbing**
Risca Ainun Jariah	**Deasy Nur Chairin Hanifa, M.Clin.Pharm., Apt**
NIM. 1811102415117	**NIDN. 1123019201**

Mengetahui,

Ketua

Program Studi S1 Farmasi

Apt. Ika Ayu Mentari, M. Farm

NIDN. 1121019201

Lampiran 3

SCREENSHOT JURNAL

KEMENTERIAN KESEHATAN REPUBLIK INDONESIA
DIREKTORAT JENDERAL
PENCEGAHAN DAN PENGENDALIAN PENYAKIT
Jalan H.R. Rasuna Said Blok X-5 Kavling 4-9 Jakarta 12950
Telepon (021) 4247608 (Hunting) Faksimile (021) 4207807

GERMAS

Yth.

1. Kepala Dinas Kesehatan Provinsi
2. Kepala Dinas Kesehatan Kabupaten/Kota
3. Pimpinan Fasilitas Pelayanan Kesehatan

di seluruh Indonesia

SURAT EDARAN

HK.02.01/I/ 2097 /2021

TENTANG

VAKSINASI COVID-19 BAGI IBU HAMIL

DAN PENYESUAIAN SKRINING DALAM PELAKSANAAN VAKSINASI COVID-19

Perkembangan kasus COVID-19 menunjukkan bahwa telah terjadi peningkatan kasus ibu hamil terkonfirmasi COVID-19 di sejumlah kota besar di Indonesia dalam keadaan berat (*severe case*). Wanita hamil memiliki peningkatan risiko menjadi berat apabila terinfeksi COVID-19, khususnya pada wanita hamil dengan kondisi medis tertentu. Dengan mempertimbangkan semakin tingginya jumlah ibu hamil yang terinfeksi COVID-19 dan tingginya risiko bagi ibu hamil apabila terinfeksi COVID-19 menjadi berat dan berdampak pada kehamilan dan bayinya, maka diperlukan upaya untuk memberikan vaksinasi COVID-19 bagi ibu hamil. Upaya pemberian vaksinasi COVID-19 bagi ibu hamil tersebut juga telah direkomendasikan oleh Komite Penasihat Ahli Imunisasi Nasional (ITAGI).

Selain sasaran ibu hamil, dalam rangka upaya pencegahan penyebaran COVID-19 pemerintah juga menetapkan sasaran anak usia 12-17 tahun sebagai sasaran penerima vaksinasi COVID-19 berdasarkan rekomendasi ITAGI. Untuk itu guna efektivitas pelaksanaan vaksinasi COVID-19 baik bagi sasaran ibu hamil, anak usia 12-17 tahun, maupun sasaran lainnya diperlukan penjelasan terhadap pelaksanaan skrining/penapisan terhadap status kesehatan sasaran sebelum dilakukan pemberian vaksinasi, sebagai salah satu prinsip dalam pelaksanaan pelayanan vaksinasi COVID-19.

Surat Edaran ini dimaksudkan untuk meningkatkan dukungan dan kerja sama pemerintah daerah, fasilitas pelayanan kesehatan, masyarakat, dan para pemangku kepentingan terkait dalam pelaksanaan vaksinasi COVID-19, termasuk pelaksanaan skrining/penapisan, baik bagi sasaran ibu hamil, anak usia 12-17 tahun, maupun sasaran lainnya.

Mengingat ketentuan:

1. Undang-Undang Nomor 4 Tahun 1984 tentang Wabah Penyakit Menular (Lembaran Negara Republik Indonesia Tahun 1984 Nomor 20, Tambahan Lembaran Negara Republik Indonesia Nomor 3237);

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Clinical Research

Maternal and Child Outcomes Reported by Breastfeeding Women Following Messenger RNA COVID-19 Vaccination

Kerri Bertrand,[1] Gordon Honerkamp-Smith,[1] and Christina D. Chambers[1,2]

Abstract

Background: In December 2020, two novel messenger RNA (mRNA) vaccines for severe acute respiratory syndrome coronavirus-2 received emergency use authorization from the U.S. Food and Drug Administration; however, the early trials excluded lactating women.
Methods: Breastfeeding women residing in the United States who received either of the two mRNA vaccines were enrolled into the Mommy's Milk Human Milk Research Biorepository at the University of California, San Diego. From December 14, 2020 to February 1, 2021, 180 women who received two doses of either mRNA vaccine were recruited into the study.
Results: Similar proportions of women reported any one or more symptoms following vaccination with either mRNA vaccine. In addition, the frequency by specific type of symptom did not differ by brand. However, following the second dose of vaccine, women who received the Moderna brand were significantly more likely to report symptoms. A small proportion of women following the first dose of either vaccine brand reported a reduction in milk supply, and significantly, more women reported a reduction in milk supply following the second dose of Moderna. Few infant events were reported for either vaccine brand following either dose, and no serious adverse events were reported.
Conclusions: These data are reassuring regarding the safety of vaccination in breastfeeding women and their breastfed children with either of the mRNA COVID-19 vaccines.

Keywords: human milk, lactation, breastfeeding, COVID-19, mRNA vaccine, vaccination, SARS-CoV-2

Introduction

Clinical trials for both the Pfizer-BioNTech BNT162b2 and Moderna messenger RNA (mRNA)-1273 COVID-19 vaccines demonstrated ability to prevent infection and severe disease, leading to emergency use authorization by the U.S. Food and Drug Administration in December 2020.[1,2]

The American College of Obstetrics and Gynecology and The Society for Maternal Fetal Medicine have recommended that these mRNA vaccines be made available for lactating women. However, initial trials excluded breastfeeding women, leading to questions about their safety in this special population.[3] One small study of 31 breastfeeding women who received an mRNA vaccine found that >60% reported vaccine-related side effects.[4] However, no data were provided on infant outcomes or milk supply. In addition, another small study of 84 breastfeeding women from Israel reported similar frequencies of vaccine-related symptoms following their first and second doses of the Pfizer-BioNTech vaccine (55% and 61%, respectively).[5] This study did not report any serious adverse events in the infants, but they did report that four infants had fevers and symptoms of upper respiratory infections during the study period following vaccination.[5]

We sought to evaluate a larger sample of vaccinated breastfeeding women for vaccine-related symptoms and their breastfed children for any nonserious and serious adverse events.

Materials and Methods

Breastfeeding women residing anywhere in the United States who received both doses of an mRNA vaccine were selected from those enrolled into the established Mommy's Milk Human Milk Research Biorepository (HMB) at the University of California, San Diego. The structure and design of the HMB have been described elsewhere.[6] Women who only received one dose of the vaccine were excluded from this analysis. Women who volunteered for the study were recruited

[1]Division of Dysmorphology and Teratology, Department of Pediatrics, University of California, San Diego, La Jolla, California, USA.
[2]Herbert Wertheim School of Public Health and Human Longevity Science, University of California, San Diego, La Jolla, California, USA.

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Short-term outcome of pregnant women vaccinated with BNT162b2 mRNA COVID-19 vaccine

S. BOOKSTEIN PERETZ[1,2#], N. REGEV[1#], L. NOVICK[1], M. NACHSHOL[1], E. GOFFER[3], A. BEN-DAVID[1,2], K. ASRAF[4], R. DOOLMAN[4], E. GAL LEVIN[2,5], G. REGEV YOCHAY[2,5] and Y. YINON[1,2]

[1]*Department of Obstetrics and Gynecology, Sheba Medical Center, Tel Hashomer, Israel;* [2]*Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel;* [3]*Institute for Medical Engineering and Science, Massachusetts Institute of Technology, Cambridge, MA, USA;* [4]*Automated Mega Laboratory, Sheba Medical Center, Tel Hashomer, Israel;* [5]*Infection Prevention & Control Unit, Sheba Medical Center, Tel Hashomer, Israel*

KEYWORDS: COVID-19; obstetric outcome; pregnancy; SARS-CoV-2 antibodies; vaccine

CONTRIBUTION

What are the novel findings of this work?
The BNT162b2 mRNA coronavirus disease 2019 (COVID-19) vaccine is safe for use in pregnant women in view of its adverse-effect profile and associated favorable short-term obstetric and neonatal outcomes. The vaccine is effective in inducing humoral immunity in pregnant women, although severe acute respiratory syndrome coronavirus 2 immunoglobulin G levels were lower when compared with those in non-pregnant vaccinated women.

What are the clinical implications of this work?
The findings of this study show that COVID-19 vaccination of pregnant women with the BNT162b2 mRNA vaccine seems to be safe and effective. Recommending COVID-19 vaccination of pregnant women should therefore be strongly considered in view of the maternal morbidity associated with COVID-19 in pregnancy.

ABSTRACT

Objectives *To determine the immunogenicity and reactogenicity of the Pfizer/BioNTech BNT162b2 mRNA coronavirus disease 2019 (COVID-19) vaccine among pregnant women compared with non-pregnant women, and to evaluate obstetric outcome following vaccination.*

Methods *This was an observational case–control study of pregnant women who were vaccinated with a two-dose regimen of the BNT162b2 vaccine during gestation between January and February 2021 (study group) and age-matched non-pregnant women who received the vaccine during the same time period (control group). Participants received a digital questionnaire 1–4 weeks after the second dose and were asked to provide information regarding demographics, medication, medical history, history of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, timing of COVID-19 vaccine doses and side effects after each vaccine dose. A second digital questionnaire, regarding current pregnancy and delivery outcomes, was sent to patients in the study group after the calculated due date. All recruited women were offered a serology blood test for SARS-CoV-2 immunoglobulin G (IgG) following the second vaccination dose and SARS-CoV-2 IgG levels were compared between the two groups.*

Results *Of 539 pregnant women who were recruited after completion of the two-dose regimen of the vaccine, 390 returned the digital questionnaire and were included in the study group and compared to 260 age-matched non-pregnant vaccinated women. The rates of rash, fever and severe fatigue following vaccination among pregnant women were comparable to those in non-pregnant women. Myalgia, arthralgia and headache were significantly less common among pregnant women after each dose, local pain or swelling and axillary lymphadenopathy were significantly less common among pregnant women after the first and second doses, respectively, while paresthesia was significantly more common among the pregnant population after the second dose. Among pregnant women, there were no significant differences in the rates of side effects according to whether the vaccine was administered during the first, second or third trimester of pregnancy, except for local pain/swelling, which was significantly less common after*

Correspondence to: Prof. Y. Yinon, Department of Obstetrics and Gynecology, Sheba Medical Center, Tel Hashomer, 52621, Israel (e-mail: yoav.yinon27@gmail.com)

#S.B.P. and N.R. contributed equally to this study.

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Article

Induction of SARS-CoV-2-Specific IgG and IgA in Serum and Milk with Different SARS-CoV-2 Vaccines in Breastfeeding Women: A Cross-Sectional Study in Northern Spain

Carolina Lechosa-Muñiz [1,2,†], María Paz-Zulueta [1,3,*,†], Jose Manuel Mendez-Legaza [4], Juan Irure-Ventura [5], Rocío Cuesta González [6], Jorge Calvo Montes [4], Marcos López-Hoyos [5,7], Javier Llorca [8,9,‡] and María Jesús Cabero-Pérez [8,10,11,‡]

[1] Faculty of Nursing, University of Cantabria, Avda Valdecilla s/n. C.P., 39008 Santander, Cantabria, Spain; carolina.lechosa@unican.es
[2] Breastfeeding Coordinator, IBCLC, Hospital Universitario Marqués de Valdecilla, C.P., 39008 Santander, Cantabria, Spain
[3] Grupo de Investigación en Derecho Sanitario y Bioética, GRIDES, IDIVAL, C/ Cardenal Herrera Oria s/n. C.P., 39011 Santander, Cantabria, Spain
[4] Department of Microbiology, Hospital Universitario Marqués de Valdecilla, C.P., 39008 Santander, Cantabria, Spain; josemanuel.mendez@scsalud.es (J.M.M.-L.); jorge.calvo@scsalud.es (J.C.M.)
[5] Department of Immunology, Hospital Universitario Marqués de Valdecilla, IDIVAL, C.P., 39008 Santander, Cantabria, Spain; juan.irure@scsalud.es (J.I.-V.); marcos.lopez@scsalud.es (M.L.-H.)
[6] Department of Pediatrics, Hospital Universitario Marqués de Valdecilla, C.P., 39008 Santander, Cantabria, Spain; rociocuestagonzalez@gmail.com
[7] Laboratory, Molecular Biology Department, University of Cantabria, Avenida del Cardenal Herrera Oria 2, C.P., 39010 Santander, Cantabria, Spain
[8] Faculty of Medicine, University of Cantabria, Avenida del Cardenal Herrera Oria 2, C.P., 39010 Santander, Cantabria, Spain; javier.llorca@unican.es (J.L.); mariajesus.cabero@unican.es (M.J.C.-P.)
[9] CIBER Epidemiology and Public Health (CIBERESP), C.P., 28029 Madrid, Spain
[10] Pediatrics Section, Hospital Universitario Marqués de Valdecilla, C.P., 39008 Santander, Cantabria, Spain
[11] IDIVAL, C/ Cardenal Herrera Oria s/n. C.P., 39011 Santander, Cantabria, Spain
* Correspondence: maria.paz@unican.es
† Shared first authorship.
‡ Shared senior authorship.

check for updates

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Abstract: Breastfeeding mothers were excluded from the clinical trials conducted for vaccines against SARS-CoV-2. Since the start of the vaccination, some doubts have arisen regarding its compatibility with breastfeeding. The aim of this study was to analyse the presence of anti-SARS-CoV-2 antibodies in breast milk and serum (IgG and IgA) of vaccinated breastfeeding women. The main variables of the observational study were: adverse related events after vaccination and determination of the presence of IgG and IgA isotypes antibodies in serum and in breast milk of vaccinated women against the SARS-CoV-2 antigens. Results: 110 breastfeeding mothers were included; 70 women (63.6%) were vaccinated with two doses of BNT162b2, 20 women (18.2%) with two doses of mRNA-1273, and 20 women (18.2%) with a single dose of ChAdOx1-S. Regarding adverse reactions and vaccine safety, 38 women had no adverse reactions; 20 (18.2%) had general malaise or adenopathies; 10 (9.1%) had a headache; and 7 (6.4%) had fever. When analysing IgG antibodies, significantly higher levels of antibodies were found in serum and breast milk from mothers vaccinated with BNT162b2 or mRNA-1273 vs. ChAdOx1-S ($p < 0.001$ and $p = 0.001$, respectively). Analysing IgA antibodies, significant differences were found when comparing mean values in serum from mothers vaccinated with BNT162b2 or mRNA-1273 vs. ChAdOx1-S (0.12, 0.16, and 0.02, respectively; $p < 0.001$) and breast milk of mothers vaccinated when comparing BNT16b2 vs. ChAdOx1-S. All vaccinated breastfeeding mothers had serum anti-S1 IgG antibodies in response to vaccination against SARS-CoV-2, regardless of the commercial vaccine administered. Conclusions: the anti-SARS-CoV-2 vaccines were well tolerated by the mothers and the breastfed infant. In addition, breastfeeding mothers offer their infants IgA and IgG isotype antibodies directed against SARS-CoV-2 protein S in breast milk.

Original Research

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Breastfeeding Mother and Child Clinical Outcomes After COVID-19 Vaccination

Jia Ming Low, MRCPCH[1,2], Le Ye Lee, MRCPCH[1,2], Yvonne Peng Mei Ng, MRCP[1,2], Youjia Zhong, MRCPCH[1,3,4], and Zubair Amin, FAAP[1,2]

Abstract

Background: Pre-approval clinical trials of the Pfizer/BioNTech messenger RNA COVID-19 vaccine, BNT162b2 did not include participants who were breastfeeding. Therefore, there is limited evidence about outcomes of breastfeeding mother–child dyads and effects on breastfeeding after vaccination.

Research Aims: To determine: (1) solicited adverse effects (e.g., axillary lymphadenopathy, mastitis, and breast engorgement), which are unique to lactating individuals; and (2) systemic and local adverse effects of COVID-19 mRNA vaccine on mothers and potential effects on their breastfed infants.

Method: This was a prospective cohort study of lactating healthcare workers ($N = 88$) in Singapore who received two doses of BNT162b2 vaccination (Pfizer/BioNTech). The outcomes of mother–child dyads within 28 days after the second vaccine dose were determined through a participant-completed questionnaire.

Results: Minimal effects related to breastfeeding were reported by this cohort; three of 88 (3.4%) participants had mastitis, one (1.1%) participant experienced breast engorgement, five of 88 (5.7%) participants reported cervical or axillary lymphadenopathy. There was no change in human milk supply after vaccination. The most common side effect was pain/redness/swelling at the injection site, which was experienced by 57 (64.8%) participants. There were no serious adverse events of anaphylaxis or hospital admissions. There were no short-term adverse effects reported in the infants of 67 lactating participants who breastfed within 72 hr after BNT162b2 vaccination. **Conclusions:** BNT162b2 vaccination was well tolerated in lactating participants and was not associated with short-term adverse effects in their breastfed infants.

Study Protocol Registration: The study protocol was registered at clinicaltrials.gov (NCT04802278).

Keywords

breastfeeding, cohort study, COVID-19, human milk, mastitis, mRNA vaccines

Background

The pre-approval clinical trials for messenger RNA (mRNA) COVID-19 vaccines did not include participants who were breastfeeding; therefore, there was only limited data about safety and outcomes of breastfeeding mother–child dyads after vaccination. Previously, researchers (Bertrand et al., 2021; Gray et al., 2021; McLaurin-Jiang et al., 2021; Perl et al., 2021) reported that 61.9%–98.3% of lactating women vaccinated with mRNA COVID-19 vaccines (BNT162b2 by Pfizer-BioNTech and mRNA-1273 by Moderna) experienced side effects. A recently updated *Drug and Lactation Database* summarized the key findings from several published and pre-print studies but did not unequivocally endorse the safety of the mRNA vaccine for lactating women (Drugs and Lactation Database [LactMed], 2021). There have also been anecdotal reports (Breastfeeding Network, 2021) of mastitis and reduction in milk supply following COVID-19 vaccinations.

This has resulted in vaccine hesitancy for COVID-19 vaccines among lactating women (Saus-Ortega, 2021) and difficulty for clinicians counseling lactating women on the

[1]Department of Paediatrics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore
[2]Department of Neonatology, Khoo Teck Puat-National University Children's Medical Institute, National University Health System, Singapore
[3]Khoo Teck Puat-National University Children's Medical Institute, National University Health System, Singapore
[4]Duke-NUS Medical School, Singapore

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Corresponding Author:
Yvonne Peng Mei Ng, Department of Neonatology, Khoo Teck Puat-National University Children's Medical Institute, National University Health System, 1E Kent Ridge Road, NUHS Tower Block, Level 12, Singapore 119228, Singapore.
Email: paeynpm@nus.edu.sg

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Maternal and Child Symptoms Following COVID-19 Vaccination Among Breastfeeding Mothers

Skyler McLaurin-Jiang,[1,2,i] Christine D. Garner,[1,2,ii] Kaytlin Krutsch,[2,3,iii] and Thomas W. Hale[1,2,iv]

Abstract

Background: The impact of COVID-19 vaccination on breastfeeding is unknown. The primary aim of this study was to determine whether vaccine-related side effects following COVID-19 vaccination were associated with an adverse impact on breastfeeding. Secondarily, we sought to determine perceived symptoms in breastfed children and maternal opinion about COVID-19 vaccination.

Materials and Methods: We conducted a cross-sectional survey of breastfeeding mothers who underwent COVID-19 vaccination >2 days before the survey. Subjects were recruited through social media and websites. Data included sociodemographic information, vaccine history, maternal and child symptoms, and impact on lactation/breastfeeding. Bivariate statistics (chi-square, Wilcoxon rank sum, and *t* tests) and multivariable logistic regression models examined the association of vaccine side effects with lactation, symptoms in breastfed children, and maternal opinion on vaccination.

Results: Analysis included 4,455 breastfeeding mothers. Maternal postvaccination symptoms were more common after the second dose ($p<0.001$). Overall, 77 (1.7%) respondents reported a negative impact on breastfeeding postvaccination, and these mothers were more likely to have experienced fatigue, headache, muscle pain, injection site pain, chills, fever, or allergic reactions. After adjusting for confounding variables, higher odds of an adverse impact on lactation were associated with lower breastfeeding intensity, dose of vaccine, and child symptoms. Even among mothers who reported an adverse impact on breastfeeding, maternal opinion about vaccination and confidence in their decision to receive the COVID-19 vaccine were high.

Conclusions: COVID-19 vaccination among breastfeeding mothers resulted in minimal disruption of lactation or adverse impact on the breastfed child. These findings may be considered in vaccination decision-making.

Keywords: COVID-19 vaccine, breastfeeding, immunization, lactation

Introduction

Breastfeeding and pregnant women were excluded from recent trials evaluating novel COVID-19 vaccines. Meanwhile, in the United States and globally, women constitute the majority of the health workforce.[1,2] With the U.S. Centers for Disease Control and Prevention (CDC) among those recommending health workers be included in the first phase of vaccine efforts, knowledge gaps related to COVID-19 vaccine safety in women of reproductive age are particularly glaring. Based on urgent ethical and clinical concerns in vaccinating this population, numerous health organizations have called for the inclusion of pregnant and lactating women in clinical trials.[3–11]

The theoretical risk of current COVID-19 vaccines adversely impacting lactation or breastfed children is quite low. However, breastfeeding mothers and their clinicians have minimal objective data to guide decisions on vaccine safety. Since the emergency use authorization of two messenger RNA (mRNA)-based COVID-19 vaccines in the United States in December 2020, COVID-19 vaccine recommendations for women who are breastfeeding have varied. Thus far, these recommendations have been based solely on expert opinion.

[1]Department of Pediatrics, School of Medicine, Texas Tech University Health Sciences Center, Amarillo, Texas, USA.
[2]InfantRisk Center, Texas Tech University Health Sciences Center, Amarillo, Texas, USA.
[3]Department of Obstetrics and Gynecology, School of Medicine, Texas Tech University Health Sciences Center, Amarillo, Texas, USA.
[i]ORCID ID (https://orcid.org/0000-0001-7160-5128).
[ii]ORCID ID (https://orcid.org/0000-0003-3824-5938).
[iii]ORCID ID (https://orcid.org/0000-0002-7453-2582).
[iv]ORCID ID (https://orcid.org/0000-0001-9349-8722).

RESEARCH LETTER

SARS-CoV-2-Specific Antibodies in Breast Milk After COVID-19 Vaccination of Breastfeeding Women

On December 20, 2020, Israel initiated a national vaccination program against COVID-19. One prioritized group was health care workers, many of whom are breastfeeding women.[1] Despite the fact that the vaccine trial did not include this population[2] and no other vaccine-related safety data had been published, breastfeeding women belonging to risk groups were encouraged to receive the vaccine.[3] The Centers for Disease Control and Prevention has also recommended that breastfeeding women belonging to vaccine-target groups be immunized.[4] We investigated whether maternal immunization results in secretion of SARS-CoV-2 antibodies into breast milk and evaluated any potential adverse events among women and their infants.

Supplemental content

Methods | We conducted a prospective cohort study of a convenience sample of breastfeeding women (either exclusive or partial) belonging to vaccine-target groups who chose to be vaccinated. Participants were recruited from all of Israel between December 23, 2020, and January 15, 2021, through advertisements and social media. All participants received 2 doses of the Pfizer-BioNTech vaccine 21 days apart. Breast milk samples were collected before administration of the vaccine and then once weekly for 6 weeks starting at week 2 after the first dose. Samples were kept frozen pending analysis. IgG levels were detected by the Elecsys Anti-SARS-CoV-2 S serology assay and read on the Cobas e801 analyzer with a level of more than 0.8 U/mL considered positive (La Roche Ltd) and IgA with the EUROIMMUN AG Anti-SARS-CoV-2 S Kit with an extinction ratio of samples over calibrator of more than 0.8 considered positive (Supplement). At enrollment, maternal and infant demographic information was collected, followed by weekly questionnaires coupled to breast milk collection soliciting information about interim well-being and vaccine-related adverse events. The study was approved by the Shamir Medical Center Institutional Review Board; written informed consent was obtained from mothers.

Changes in the proportion of participants with positive test results and in antibody levels during the study were evaluated using paired-sample *t* tests, comparing antibody levels at each point with the baseline and correcting for multiple testing using the Benjamini-Hochberg procedure. A 2-sided significance threshold was set at $P < .05$. Analyses were performed with R version 3.6

Results | Eighty-four women completed the study, providing 504 breast milk samples. Women were a mean (SD) age of 34 (4) years and infants 10.32 (7.3) months (Table).

Table. Maternal and Infant Characteristics

	No. (%)
Study participants, No.	84
Maternal features	
Maternal age, mean (SD), y	34 (4)
No. of children, mean (SD)	2.36 (0.98)
Chronic diseases	22 (26.2)
Gestational diabetes	3 (3.6)
First vaccine adverse effects	47 (55.9)
Local pain	40 (47.6)
Fatigue	8 (9.5)
Fever	0
Other	12 (14.3)
Second vaccine adverse effects	52 (61.9)
Local pain	34 (40.5)
Fatigue	28 (33.3)
Fever	10 (11.9)
Other	22 (26.2)
Infant related features	
Vaginal delivery mode	78 (92.9)
Infant age at time of first maternal vaccine, mean (SD), mo	10.32 (7.31)
Birth week, mean (SD)	39.01 (1.95)
Birth weight, mean (SD), g	3175.27 (502.33)
Exclusive breastfeeding	35 (41.6)

Mean levels of anti-SARS-CoV-2-specific IgA antibodies in the breast milk increased rapidly and were significantly elevated at 2 weeks after the first vaccine (2.05 ratio; $P < .001$), when 61.8% of samples tested positive, increasing to 86.1% at week 4 (1 week after the second vaccine). Mean levels remained elevated for the duration of follow-up, and at week six, 65.7% of samples tested positive. Anti-SARS-CoV-2-specific IgG antibodies remained low for the first 3 weeks, with an increase at week 4 (20.5 U/mL; $P = .004$), when 91.7% of samples tested positive, increasing to 97% at weeks 5 and 6 (Figure).

No mother or infant experienced any serious adverse event during the study period. Forty-seven women (55.9%) reported a vaccine-related adverse event after the first vaccine dose and 52 (61.9%) after the second vaccine dose, with local pain being the most common complaint (Table). Four infants developed fever during the study period 7, 12, 15, and 20 days after maternal vaccination. All had symptoms of upper respiratory tract infection including cough and congestion, which resolved without treatment except for 1 infant who was admitted for neonatal fever evaluation due to his age and was treated with antibiotics pending culture results. No other adverse events were reported.

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Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons

Tom T. Shimabukuro, M.D., Shin Y. Kim, M.P.H., Tanya R. Myers, Ph.D., Pedro L. Moro, M.D., Titilope Oduyebo, M.D., Lakshmi Panagiotakopoulos, M.D., Paige L. Marquez, M.S.P.H., Christine K. Olson, M.D., Ruiling Liu, Ph.D., Karen T. Chang, Ph.D., Sascha R. Ellington, Ph.D., Veronica K. Burkel, M.P.H., Ashley N. Smoots, M.P.H., Caitlin J. Green, M.P.H., Charles Licata, Ph.D., Bicheng C. Zhang, M.S., Meghna Alimchandani, M.D., Adamma Mba-Jonas, M.D., Stacey W. Martin, M.S., Julianne M. Gee, M.P.H., and Dana M. Meaney-Delman, M.D., for the CDC v-safe COVID-19 Pregnancy Registry Team*

ABSTRACT

BACKGROUND

Many pregnant persons in the United States are receiving messenger RNA (mRNA) coronavirus disease 2019 (Covid-19) vaccines, but data are limited on their safety in pregnancy.

METHODS

From December 14, 2020, to February 28, 2021, we used data from the "v-safe after vaccination health checker" surveillance system, the v-safe pregnancy registry, and the Vaccine Adverse Event Reporting System (VAERS) to characterize the initial safety of mRNA Covid-19 vaccines in pregnant persons.

RESULTS

A total of 35,691 v-safe participants 16 to 54 years of age identified as pregnant. Injection-site pain was reported more frequently among pregnant persons than among nonpregnant women, whereas headache, myalgia, chills, and fever were reported less frequently. Among 3958 participants enrolled in the v-safe pregnancy registry, 827 had a completed pregnancy, of which 115 (13.9%) were pregnancy losses and 712 (86.1%) were live births (mostly among participants vaccinated in the third trimester). Adverse neonatal outcomes included preterm birth (in 9.4%) and small size for gestational age (in 3.2%); no neonatal deaths were reported. Although not directly comparable, calculated proportions of adverse pregnancy and neonatal outcomes in persons vaccinated against Covid-19 who had a completed pregnancy were similar to incidences reported in studies involving pregnant women that were conducted before the Covid-19 pandemic. Among 221 pregnancy-related adverse events reported to the VAERS, the most frequently reported event was spontaneous abortion (46 cases).

CONCLUSIONS

Preliminary findings did not show obvious safety signals among pregnant persons who received mRNA Covid-19 vaccines. However, more longitudinal follow-up, including follow-up of large numbers of women vaccinated earlier in pregnancy, is necessary to inform maternal, pregnancy, and infant outcomes.

The authors' affiliations are listed in the Appendix. Address reprint requests to Dr. Shimabukuro at the Immunization Safety Office, Division of Healthcare Quality Promotion, National Center for Emerging and Zoonotic Infectious Diseases, Centers for Disease Control and Prevention, 1600 Clifton Rd., Atlanta, GA 30329, or at tshimabukuro@cdc.gov.

*The members of the CDC v-safe COVID-19 Pregnancy Registry Team are listed in the Supplementary Appendix, available at NEJM.org.

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OBSTETRICS

COVID-19 vaccination during pregnancy: coverage and safety

Helena Blakeway, MD; Smriti Prasad, MD; Erkan Kalafat, MD, MSc; Paul T. Heath, FRCPCH; Shamez N. Ladhani, PhD; Kirsty Le Doare, PhD; Laura A. Magee, FRCOG; Pat O'Brien, FRCOG; Arezou Rezvani, BSc, MSc; Peter von Dadelszen, FRCOG; Asma Khalil, MD

BACKGROUND: Concerns have been raised regarding a potential surge of COVID-19 in pregnancy, secondary to the rising numbers of COVID-19 in the community, easing of societal restrictions, and vaccine hesitancy. Although COVID-19 vaccination is now offered to all pregnant women in the United Kingdom; limited data exist on its uptake and safety.

OBJECTIVE: This study aimed to investigate the uptake and safety of COVID-19 vaccination among pregnant women.

STUDY DESIGN: This was a cohort study of pregnant women who gave birth at St George's University Hospitals National Health Service Foundation Trust, London, United Kingdom, between March 1, 2020, and July 4, 2021. The primary outcome was uptake of COVID-19 vaccination and its determinants. The secondary outcomes were perinatal safety outcomes. Data were collected on COVID-19 vaccination uptake, vaccination type, gestational age at vaccination, and maternal characteristics, including age, parity, ethnicity, index of multiple deprivation score, and comorbidities. Further data were collected on perinatal outcomes, including stillbirth (fetal death at ≥24 weeks' gestation), preterm birth, fetal and congenital abnormalities, and intrapartum complications. Pregnancy and neonatal outcomes of women who received the vaccine were compared with that of a matched cohort of women with balanced propensity scores. Effect magnitudes of vaccination on perinatal outcomes were reported as mean differences or odds ratios with 95% confidence intervals. Factors associated with antenatal vaccination were assessed with logistic regression analysis.

RESULTS: Data were available for 1328 pregnant women of whom 140 received at least 1 dose of the COVID-19 vaccine before giving birth and 1188 women who did not; 85.7% of those vaccinated received their vaccine in the third trimester of pregnancy and 14.3% in the second trimester of pregnancy. Of those vaccinated, 127 (90.7%) received a messenger RNA vaccine and 13 (9.3%) a viral vector vaccine. There was evidence of reduced vaccine uptake in younger women ($P=.001$), women with high levels of deprivation (ie, fifth quintile of the index of multiple deprivation; $P=.008$), and women of Afro-Caribbean or Asian ethnicity compared with women of White ethnicity ($P<.001$). Women with prepregnancy diabetes mellitus had increased vaccine uptake ($P=.008$). In the multivariable model the fifth deprivation quintile (most deprived) (adjusted odds ratio, 0.10; 95% confidence interval, 0.02–0.10; $P=.003$) and Afro-Caribbean ethnicity (adjusted odds ratio, 0.27; 95% confidence interval, 0.06–0.85; $P=.044$) were significantly associated with lower antenatal vaccine uptake, whereas prepregnancy diabetes mellitus was significantly associated with higher antenatal vaccine uptake (adjusted odds ratio, 10.5; 95% confidence interval, 1.74–83.2; $P=.014$). In a propensity score–matched cohort, the rates of adverse pregnancy outcomes of 133 women who received at least 1 dose of the COVID-19 vaccine in pregnancy were similar to that of unvaccinated pregnant women ($P>.05$ for all): stillbirth (0.0% vs 0.2%), fetal abnormalities (2.2% vs 2.5%), postpartum hemorrhage (9.8% vs 9.0%), cesarean delivery (30.8% vs 34.1%), small for gestational age (12.0% vs 12.8%), maternal high-dependency unit or intensive care admission (6.0% vs 4.0%), or neonatal intensive care unit admission (5.3% vs 5.0%). Intrapartum pyrexia (3.7% vs 1.0%; $P=.046$) was significantly increased but the borderline statistical significance was lost after excluding women with antenatal COVID-19 infection ($P=.079$). Mixed-effects Cox regression showed that vaccination was not significantly associated with birth at <40 weeks' gestation (hazard ratio, 0.93; 95% confidence interval, 0.71–1.23; $P=.624$).

CONCLUSION: Of pregnant women eligible for COVID-19 vaccination, less than one-third accepted COVID-19 vaccination during pregnancy, and they experienced similar pregnancy outcomes with unvaccinated pregnant women. There was lower uptake among younger women, non-White ethnicity, and lower socioeconomic background. This study has contributed to the body of evidence that having COVID-19 vaccination in pregnancy does not alter perinatal outcomes. Clear communication to improve awareness among pregnant women and healthcare professionals on vaccine safety is needed, alongside strategies to address vaccine hesitancy. These strategies include postvaccination surveillance to gather further data on pregnancy outcomes, particularly after first-trimester vaccination, and long-term infant follow-up.

Key words: coverage, COVID-19, immunization, mRNA, pregnancy, safety vaccine uptake, SARS-CoV-2, vaccination, viral vector

Introduction

The COVID-19 pandemic has caused loss of life and poorer health outcomes, outside and in pregnancy, despite worldwide aggressive public health measures to control the spread.[1] Mass vaccination is a key method by which countries are aiming to control the pandemic.[2]

Theoretically, COVID-19 vaccines are safe for use in pregnancy, as they do not contain a live attenuated virus.[3] For COVID-19 vaccination in pregnancy, there has been no major safety signal from animal reproductive toxicology studies, the very small number of inadvertent pregnancies in vaccine trials, the Centers for Disease Control and

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Human Milk SARS-CoV-2 Antibodies up to 6 Months After Vaccination

Stephanie E. Perez, BS,[a,b] Luis Diego Luna Centeno, BA,[a,b] Wesley A. Cheng, BS,[a] Carolyn Jennifer Marentes Ruiz, MD,[a] Yeaun Lee, PhD,[a] Zion Congrove-Wilson, MS,[a] Rebecca L. Powell, PhD,[c] Lisa Stellwagen, MD,[d] Pia S. Pannaraj, MD, MPH[a,e]

abstract

BACKGROUND: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)–specific antibodies have been detected in human milk up to 6 weeks post–coronavirus disease 2019 (COVID-19) vaccination. We evaluated SARS-CoV-2–specific antibodies, neutralization activity, effect of pasteurization, and persistence through 6 months after vaccination.

METHODS: This prospective longitudinal study enrolled 30 pregnant or lactating women. SARS-CoV-2 antibodies and neutralization capacity were analyzed using an enzyme-linked immunosorbent assay compared at prevaccination and 1, 3, and 6 months postvaccination, and through Holder pasteurization.

RESULTS: Human milk SARS-CoV-2–specific IgG levels peaked at 1 month postvaccination and persisted above prevaccination levels for at least 6 months ($P = .005$). SARS-CoV-2–specific IgA was detected at 1 and 3 months (both $P < .001$) but waned by 6 months compared with baseline ($P = .07$). Milk SARS-CoV-2–specific IgG and IgA correlated with serum IgG at the same time point ($R^2 = 0.37$, $P < .001$ and $R^2 = 0.19$, $P < .001$). Neutralization activity was seen in 83.3%, 70.4%, and 25.0% of milk samples at 1, 3, and 6 months postvaccination. Neutralization most strongly correlated with SARS-CoV-2–specific IgG ($R^2 = 0.57$, $P < .001$). Pre- and postpasteurization samples showed similar IgG (0.84 vs 1.07, $P = .36$) and neutralizing activity (57.7% vs 58.7% inhibition, $P = .27$), but lower IgM and IgA levels postpasteurization (0.09 vs 0.06, $P = .004$ and 0.21 vs 0.18, $P = .043$).

CONCLUSIONS: The data suggest that human milk SARS-CoV-2–specific antibodies may be available to milk-fed infants for up to 6 months. In addition, donor milk from vaccinated mothers retain IgG and neutralizing activity.

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[a]*Division of Infectious Diseases, Children's Hospital Los Angeles, Los Angeles, California;* [b]*Keck School of Medicine, University of Southern California, Los Angeles, California;* [c]*Division of Infectious Diseases, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, New York;* [d]*Department of Pediatrics, University of California, San Diego and University of California Health Milk Bank, San Diego, California; and* [e]*Departments of Pediatrics and Molecular Microbiology and Immunology, Keck School of Medicine, University of Southern California, Los Angeles, California*

**Contributed equally as co-first authors*

Ms Perez and Mr Luna Centeno collected data and drafted the initial manuscript; Mr Cheng and Dr Marentes Ruiz designed the data collection instruments and collected data; Dr Lee analyzed the data and reviewed and revised the manuscript; Mr Congrove-Wilson and Dr Stellwagen collected data and reviewed and revised the manuscript; Dr Powell helped design analysis methods and reviewed and revised the manuscript; Dr Pannaraj conceptualized and designed the study, supervised the data collection and analysis, and reviewed and revised the manuscript for important intellectual content; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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WHAT'S KNOWN ON THIS SUBJECT: Data suggests that maternal COVID-19 messenger RNA (mRNA) vaccination stimulates the presence of SARS-CoV-2 antibodies in human milk up to 6 weeks, but less is known about the duration of antibody neutralization ability and persistence after pasteurization.

WHAT THIS STUDY ADDS: In this longitudinal prospective study of 30 lactating women, vaccination induced a strong SARS-CoV-2–specific antibody response in human milk which lasted at least 6 months and correlated with neutralizing activity that is not significantly reduced with pasteurization methods.

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Efficient maternal to neonatal transfer of antibodies against SARS-CoV-2 and BNT162b2 mRNA COVID-19 vaccine

Ofer Beharier,[1,2] Romina Plitman Mayo,[2] Tal Raz,[3] Kira Nahum Sacks,[4] Letizia Schreiber,[5] Yael Suissa-Cohen,[1] Rony Chen,[6] Rachel Gomez-Tolub,[6] Eran Hadar,[6] Rinat Gabbay-Benziv,[7] Yuval Jaffe Moshkovich,[7] Tal Biron-Shental,[8] Gil Shechter-Maor,[9] Sivan Farladansky-Gershnabel,[9] Hen Yitzhak Sela,[9] Hedi Benyamini-Raischer,[10] Nitzan D. Sela,[10] Debra Goldman-Wohl,[1] Ziv Shulman,[11] Ariel Many,[12] Haim Barr,[13] Simcha Yagel,[1] Michal Neeman,[3] and Michal Kovo[4]

[1]Department of Obstetrics and Gynecology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel. [2]Department of Biological Regulation, Weizmann Institute of Science, Rehovot, Israel. [3]Koret School of Veterinary Medicine, The Robert H. Smith Faculty of Agriculture, Food & Environment, The Hebrew University of Jerusalem, Rehovot, Israel. [4]Department Obstetrics and Gynecology, Wolfson Medical Center, Holon; affiliated to Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel. [5]Department of Pathology, Wolfson Medical Center, Holon; affiliated to Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel. [6]Helen Schneider Hospital for Women, Rabin Medical Center, Petach Tikva; affiliated to Sackler Faculty of Medicine, Tel Aviv University, Israel. [7]The Hillel Yaffe Medical Center, Hadera, Israel; affiliated to the Bruce Rappaport Faculty of Medicine, Technion, Israel Institute of Technology, Haifa, Israel. [8]Department of Obstetrics and Gynecology, Meir Medical Center, Kfar Saba, Israel, affiliated to Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel. [9]Department of Obstetrics and Gynecology, Shaare Zedek Medical Center and Faculty of Medicine, Hebrew University of Jerusalem, Israel. [10]Department of Obstetrics and Gynecology, Emek Medical Center, Afula, Israel affiliated with Rappaport Faculty of Medicine, Technion, Haifa, Israel. [11]Department of Immunology, Weizmann Institute of Science, Rehovot, Israel. [12]Lis Hospital for Women, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel; affiliated to Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel. [13]The Nancy and Stephen Grand Israel National Center for Personalized Medicine (G-INCPM), Weizmann Institute of Science, Rehovot, Israel.

BACKGROUND. The significant risks posed to mothers and fetuses by COVID-19 in pregnancy have sparked a worldwide debate surrounding the pros and cons of antenatal SARS-CoV-2 inoculation, as we lack sufficient evidence regarding vaccine effectiveness in pregnant women and their offspring. We aimed to provide substantial evidence for the effect of the BNT162b2 mRNA vaccine versus native infection on maternal humoral, as well as transplacentally acquired fetal immune response, potentially providing newborn protection.

METHODS. A multicenter study where parturients presenting for delivery were recruited at 8 medical centers across Israel and assigned to 3 study groups: vaccinated ($n = 86$); PCR-confirmed SARS-CoV-2 infected during pregnancy ($n = 65$), and unvaccinated noninfected controls ($n = 62$). Maternal and fetal blood samples were collected from parturients prior to delivery and from the umbilical cord following delivery, respectively. Sera IgG and IgM titers were measured using the Milliplex MAP SARS-CoV-2 Antigen Panel (for S1, S2, RBD, and N).

RESULTS. The BNT162b2 mRNA vaccine elicits strong maternal humoral IgG response (anti-S and RBD) that crosses the placenta barrier and approaches maternal titers in the fetus within 15 days following the first dose. Maternal to neonatal anti-COVID-19 antibodies ratio did not differ when comparing sensitization (vaccine vs. infection). IgG transfer ratio at birth was significantly lower for third-trimester as compared with second trimester infection. Lastly, fetal IgM response was detected in 5 neonates, all in the infected group.

CONCLUSION. Antenatal BNT162b2 mRNA vaccination induces a robust maternal humoral response that effectively transfers to the fetus, supporting the role of vaccination during pregnancy.

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Introduction

The worldwide pandemic of COVID-19 continues to spread, with substantial morbidity and mortality. To date, more than 80,000 pregnant women have been infected in the U.S. alone, and the estimated global number of pregnant women infected with COVID-19 is likely to reach millions this year. Recent data demonstrated that pregnant women with COVID-19 infection are at increased risk for intensive care unit (ICU) admission, mechanical ventilation, and death, compared with properly matched nonpregnant women (1–9). Furthermore, COVID-19 illness increases the risk for pregnancy complications such as preterm birth, pregnancy-induced hypertensive diseases, and thromboembolic diseases (10). Although accumulating data suggest that the risk for

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RESEARCH Open Access

COVID-19 mRNA vaccine and antibody response in lactating women: a prospective cohort study

Nadia Charepe[1,2*], Juliana Gonçalves[3,4], A. Margarida Juliano[3,4], David G. Lopes[2,5], Helena Canhão[1,2,5], Helena Soares[2,3,4] and e Fátima Serrano[1,2]

Abstract

Background: Immunological protection via breastfeeding is well known. The immunological profile of human milk changes during lactation. No clinical trials have been conducted in lactating women with the newest mRNA vaccines against SARS- CoV-2. A Few studies have shown the presence of antibodies in breastmilk after vaccination. The aim of this work is to study possible antibodies transfer via breastmilk and also the immunological characteristics of lactating women compared to non-lactating women, after using the BNT162b2 Pfizer vaccine.

Methods: This is a prospective cohort study with a convenience homogenous sample of 24 healthcare workers (14 lactating and 10 non-lactating women) enrolled at the time of COVID-19 vaccination. Clinical data was registered in a questionnaire. Titers of SARS-CoV-2 spike IgG, IgA and IgM were quantified in post vaccination blood and human milk. Antibody quantification was performed by an in-house ELISA to SARS-CoV-2 trimeric spike protein.

Results: All women showed immunity after vaccination with positive antibodies for IgM, IgA and IgG antibodies. The dominant serum antibody response was IgG. Modest levels of antibodies in breastmilk of lactating mothers were observed in this study, especially IgG in 42.9%. There was a moderate association between higher titers of IgG and a longer duration of breastfeeding (R= 0.55, p=0.041).

Conclusions: Evidence of antibody transfer in human milk after COVID-19 vaccination is scarce. The presence of antibodies in human milk is reported, but immunization through breastfeeding is still to be established.

Keywords: Breastfeeding, Covid-19, mRNA vaccination, Antibodies

Background

In the first months of life, neonates are at greater risk of infections, due to their immature immune system and breastfeeding will boost immunological responses [1]. Additionally, breastfeeding is proven to be effective against acute and prolonged infections, and has an influence on infant immune response after mother's vaccine immunization [2]. Secretory IgA (SIgA) represents 90% of the antibodies in human milk, followed by IgM and IgG antibodies [1]. For this reason, and for its biological properties, SIgA is very important, as it is essential in defending mucous membranes [1]. Nevertheless, specific characteristics of lactating mothers may influence the kinetics of human milk antibodies due to the differences of previous infections (time since preexisting disease immunity), age, genetic factors, and individual immune response [3].

The arrival of COVID-19 vaccines, specifically mRNA vaccines against SARS-CoV-2 such as BNT162b2 Pfizer, has raised the question whether they are safe for use in

* Correspondence: nadia.charepe@edu.nmsunl.pt
[1] Centro Hospitalar Universitário de Lisboa Central (CHULC), Lisboa, Portugal
[2] Comprehensive Health Research Centre, NOVA Medical School, Universidade NOVA de Lisboa, Lisboa, Portugal
Full list of author information is available at the end of the article

JAMA | Original Investigation

Immunogenicity of COVID-19 mRNA Vaccines in Pregnant and Lactating Women

Ai-ris Y. Collier, MD; Katherine McMahan, MS; Jingyou Yu, PhD; Lisa H. Tostanoski, PhD; Ricardo Aguayo, BS; Jessica Ansel, NP; Abishek Chandrashekar, MS; Shivani Patel, BA; Esther Apraku Bondzie, BA; Daniel Sellers, BS; Julia Barrett, BS; Owen Sanborn, BS; Huahua Wan, MS; Alquan Chang, BA; Tochi Anioke, BS; Joseph Nkolola, PhD; Connor Bradshaw, BS; Catherine Jacob-Dolan, BS; Jared Feldman, BS; Makda Gebre, MSc; Erica N. Borducchi, PhD; Jinyan Liu, PhD; Aaron G. Schmidt, PhD; Todd Suscovich, PhD; Caitlyn Linde, PhD; Galit Alter, PhD; Michele R. Hacker, ScD; Dan H. Barouch, MD, PhD

IMPORTANCE Pregnant women are at increased risk of morbidity and mortality from COVID-19 but have been excluded from the phase 3 COVID-19 vaccine trials. Data on vaccine safety and immunogenicity in these populations are therefore limited.

OBJECTIVE To evaluate the immunogenicity of COVID-19 messenger RNA (mRNA) vaccines in pregnant and lactating women, including against emerging SARS-CoV-2 variants of concern.

DESIGN, SETTING, AND PARTICIPANTS An exploratory, descriptive, prospective cohort study enrolled 103 women who received a COVID-19 vaccine from December 2020 through March 2021 and 28 women who had confirmed SARS-CoV-2 infection from April 2020 through March 2021 (the last follow-up date was March 26, 2021). This study enrolled 30 pregnant, 16 lactating, and 57 neither pregnant nor lactating women who received either the mRNA-1273 (Moderna) or BNT162b2 (Pfizer-BioNTech) COVID-19 vaccines and 22 pregnant and 6 nonpregnant unvaccinated women with SARS-CoV-2 infection.

MAIN OUTCOMES AND MEASURES SARS-CoV-2 receptor binding domain binding, neutralizing, and functional nonneutralizing antibody responses from pregnant, lactating, and nonpregnant women were assessed following vaccination. Spike-specific T-cell responses were evaluated using IFN-γ enzyme-linked immunospot and multiparameter intracellular cytokine–staining assays. Humoral and cellular immune responses were determined against the original SARS-CoV-2 USA-WA1/2020 strain as well as against the B.1.1.7 and B.1.351 variants.

RESULTS This study enrolled 103 women aged 18 to 45 years (66% non-Hispanic White) who received a COVID-19 mRNA vaccine. After the second vaccine dose, fever was reported in 4 pregnant women (14%; SD, 6%), 7 lactating women (44%; SD, 12%), and 27 nonpregnant women (52%; SD, 7%). Binding, neutralizing, and functional nonneutralizing antibody responses as well as CD4 and CD8 T-cell responses were present in pregnant, lactating, and nonpregnant women following vaccination. Binding and neutralizing antibodies were also observed in infant cord blood and breast milk. Binding and neutralizing antibody titers against the SARS-CoV-2 B.1.1.7 and B.1.351 variants of concern were reduced, but T-cell responses were preserved against viral variants.

CONCLUSION AND RELEVANCE In this exploratory analysis of a convenience sample, receipt of a COVID-19 mRNA vaccine was immunogenic in pregnant women, and vaccine-elicited antibodies were transported to infant cord blood and breast milk. Pregnant and nonpregnant women who were vaccinated developed cross-reactive antibody responses and T-cell responses against SARS-CoV-2 variants of concern.

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Dan H. Barouch, MD, PhD, Center for Virology and Vaccine Research, 330 Brookline Ave, E/CLS-1043, Boston, MA 02115 (dbarouch@bidmc.harvard.edu).

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Research Letter

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Vaccination in Pregnancy

Measures of Immunity and Placental Histopathology

Elisheva D. Shanes, MD, Sebastian Otero, BA, Leena B. Mithal, MD, MSCI, Chiedza A. Mupanomunda, BS, Emily S. Miller, MD, MPH, and Jeffery A. Goldstein, MD, PhD

INTRODUCTION

Vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been approved for emergency use, but, despite elevated risk of severe disease, pregnant women were excluded from the clinical trials that led to their authorization.[1] Placental findings can indicate potential clinical risk and could be an early signal for rare injury seen only after widespread use in the pregnant population.[2–6]

Maternal SARS-CoV-2 infection has been associated with decidual arteriopathy, fetal vascular malperfusion, and chronic histiocytic intervillositis.[7–9] mRNA vaccines induce an immune response through activation of TLR3, which has been linked to decidual arteriopathy, growth restriction, preterm delivery, and fetal loss in mouse models.[10–14]

Our objective was to evaluate the frequency of these key placental lesions in patients who received SARS-CoV-2 vaccination in pregnancy.

METHODS

The study methods have been described previously and were approved by the Northwestern University institutional review board.[7,15] We report results from patients who tested negative for SARS-CoV-2 infection on polymerase chain reaction who received vaccine (delivering between January and April 2021) and unvaccinated women in a control group (negative for SARS-CoV-2 infection on polymerase chain reaction, immunoglobulin G– and immunoglobulin M–negative, delivering between April 2020 and April 2021) from an ongoing coronavirus disease 2019 (COVID-19) cohort study. Antibody testing used the ACCESS SARS-CoV-2 spike protein RBD test.

Statistical testing was performed with unpaired *t* tests or Fisher exact test for demographics and logistic regression with gestational age as a covariate for placental lesions (Python SciPy 1.6.1). A post hoc power calculation was performed, demonstrating at least 80% power to identify a 2.5-fold or higher increased risk of any lesion with a baseline prevalence of 10% or greater and a threefold or higher increased risk of any lesion with a baseline prevalence of 7% or greater (Stata 15.0).

RESULTS

We report findings in 84 women who received a SARS-CoV-2 vaccine during pregnancy and 116 women in a control group who did not receive a vaccine (Table 1). Women with vaccination were more likely to deliver vaginally. The first inoculation was 46±24 days before delivery for the 75 patients with known vaccination timing. Vaccinated women showed robust antibody responses, whereas women in the control group were negative (Fig. 1 and Table 1).

Placental examination in women with vaccination showed no increased incidence of decidual arteriopathy, fetal vascular malperfusion, low-grade chronic villitis, or chronic histiocytic intervillositis compared

From the Feinberg School of Medicine, Northwestern University, and the Ann and Robert H. Lurie Children's Hospital of Chicago, Chicago, Illinois.

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Corresponding author: Jeffery A. Goldstein, MD, PhD, Olson 2-455, Feinberg School of Medicine, Chicago IL; email: ja-goldstein@northwestern.edu.

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Case Report

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Antibodies in Neonatal Cord Blood After Vaccination in Pregnancy

Lisa Gill, MD, MS, and Cresta W. Jones, MD

BACKGROUND: Studies evaluating the safety and efficacy of currently available vaccines for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) do not include pregnant participants. No data are available to counsel on vaccine safety and potential for neonatal passive immunity.

CASE: A 34-year-old multigravid patient working in health care received the Pfizer-BioNTech (BNT162b2) mRNA vaccine for SARS-CoV-2 in the third trimester of pregnancy. Uncomplicated spontaneous vaginal delivery of a female neonate with Apgar scores of 9 and 9 occurred at term. The patient's blood as well as neonatal cord blood were evaluated for SARS-CoV-2–specific antibodies. Both the patient and the neonate were positive for antibodies at a titer of 1:25,600.

CONCLUSION: In this case, passage of transplacental antibodies for SARS-CoV-2 was shown after vaccination in the third trimester of pregnancy.

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Teaching Points

1. Pregnant patients have been excluded from SARS-CoV-2 vaccine trials, leading to uncertainty regarding safety, efficacy, and potential for neonatal passive immunity.
2. Vaccination in pregnancy produced a robust immune response for the patient, with subsequent transplacental transfer of neutralizing antibodies.

Newly available vaccines for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are of great interest to patients and health care professionals. Initial studies of the two currently available mRNA vaccines have shown them to be safe and effective in nonpregnant adults.[1,2] Importantly, pregnant and lactating individuals were excluded from initial safety and efficacy trials, despite data demonstrating higher risks of severe infection and pregnancy-related morbidity and mortality.[3] The American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine released a joint statement in January 2021 advocating that pregnant individuals at high risk for contracting the virus should be able to decide whether they will receive the vaccination during pregnancy or while breastfeeding.[4]

In addition to safety, the potential for transplacental transfer of neutralizing maternal antibodies is also a consideration. The neonatal period is marked by an immature immune system, making it a vulnerable period for infection. Maternal antibodies generated during pregnancy are able to cross the placenta into the fetal circulation, providing immune protection for the neonate. This has been demonstrated previously in pregnant patients receiving several other vaccines in pregnancy.[5–7]

In this case, we report on a pregnant individual who received the Pfizer-BioNTech (BNT162b2) mRNA vaccine for SARS-CoV-2 at 32 weeks of gestation, with documented antibodies present in neonatal cord blood.

CASE

We present the case of a 34-year-old multigravid patient (G4P2012) who works as a nurse in a large health care system. System guidance allowed for pregnant individuals to opt in to receive a vaccine when it was available based on the tier system established by the Centers for Disease Control and Prevention. The patient's pregnancy was complicated by a history of fetal growth restriction in both prior pregnancies and hemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome in one prior pregnancy. Fetal growth was monitored by ultrasonography and was normal throughout the pregnancy.

From the Department of Obstetrics, Gynecology and Women's Health, Division of Maternal-Fetal Medicine, University of Minnesota, Minneapolis, Minnesota.

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Corresponding author: Lisa Gill, MD, MS, Department of Obstetrics, Gynecology and Women's Health, Division of Maternal-Fetal Medicine, University of Minnesota, Minneapolis, MN; e-mail: lgill@umn.edu.

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OBSTETRICS

Coronavirus disease 2019 vaccine response in pregnant and lactating women: a cohort study

Kathryn J. Gray, MD, PhD; Evan A. Bordt, PhD; Caroline Atyeo, BS; Elizabeth Deriso, PhD; Babatunde Akinwunmi, MD, MPH, MMSc; Nicola Young, BA; Aranxta Medina Baez, BS; Lydia L. Shook, MD; Dana Cvrk, CNM; Kaitlyn James, PhD, MPH; Rose De Guzman., PhD; Sara Brigida, BA; Khady Diouf, MD; Ilona Goldfarb, MD, MPH; Lisa M. Bebell, MD; Lael M. Yonker, MD; Alessio Fasano, MD; S. Alireza Rabi, MD; Michal A. Elovitz, MD; Galit Alter, PhD; Andrea G. Edlow, MD, MSc

BACKGROUND: Pregnant and lactating women were excluded from initial coronavirus disease 2019 vaccine trials; thus, data to guide vaccine decision making are lacking.

OBJECTIVE: This study aimed to evaluate the immunogenicity and reactogenicity of coronavirus disease 2019 messenger RNA vaccination in pregnant and lactating women compared with: (1) nonpregnant controls and (2) natural coronavirus disease 2019 infection in pregnancy.

STUDY DESIGN: A total of 131 reproductive-age vaccine recipients (84 pregnant, 31 lactating, and 16 nonpregnant women) were enrolled in a prospective cohort study at 2 academic medical centers. Titers of severe acute respiratory syndrome coronavirus 2 spike and receptor-binding domain immunoglobulin G, immunoglobulin A, and immunoglobulin M were quantified in participant sera (n=131) and breastmilk (n=31) at baseline, at the second vaccine dose, at 2 to 6 weeks after the second vaccine, and at delivery by Luminex. Umbilical cord sera (n=10) titers were assessed at delivery. Titers were compared with those of pregnant women 4 to 12 weeks from the natural infection (n=37) by enzyme-linked immunosorbent assay. A pseudovirus neutralization assay was used to quantify neutralizing antibody titers for the subset of women who delivered during the study period. Postvaccination symptoms were assessed via questionnaire. Kruskal-Wallis tests and a mixed-effects model, with correction for multiple comparisons, were used to assess differences among groups.

RESULTS: Vaccine-induced antibody titers were equivalent in pregnant and lactating compared with nonpregnant women (pregnant, median, 5.59; interquartile range, 4.68–5.89; lactating, median, 5.74; interquartile range, 5.06–6.22; nonpregnant, median, 5.62; interquartile range, 4.77–5.98, $P=.24$). All titers were significantly higher than those induced by severe acute respiratory syndrome coronavirus 2 infection during pregnancy ($P<.0001$). Vaccine-generated antibodies were present in all umbilical cord blood and breastmilk samples. Neutralizing antibody titers were lower in umbilical cord than maternal sera, although this finding did not achieve statistical significance (maternal sera, median, 104.7; interquartile range, 61.2–188.2; cord sera, median, 52.3; interquartile range, 11.7–69.6; $P=.06$). The second vaccine dose (boost dose) increased severe acute respiratory syndrome coronavirus 2–specific immunoglobulin G, but not immunoglobulin A, in maternal blood and breastmilk. No differences were noted in reactogenicity across the groups.

CONCLUSION: Coronavirus disease 2019 messenger RNA vaccines generated robust humoral immunity in pregnant and lactating women, with immunogenicity and reactogenicity similar to that observed in nonpregnant women. Vaccine-induced immune responses were statistically significantly greater than the response to natural infection. Immune transfer to neonates occurred via placenta and breastmilk.

Key words: antibodies, breastfeeding, breastmilk, cord blood, COVID-19 vaccine, maternal immunity, mRNA, neonatal immunity, pregnancy

Introduction

More than 73,600 infections and 80 maternal deaths have occurred in pregnant women in the United States alone as of March 1, 2021.[1] Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is more severe in pregnant women compared with their nonpregnant counterparts, with an increased risk of hospital admission, intensive care unit stay, and death.[2] Despite their higher risk, pregnant and lactating women were not included in any initial coronavirus disease 2019 (COVID-19) vaccine trials, although the first vaccine trial began in pregnant women in February 2021 (Pfizer/BioNTech, ClinicalTrials.gov identifier: NCT04754594).

The COVID-19 pandemic has given rise to hundreds of vaccine platforms in development to fight SARS-CoV-2.[3,4] However, few of these platforms have been tested or are specifically designed to elicit immunity in vulnerable populations, including pregnant women. Pregnant women have long been left out of therapeutic and vaccine research, reportedly owing to heightened safety concerns in this population.[5–8] Although the American College of Obstetricians and Gynecologists and the Society for Maternal-Fetal Medicine encouraged the Food and Drug Administration to include pregnant women in the COVID-19 vaccine emergency use authorization (EUA) owing to the risk of increased disease severity in this population, evidence about vaccine immunogenicity to guide patient decision making and provider counseling is lacking.[9–11] In particular, given the novelty of the first emergency approved COVID-19 vaccines, both of which use messenger RNA (mRNA) to deliver

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ARTICLE

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BNT162b2 mRNA vaccine elicited antibody response in blood and milk of breastfeeding women

Michal Rosenberg-Friedman[1,2,7], Aya Kigel[3,7], Yael Bahar[3], Michal Werbner[4], Joel Alter[5], Yariv Yogev[1,2], Yael Dror[3], Ronit Lubetzky[2,6], Moshe Dessau[5], Meital Gal-Tanamy[4], Ariel Many[1,2] & Yariv Wine[3]✉

The importance of breastmilk in postnatal life lies in the strong association between breastfeeding and the reduction in the risk of infection and infection-related infant mortality. However, data regarding the induction and dynamics of breastmilk antibodies following administration of the Pfizer-BioNTech BNT162b2 COVID-19 mRNA vaccine is scarce, as pregnant and lactating women were not included in the initial vaccine clinical trials. Here, we investigate the dynamics of the vaccine-specific antibody response in breastmilk and serum in a prospective cohort of ten lactating women who received two doses of the mRNA vaccine. We show that the antibody response is rapid and highly synchronized between breastmilk and serum, reaching stabilization 14 days after the second dose. The response in breastmilk includes both IgG and IgA with neutralization capacity.

[1] Department of Obstetrics and Gynecology, Lis Maternity & Women's Hospital, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel. [2] Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel. [3] The Shmunis School of Biomedicine and Cancer Research, The George S. Wise Faculty of Life Sciences, Tel Aviv University, Tel Aviv, Israel. [4] Molecular Virology Lab, The Azrieli Faculty of Medicine, Bar-Ilan University, Safed, Israel. [5] The Laboratory of Structural Biology of Infectious Diseases, The Azrieli Faculty of Medicine, Bar-Ilan University, Safed, Israel. [6] Department of Pediatrics, Dana Dwek Children's Hospital, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel. [7] These authors contributed equally: Michal Rosenberg-Friedman, Aya Kigel. ✉email: yarivwine@biu.ac.il

Research Letter

Antibody Response to Coronavirus Disease 2019 (COVID-19) Messenger RNA Vaccination in Pregnant Women and Transplacental Passage Into Cord Blood

Malavika Prabhu, MD, Elisabeth A. Murphy, PhD, Ashley C. Sukhu, BS, Jim Yee, BS, Sunidhi Singh, BA, Dorothy Eng, BA, BS, Zhen Zhao, PhD, Laura E. Riley, MD, and Yawei J. Yang, MD, PhD

INTRODUCTION

Pregnant women were excluded from initial clinical trials for coronavirus disease 2019 (COVID-19) vaccines[1,2]; thus, the understanding of the immunologic response to vaccination in pregnancy and the transplacental transfer of maternal antibodies is limited.[3,4]

METHODS

Between January 28, 2021, and March 31, 2021, we studied 122 pregnant women with cord blood available at the time of birth at a single academic medical center. Women who self-reported receipt of one or both doses of a messenger RNA (mRNA)-based COVID-19 vaccine and gave birth to a singleton neonate (gestational age between 35 0/7 and 41 2/7 weeks) were included in the study. Semi-quantitative testing for antibodies against S-receptor binding domain[5,6] was performed on leftover clinical sera of maternal peripheral blood to identify antibodies mounted against the vaccine and on leftover clinical sera of cord blood to study passive immunity. Only women who tested negative for antibodies against the nucleocapsid protein antigen[7] were included to ensure antibodies were not the result of past severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. The relationship between immunoglobin (Ig)G antibody levels and time was studied using analysis of variance. The relationship between maternal and cord blood IgG levels and between IgG placental transfer (neonatal/maternal) ratio and time was studied using Pearson correlation analysis and linear regression. The study was approved by the Weill Cornell Medicine Institutional Review Board.

RESULTS

By the time of delivery, 55 pregnant women had received one dose of an mRNA vaccine and 67 had received both vaccine doses. Eighty-five women received the Pfizer-BioNTech vaccine, and 37 women received the Moderna vaccine. All women tested negative for SARS-CoV-2 infection using reverse-transcriptase polymerase chain reaction on nasopharyngeal swabs, and all women and neonates were asymptomatic at birth and until time of discharge.

Eighty-seven pregnant women tested at birth produced an IgG response, 19 women produced both an IgM and IgG response, and 16 women had no detectable antibody response, the latter of whom were within 4 weeks of vaccine dose 1 (Fig. 1A). As the number of weeks elapsed, the number of women who mounted an antibody response and who conferred passive immunity to their neonates increased (Fig. 1A). All women and cord blood samples, except for one, had detectable IgG antibodies by 4 weeks after vaccine dose 1 (Fig. 1A). The one dyad with no transfer of antibodies to the neonate was 10 weeks from dose 1 and 6 weeks from dose 2. The earliest

From the Department of Obstetrics and Gynecology and the Department of Pathology and Laboratory Medicine, Weill Cornell Medicine, the Laboratory of Molecular Neuro-oncology, the Rockefeller University, and the Department of Pathology and Laboratory Medicine, New York-Presbyterian Hospital/Weill Cornell Medical Center, New York, New York.

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Corresponding author: Yawei J. Yang, MD, PhD, Department of Pathology and Laboratory Medicine, Weill Cornell Medicine, New York, NY; email: yangyj@med.cornell.edu.

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vaccines

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Communication

Evaluation of SARS-CoV-2 Spike Protein Antibody Titers in Cord Blood after COVID-19 Vaccination during Pregnancy in Polish Healthcare Workers: Preliminary Results

Wojciech Zdanowski [1,2,*] and Tomasz Waśniewski [1,2]

[1] Department of Gynaecology and Obstetrics, Gynaecological Oncology Clinical Ward, Regional Specialist Hospital, ul. Żołnierska 18, 10-561 Olsztyn, Poland; tomasz.wasniewski@uwm.edu.pl
[2] Department of Obstetrics and Gynaecology, School of Medicine, Collegium Medicum, University of Warmia and Mazury, 10-561 Olsztyn, Poland
* Correspondence: wojciech.zdanowski@uwm.edu.pl; Tel.: +48-502-978-651

Abstract: Background: The coronavirus disease 2019 (COVID-19) pandemic has given rise to the need to develop a vaccine as quickly as possible. As pregnant women are at increased risk of contracting severe COVID-19, with higher mortality, it is essential to assess the safety of the vaccines administered during pregnancy. Methods: The aim of this study was to determine the titer of specific maternal and cord antibodies against severe acute respiratory syndrome coronavirus 2 S protein after antenatal vaccination. The secondary objective was to evaluate the ratio of the umbilical cord to the maternal antibody titers. Patients included in the study were enrolled after undergoing voluntary vaccination against COVID-19 during pregnancy at different weeks of gestation. All patients analyzed in our initial study were vaccinated with the BNT162b2 mRNA COVID-19 vaccine. Results: The results of the current study document high anti-S total IgG antibody titers in cord serum at birth in all mother–infant pairs analyzed. The mean umbilical cord blood sample IgG antibody titer anti-S protein was 1026.51 U/mL (±SD 769.25). The mean cord-to-maternal anti-S IgG antibody ratio was 1.28 (±SD 0.798). A significant positive correlation was observed between the week of gestation at which the first dose was administered and the week of gestation at which the second dose was administered, and the respective cord-to-maternal ratio ($r = 0.48$; $p = 0.0029$) for the first dose and ($r = 0.39$; $p = 0.0102$) for the second dose. Conclusions: To date, despite the prevalence of COVID-19 vaccination, there is a lack of conclusive evidence supporting the safety and efficacy of vaccination of pregnant women. Therefore, the results we present are complementary. Our study suggests that maternal immunization may provide neonatal protection through the transplacental transfer of antibodies. Of particular importance is the demonstration that antibody transfer is correlated with the time from vaccination to delivery, which may allow future determination of the optimal timing of COVID-19 vaccination in pregnant women.

Keywords: COVID-19; pregnancy; vaccine

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1. Introduction

The coronavirus disease 2019 (COVID-19) pandemic has become an indefinite global public health crisis. The elevated vulnerability of women during pregnancy, as well as experiences from previous coronavirus outbreaks, have heightened concerns around maternal and fetal complications [1]. Pregnant women are at an increased risk of developing severe COVID-19, with higher mortality rates, compared to non-pregnant women. The efficacy and safety of vaccines for use in pregnant women, fetuses, and infants remain undefined. Pregnant and lactating women have been excluded from clinical trials of existing COVID-19 vaccines [2–4]. According to the recommendations issued by the American College of Obstetricians and Gynecologists, the Center for Disease Control and Prevention, and the Royal College of Obstetricians and Gynecologists, COVID-19

Lampiran 4

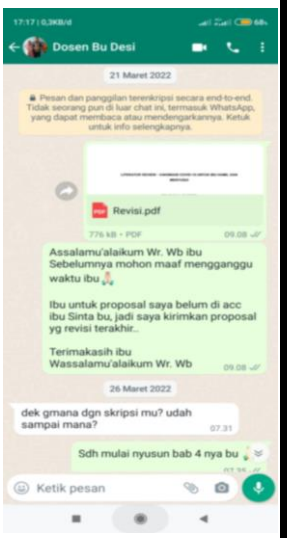
Lembar Konsultasi

KARTU BIMBINGAN SKRIPSI

Nama Mahasiswa : Risca Airun Jariah
NIM : 1811102415117
Pembimbing : Apt. Deasy Nurchairin Harifa, M.Clin., pharm.

No	Tanggal	Materi Bimbingan	Arahan/Masukan	Paraf	
				Mahasiswa	Dosen
1	01/09-21	pendaftaran KDM klinis	menentukan jenis penelitian yang ingin di teliti		
2	09/09-21	penentuan judul	persetujuan judul proposal skripsi, dan arahan dalam penyusunan proposal.		

No	Tanggal	Materi Bimbingan	Arahan/Masukan	Paraf	
				Mahasiswa	Dosen
3.	04/11-21	mengumpulkan proposal revisi Bab 1-3.	Revisi proposal		
4.	05/11-21	mengumpulkan proposal yang telah direvisi	Revisi proposal, lengkapi proposal		
5.	20/11-21	mengumpulkan proposal yang telah direvisi	Pendaftaran sempro.		

No	Tanggal	Materi Bimbingan	Arahan/Masukan	Bukti Konsultasi
6.	26/01/22	Revisi Proposal	Revisi proposal skripsi, dan lanjut mengerjakan bab IV dan V	
7.	21/03/22	Pengumpulan proposal skripsi	Melanjutkan penulisan skripsi bab IV dan V	
8.	4/04/22	Pengumpulan Skripsi Bab 4	Tambahkan literatur dan lanjut mengerjakan hingga bab IV	

9.	09/04/22	Mengumpulkan naskah skripsi bab 1-5	Revisi Bab 1-5	
10.	07/06/22	Mengumpulkan naskah skripsi bab 1-5	ACC naskah skripsi, meminta ttd untuk uji turnitin	

Lampiran 5

Hasil Uji Plagiasi

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by Risca Ainun Jariah

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