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SARS-CoV-2 mRNA vaccination in lactating mothers: an observational study to assess longer-term immune responses in blood and breast milk, infections and health status after coronavirus (COVID-19) mRNA vaccination in Zurich, Switzerland

Submission date
28/07/2023

Recruitment status
No longer recruiting

Registration date
28/07/2023

Overall study status
Completed

Last Edited
28/07/2023

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Due to safety reasons, lactating women have been excluded in the early stages of the clinical trials of mRNA vaccines against SARS-CoV-2. In affected persons, this has led to great uncertainty and was associated with major restrictions in the daily life – even after the approval of the mRNA vaccines for pregnant and lactating women. A few articles focusing on longitudinal assessments of the immunogenic profile in blood and breast milk of lactating individuals have now been published. However, continuous research in field is urgently needed as antibody transfer from mother to breast milk and breastfed infant respectively is still not very well understood.
The aim of this study is to assess antibody responses in the blood and breast milk of lactating women for up to 6 weeks after the administration of the first mRNA vaccine (monovalent BNT-162b2 or mRNA-1273). In order to provide a complete picture in lactating women and their breastfed children, the researchers did not only focus on immunological data but also on post-vaccination symptoms (PVS) and the occurrence of SARS-CoV-2 infections after vaccination for up to 6 months after study enrolment.

Who can participate?
Lactating women receiving any of the mRNA SARS-CoV-2 vaccines approved in Switzerland at the Corona Center of the UZH are randomly selected and invited for study participation.

What does the study involve?
1. Questionnaires
All participants will be asked to fill out a self-administered electronic questionnaire at enrolment (baseline; usually day of first vaccine dose), 3-4 weeks, 6 weeks, 3 months and 6 months after

baseline. The questionnaires can be filled out before or during the study visits and will collect the following information:
1. Sociodemographic information
2. Medical and smoking history
3. SARS-CoV-2 related information (e.g. infection, symptoms, doctor visits and hospitalizations, and treatment)
4. Vaccination-related information (e.g. type of SARS-CoV-2 vaccine received, vaccine-related adverse effects)
5. Information regarding SARS-CoV-2 exposure (e.g. contacts with an infected person, professional exposure, receipt of a SwissCovid app warning)

2. Collection of biological material
Participants will be invited for a total of three study visits during which blood and breast milk samples are collected. The collection of blood and breast milk samples will be conducted at baseline before receipt of the first vaccine and at 3-4 weeks and 6 weeks after baseline.
The study visits will take place at the Corona Center of the UZH and are expected to take 20-30 minutes during which:
1. Study personnel will check the clinical follow-up questionnaires and will provide assistance to participants if incomplete.
2. Trained personnel will collect two peripheral venous blood samples (total 30 ml) and breast milk samples (30 ml)
3. Participants will be given an information sheet explaining how to interpret the test results (i. e., the possibility of false positive or false negative results, the uncertainty of the extent of protection against (re)infection).
Blood and breast milk samples will subsequently be tested for SARS-CoV-2 antibodies. Participants will receive their test results by postal mail and will be called by the study personnel if no antibodies are detected after 1 month, or if antibody levels decline below the detection threshold with time.

The vaccination cards of participants will be scanned and archived as a medical record of the SARS-CoV-2 vaccination, as well as further vaccinations received during childhood and adulthood. The participants' treating physicians may be contacted for more detailed information regarding relevant clinical outcomes and/or medical consequences for all participants reporting a health care contact at the follow-up evaluations.

What are the possible benefits and risks of participating?
This study will significantly advance the understanding of how immunity develops with the SARS-COV-2 mRNA vaccines in lactating women in terms of humoral response in blood and breast milk. This information will be highly relevant for public health decision-makers and patients both locally in Switzerland and internationally. Participants directly benefit from information about their antibody responses. Minimal risk to participants is anticipated during biological sample collection. Possible complications occurring during biological sample collection will be minimized by adopting standard sample collection protocols and working with trained personnel.

Where is the study run from?
The Corona Center of the University of Zurich, Epidemiology, Biostatistics and Prevention Institute (EBPI) (Switzerland)

When is the study starting and how long is it expected to run for?
September 2021 to August 2022

Who is funding the study?
The Uniscientia Foundation (Switzerland)

Who is the main contact?
Prof. Dr. med. Jan Fehr

Study website
https://www.ebpi.uzh.ch/en/translational_research/community_and_health/sars_cov_2_mrna_vaccination_lactating_mothers_vlac.html

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
Nil known

Study information

Scientific Title
SARS-CoV-2 mRNA vaccination in lactating mothers (VLAC): characterization of immune responses in serum and breast milk of lactating women

Acronym
VLAC

Study objectives
The overall aim of this prospective and population-based cohort study is to assess the development of vaccine-induced short- and mid-term immunity. The primary and secondary objectives are the following:

Primary objective:
1. To characterize IgG and IgA antibodies against the trimeric SARS-CoV-2 spike protein in serum and breastmilk: antigen specificity and phenotype produced in response to the mRNA SARS-CoV-2 vaccines over time in lactating women.

Secondary objectives:
1. To assess neutralizing antibodies against the trimeric SARS-CoV-2 spike protein of SARS CoV-2 variants in serum
2. To evaluate the occurrence and severity of SARS-CoV-2 infections among lactating women and their infants who received a SARS-CoV-2 vaccine.
3. To evaluate the occurrence and severity of adverse effects among lactating women and their infants who received a SARS-CoV-2 vaccine.
4. To compare the humoral immune response in breast milk between lactating women with SARS-CoV-2 infection and those who received a SARS-CoV-2 vaccine.
5. To evaluate factors that influence the immune response in breast milk.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 01/11/2021, Cantonal Ethics Committee Zurich (Stampfenbachstrasse 121, Zurich, 8090, Switzerland; +41 (0)43 259 79 70; Info.KEK@kek.zh.ch), ref: BASEC 2021-01835

Study design
Observational prospective cohort study

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Community, University/medical school/dental school

Study type(s)
Prevention, Safety, Efficacy

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied
COVID-19 (SARS-CoV-2 infection)

Interventions

Individuals receiving any of the mRNA SARS-CoV-2 vaccines approved in Switzerland at the Corona Center of the UZH, who are randomly selected and invited for study participation will be asked to provide informed consent for study participation. The study procedures are the same for all different vaccines and include the following:

1. Questionnaires
All participants will be asked to fill out a self-administered electronic questionnaire at enrolment (baseline; usually day of first vaccine dose), and 3-4 weeks, 6 weeks, 3 months and 6 months after baseline. The questionnaires can be filled before or during the study visits (see below) and will collect the following information:
1. Sociodemographic information
2. Medical and smoking history
3. SARS-CoV-2 related information (e.g. infection, symptoms, doctor visits and hospitalizations, and treatment)
4. Vaccination-related information (e.g. type of SARS-CoV-2 vaccine received, vaccine-related adverse effects)
5. Information regarding SARS-CoV-2 exposure (e.g. contacts with an infected person, professional exposure, receipt of a SwissCovid app warning)

2. Collection of biological material
Participants will be invited for a total of three study visits during which blood samples are collected. The collection of blood samples will be conducted at baseline before receipt of the first vaccine, and at 3-4 weeks and 6 weeks after baseline. The study visits will take place at the Corona Center of the UZH and are expected to take 20-30 minutes during which:
1. Study personnel will check the clinical follow-up questionnaires and will provide assistance to participants if incomplete.
2. Trained personnel will collect two peripheral venous blood samples in EDTA tubes by venipuncture (total 20 ml) and breast milk samples in specified tubes (30ml)
3. Participants will be given an information sheet explaining how to interpret serological test results (i.e., possibility of false positive or false negative results, uncertainty of the extent of protection against (re)infection).

Blood and breast milk samples will subsequently be tested for SARS-CoV-2 antibodies. Participants will receive their test result by postal mail and will be called by the study personnel if no antibodies are detected after one month, or if antibody levels decline below the detection threshold with time.

Further data sources - Collection of supplementary medical information
The vaccination cards of participants will be scanned and archived as a medical record of the SARS-CoV-2 vaccination, as well as further vaccinations received during childhood and adulthood. The participants' treating physicians may be contacted for more detailed information regarding relevant clinical outcomes and/or medical consequences for all participants reporting a health care contact at the follow-up evaluations.

Intervention Type
Other

Primary outcome measure
1. Presence of anti-SARS-CoV-2 IgG antibodies in blood and breast milk before receiving the first dose of a vaccine (baseline), at 3-4 weeks and at 6 weeks, tested using the Corona Immunitas serology test from CHUV (Centre Hospitalier Universitaire Vaudois)

2. Presence of anti-SARS-CoV-2 IgA antibodies in blood and breast milk before receiving the first dose of a vaccine (baseline), at 3-4 weeks and at 6 weeks, tested using the Corona Immunitas serology test from CHUV (Centre Hospitalier Universitaire Vaudois)

Secondary outcome measures
1. Proportion of individuals with measurable neutralizing antibodies against the trimeric SARS-CoV-2 spike protein of SARS-CoV-2 variants in serum and breast milk before receiving the first dose of an mRNA SARS-CoV-2 vaccine (baseline), before the second vaccine dose (usually 4 weeks after the first vaccine dose) and 2 weeks after the second vaccine dose (usually 6 weeks after the first vaccine dose), tested using a cell-free neutralization assay based on the competitive inhibition of ACE2 binding to spike protein trimer-bearing beads.
3. Proportion of lactating women and their infants who received a SARS-CoV-2 and experience a SARS-CoV-2 infection after vaccination, assessed with own standardized questionnaires including the information about positive results in SARS-CoV-2 PCR or rapid antigen tests
4. Proportion of lactating women and their infants who experience adverse effects after vaccination of the mother, assessed using own standardized symptom diary handed out at baseline and subsequently collected 6 weeks after baseline.
5. Comparison of differences in antibody level in breast milk according to the age of the mother, age of the baby, duration of lactation, circumstances of birth (e.g., prematurity) and other factors

Overall study start date
01/09/2021

Completion date
12/08/2022

Eligibility

Key inclusion criteria
1. Lactating women receiving any of the mRNA SARS-CoV-2 vaccines approved in Switzerland at the Corona Center of the UZH
2. Aged ≥18 years
3. Able to follow the study procedures
4. Providing informed consent

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Sex
Female

Target number of participants
80

Total final enrolment
45

Key exclusion criteria
1. Non-lactating individuals
2. Having insufficient knowledge of the German language
3. Previously received SARS-CoV-2 vaccine

Date of first enrolment
02/11/2021

Date of final enrolment
21/02/2022

Locations

Countries of recruitment
Switzerland

Study participating centre
University of Zurich (UZH), Corona Center of the University of Zurich, Epidemiology, Biostatistics and Prevention Institute (EBPI)
Hirschengraben 84
Zurich
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8001

Sponsor information

Organisation
University of Zurich

Sponsor details
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Sponsor type
University/education

Website

http://www.uzh.ch/index_en.html

ROR
https://ror.org/02crff812

Funder(s)

Funder type
Charity

Funder Name
Uniscientia Foundation

Alternative Name(s)

Funding Body Type
Private sector organisation

Funding Body Subtype
Trusts, charities, foundations (both public and private)

Location
Switzerland

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
01/01/2024

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be available upon request from Dipl. Med. Patrick Wiech (patrick.wiech@uzh.ch). Data will be depersonalized and include baseline questionnaire answers as well as the immunologic parameters. Access to the data will be granted individually upon request.

IPD sharing plan summary
Available on request