Fucosylation of antibodies in multi-inflammatory syndrome in children after SARS-CoV-2 infection

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To study the antibody response as a disease modifying factor in the context of COVID-19, we will compare the anti-CoV antibody composition, quality and interaction with immune receptors.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Autoimmune disorders
Study type	Observational invasive

Summary

ID

NL-OMON54254

Source
ToetsingOnline

Brief title
FLAMINGO

Condition

- Autoimmune disorders
- Viral infectious disorders
- Respiratory tract infections

Synonym
Covid, inflammatory disease

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht

Source(s) of monetary or material Support: NWO

Intervention

Keyword: Antibodies, Fucosylation, Multi-inflammatory syndrome in children, SARS-CoV-2

Outcome measures

Primary outcome

Fucosylation of SARS-CoV-2 IgG antibodies defined as percentage of fucose-containing glycans attached to N297 in the IgG-Fc. Focus will be on the main subclass generated (IgG1 and IgG3).

Secondary outcome

We compare the anti-CoV antibody response and interaction with immune receptors between cases and controls by:

- Anti-CoV antibody levels, (sub)class and antigen specificity (ELISA)

- Anti-CoV antibody glycosylation

- Interaction of serum-derived patient anti-CoV antibodies with a biosensor equipped with all human Fc-gamma receptors

- Inflammatory markers of juvenile idiopathic arthritis (see UCAN CAN-DU protocol)

-To study gene expression profiles to distinguish between inflammatory and infectious causes of fever.

Study description

Background summary

The COVID-19 pandemic caused by SARS-CoV-2, has 24 million confirmed cases and more than 800.000 deaths. Patient responses to SARS-CoV-2 (COVID-19) are highly

diverse, ranging from asymptomatic or mild self-limiting infection, to a severe upper airway inflammation leading to respiratory distress, often with a fatal outcome. This suggests different paths taken by the immune system to combat the disease, so far there is no clear evidence that can make a distinction between these two different immunological and pathological paths. It is also not known how the immune response to COVID in MIS-C compares to other hyperinflammatory diseases in childhood such as juvenile idiopathic arthritis.

In the recent past, have discovered that antibody responses to enveloped viral infections can be altered. Posttranslational modification through glycosylation can either give a protective response or enhance the disease phenotype through an overreacting immune response. There have been many cases of children and adolescents with COVID-19-assocated multisystem inflammatory conditions, which seems to develop after a COVID-19 infection. The multisystem inflammatory syndrome in children (MIS-C) can lead to shock and multiple organ failure requiring intensive care. The pathophysiology of MIS-C is still unclear.

Study objective

To study the antibody response as a disease modifying factor in the context of COVID-19, we will compare the anti-CoV antibody composition, quality and interaction with immune receptors.

Study design

This is a non-interventional, observational case-control study:
Cases: laboratory-confirmed SARS-CoV-2 infection with MIS-C. We will recruit retrospective and prospective cases. A single blood draw is taken from retrospective cases and two blood draws from prospective cases. For the main analysis all cases will be pooled. Furthermore they will get a short questionary.

Controls: three control populations will be distinguished in (A) children suspected of MIS-C but with negative COVID diagnostics, (B) children with proven acute COVID respiratory infection and (C) otherwise healthy children prior to elective surgery. A single blood draw prior to surgery is taken from control group 3 and two blood draws from control group 1 and control group 2. Furthermore they will get a short questionary.

Study burden and risks

There will be a blood draw, which is the most stressful part.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)
Babies and toddlers (28 days-23 months)

Inclusion criteria

Children 0-16 years of age with a laboratory confirmed COVID-19 (RIVM) and MIS-C.

Exclusion criteria

Severe immune-related comorbidity (humoral immunodeficiency, cellular immunodeficiency, treatment for cancer, treatment with biologicals, IVIG treatment at moment of inclusion).

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	14-01-2021
Enrollment:	120
Type:	Actual

Ethics review

Approved WMO Date:	18-01-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	24-06-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-07-2023
Application type:	Amendment
Review commission:	METC NedMec

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	NL75633.041.20