COVID-19 serology, virology, and host factors among healthcare workers

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In this study, we therefore aim to establish the kinetics of the humoral immune response against SARS-CoV-2, and relate this to the viral characteristics, microbiome and host factors of healthcare workers.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Viral infectious disorders
Study type	Observational non invasive

Summary

ID

NL-OMON55118

Source
ToetsingOnline

Brief title
COVID-19 infection among healthcare workers

Condition

- Viral infectious disorders

Synonym
COVID-19, SARS-CoV-2

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: Health Holland (recieves from Ministry of economic affairs and climate policy)

Intervention

Keyword: COVID-19, Heathcare workers, SARS-CoV-19, Serology

Outcome measures

Primary outcome

1 - The association between SARS-CoV-2 serology (IgG / IgM antibodies) with symptom severity and duration of healthcare workers

COVID-19 disease severity classification

For the initial presentation of patients we will use the severity scale published by the WHO (COVID-19 Interim Guidance 27-5-2020, page 13). Categories are Mild Disease (Symptomatic COVID-19), Moderate Disease (Pneumonia), Severe Disease (severe pneumonia), Critical disease (ARDS or sepsis). Given the nature of our populations. We expect that the majority of the healthcare workers included will be classified as *Mild disease*.

As the pandemic is ongoing and we are still learning about potential clinical subcategories, we will continuously assess clinical criteria with experienced physicians and according to international standards. Indicators for disease severity that we will record for all patients include underlying diseases, days since onset of symptoms, cough, maximum measured body temperature, running nose and shortness of breath (a detailed questionnaire is provided as part of the point to point reply). In the hospitalized patients we will also record days of hospitalization, need for oxygen suppletion (in L/min), ICU admittance, need for ventilation and duration of ventilator support, need for rehabilitation after hospital admittance, multi-organ complications (e.g. need for

kidney-replacement therapy, creatinine change compared to baseline, cardiac failure), thrombotic complications (and affected organ by thrombosis).

Secondary outcome

2 - the validation of an in-house serological test for SARS-CoV-2 (IgG / IgM) for persons with mild infection
(UMC Utrecht diagnostic objective)

3 - the association between SARS-CoV-2 serology (presence or absence of SARS-CoV-2 IgG antibodies at visit 3), and three immunological host factors: serum inflammatory marker profile, peripheral blood cell and nasal epithelial cell phenotype
(UMC Utrecht research objective)

4 - the association of the respiratory microbiome composition in determining the symptom duration in COVID-19 patients
(UMC Utrecht research objective)

5 - the percentage of healthcare workers with SARS-CoV-2 who are still contagious 24 hours after the last symptoms have resolved
(contributing to the national study on healthcare worker serology)

6 - the percentage of healthcare workers with negative SARS CoV-2 PCR, but with antibodies (IgG / IgM) against SARS CoV-2

(contributing to the national study on healthcare worker serology)

Study description

Background summary

The majority of people infected with SARS-CoV-2 have mild disease. At the start of the epidemic, initial surveillance of SARS-CoV-2 was directed at persons that present at the hospital, who have serious SARS-CoV-2 symptoms that require admission. Patients with more severe symptoms are thought to be at increased risk of transmitting SARS-CoV-2 to other individuals. Transmission of SARS-CoV-2 during mild disease course is considered rare, provided social distancing is adequately applied. However, for healthcare workers, social distancing may not be possible, as physical proximity to admitted patients is often required. As such, there is concern to contract and spread SARS-CoV-2 to vulnerable patients in the hospital, illustrating the need for additional information on symptom severity, and the potential to infect others. In addition, it remains unclear to what extent healthcare workers generate antibodies against SARS-CoV-2, and whether this prevents re-infection. Importantly, recent studies indicated that people who experience mild disease may develop a less potent antibody response to SARS-CoV-2. For these reasons, reliable assessment of antibody generation in the blood of healthcare workers is urgent. To investigate which health care workers are vulnerable to infection, we will additionally map host and virological factors related to SARS-CoV-2.

Study objective

In this study, we therefore aim to establish the kinetics of the humoral immune response against SARS-CoV-2, and relate this to the viral characteristics, microbiome and host factors of healthcare workers.

Study design

A single center, longitudinal, observational, investigator initiated study

Study burden and risks

We aim to include 75 SARS-CoV-2 positive healthcare workers for follow up. Based on the current prevalence among tested healthcare workers of 10%, we expect to include a total of 750 healthcare workers in the study.

All included individuals will be healthcare workers with symptoms associated with SARS CoV-2 who are tested according to the regular procedure in the UMCU

for healthcare workers. One nose-throat swab at day 0 (visit 0) and one after symptoms have resolved (visit 2) will be performed (standard of care). In asymptomatic healthcare workers a control nose-throat swab is performed after 5 days. If the SARS-CoV-2 PCR at visit 2 is positive, the PCR test will be repeated weekly until negative. During this study, healthcare workers will be asked to visit the UMC Utrecht test location two additional times (4 visits total). The nose brush (for isolation of nasal epithelial cells) will only be performed for SARSCoV-
2 positive patients. All visits that include a nose throat swab are standard of care (visit 0 and 2). The testing of blood at any timepoint is not standard of care. At visit 3, three weeks after the first symptoms have occurred, only blood tests are performed (no swab is done). If symptoms persist, timepoint X can be delayed to a maximum of three months.
If the SARS-CoV-2 PCR is positive at visit 2, the test will be repeated weekly until the participant is SARS-CoV-2 PCR negative. Retesting when the PCR is positive with a CT value < 32 is standard of care for healthcare workers, retesting after a PCR with a CT value > 32 is additional.

Visit 0: COVID test healthcare worker with symptoms (standard of care)
- Nose-throat swab (for SARS-CoV-2 testing)*

Visit 1: blood test and nose brush
- Inclusion: sign PIF
- Questionnaire
- Symptom diary (day 1 - day 21)
- 4 blood tubes (2 serum, 2 heparin)
- Nose brush (nasal epithelial cells, the nose brush is only performed if SARS-CoV-2 PCR is positive)
This material will be collected by a physician and medical students specifically allocated to this project.

Visit 2: control nose-throat swab after resolution of symptoms**
- Nose-throat swab (for SARS-CoV-2 testing)*

Visit 3: blood test after 3 weeks
- 4 blood tubes (2 serum, 2 heparin)
* This swab is part of the regular procedure for healthcare workers of the UMCU. The swab is repeated until the PCR is negative.
** In asymptomatic healthcare workers a control nose-throat swab is performed after 5 days.
If SARS-CoV-2 negative participants become SARS-CoV-2 positive during follow-up the participant will be transferred to the SARS-CoV-2 positive study group. The questionnaire and symptom diary will be sent again, a nose brush will be performed and visit 3 will be postponed to 3 weeks after onset of their first SARS-CoV-2 symptoms.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

All healthcare workers who have symptoms associated with SARS-CoV-2

Exclusion criteria

None

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Health services research

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	19-01-2021
Enrollment:	750
Type:	Actual

Ethics review

Approved WMO Date:	15-10-2020
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	02-03-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL73903.041.20