COVID-19 in Pediatric Patients: clinical and immunological features

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Primary objective: To obtain a detailed immunological profile of children presenting to Dutch hospitals with acute SARS-CoV-2 infection or with a SARS-CoV-2 related post-infectious inflammatory syndrome. Secondary objectives: (1) To correlate the...

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

Summary

ID

NL-OMON54119

Source
ToetsingOnline

Brief title
COPP-IMM

Condition

- Immune disorders NEC
- Viral infectious disorders

Synonym
COVID-19 in children; multi-system inflammatory in children (MIS-C)

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Bontius Stichting en LUF

Intervention

Keyword: children, COVID-19, immunology, MIS-C

Outcome measures

Primary outcome

We will perform detailed immunological analyses in a two-tiered approach. In the first tier we will do a rapid, more general assessment of the immune system. This will include a detailed phenotypical analysis of the cells of the innate and adaptive immune system using spectral flow cytometry, a multiplex analysis of inflammatory cytokines using Luminex bead arrays and a quantitative and qualitative analysis of anti-SARS-CoV-2 antibodies. Depending on the results of the investigations in the first tier, we will choose which in-depth immunological analyses will be done in the second tier. Investigations in the second tier will focus on the innate immune system, the adaptive immune system (either T-cell responses or B-cell responses) and/or biomarker discovery of serum proteins.

Main study parameter/endpoints of the reinfection substudy

1. To determine the incidence rate of reinfections with SARS-CoV-2.

2. To investigate risk factors (demographic, clinical, virological, immunological) for SARS-CoV-2 reinfections.

3. To understand which factors determine the longevity and breadth of protective SARS-CoV-2-specific humoral immunity.

4. To determine the health impact of SARS-CoV-2 reinfections or their sequelae.

Secondary outcome

We will correlate the immunological profiles with detailed clinical outcome measures of the patients. We will collect these clinical outcome measures in the same manner as in our related cohort study *Clinical features of COVID-19 in Pediatric Patients* (COPP-study). Clinical parameters collected include: severity of disease (need of supplemental oxygen); underlying illnesses; age at presentation; clinical syndrome; laboratory parameters at diagnosis and during illness; response to treatment; clinical outcome, and patient reported outcome measures at 6 weeks follow-up.

Secondary study parameter/endpoints of the reinfection substudy
To determine the incidence rate of (co-)infections (such as influenza viruses and RSV).

Study description

Background summary

The immune response of children to infection with SARS-CoV-2 is markedly different to the immune response of adults with COVID-19. Children are less likely to develop severe COVID-19, but some children do need supplemental oxygen or intensive care. In rare cases, children who have been infected with SARS-CoV-2 develop a potentially life-threatening post-infectious inflammatory syndrome termed *multisystem inflammatory syndrome in children* (MIS-C). To better understand and treat these severe sequelae of SARS-CoV-2 infection in children, comprehensive immunological analysis in parallel with the collection of detailed clinical information is needed.

For the substudy on reinfections:
Reinfections with SARS-CoV-2 occur frequently due to declining immunity after previous infection and/or vaccination and the emergence of new virus variants that partially circumvent existing immunity. It is currently unknown if

children with a history of severe COVID-19 and/or MIS-C are at an increased risk of severe sequelae after reinfection. This substudy is part of a ZonMw funded collaboration between 7 different existing COVID-19 cohorts in the Netherlands (children and adults): *Riding the waves in the pandemic tail: incidence, risk factors and impact of SARS-COV-2 reinfections*, or *RTW-study*.

Study objective

Primary objective: To obtain a detailed immunological profile of children presenting to Dutch hospitals with acute SARS-CoV-2 infection or with a SARS-CoV-2 related post-infectious inflammatory syndrome.

Secondary objectives: (1) To correlate the immunological profiles with detailed clinical parameters. We will collect clinical data in this COPP-IMM study in the same way as in our related observational cohort study *Clinical features of COVID-19 in Pediatric Patients* (COPP-study). Clinical parameters include: severity of disease, underlying illnesses, age at presentation, clinical syndrome, laboratory parameters at diagnosis, outcome. (2) To identify immunological targets of therapy.

Main study parameter/endpoints of the reinfection substudy
The overall aim is to to investigate risk factors, including existing SARS-CoV-2-specific antibody and T cell immunity, and health impact of reinfections, including the nature, severity and duration of symptoms, during the autumn, winter and spring seasons of 2022-2023, in children previously seen in or admitted to hospital with COVID-19 or MIS-C.

Study design

Study design: Multicenter prospective cohort study

Study burden and risks

Blood samples for this study will be collected after confirmation of the diagnosis COVID-19 or MIS-C and after the patient and/or the caregiver have consented for participation. The amount of blood drawn depends on the body weight of the patient, and ranges from 5 to 50 mL. To ensure minimal burden as possible, the collection of the blood sample will be combined with a blood sample collection for routine clinical care and/or will be drawn from an indwelling venous catheter, if possible. If this is not possible, a venepuncture will be done to collect material for this study. In this case, there will some burden to the patient. To ensure that this burden is minimal, we will apply a topical anaesthetic (lidocaine/prilocaine or lidocaine/tetracaine as per local guidelines) and will instruct local researchers on positive language before and during the procedure.
The risk of this study to the participants is negligible. There is no direct

benefit of this study for the participants. The results from this study will benefit the target group, i.e. children with COVID-19 or MIS-C, by identifying immunological targets of therapy.

For the reinfection substudy:
The blood sampling and swabs will cause some burden. To ensure that this burden is minimal, will use positive language before and during the sampling. The finger will be warmed. The risk of this study to the participants is negligible. There is no direct benefit of this study for the participants. The results from this study will benefit the target group, i.e. children with a history of COVID-19 or MIS-C, by identifying risk factors, clinical features and immunological characteristics of reinfection.

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)
Newborns
Premature newborns (<37 weeks pregnancy)

Inclusion criteria

- age up to and including 17 years
- clinical or microbiological diagnosis of COVID-19 or MIS-C
- presentation in hospital (outpatient department, emergency department, or clinical admission)

Study population of the substudy on reinfections: enrolled participants of the initial studies COPP/COPP-IMM will be approached to also participate in the current substudy.

Inclusion criteria for this substudy:
- Children with a prior COVID-19 infection and/or MIS-C, treated as in- or outpatients in Dutch hospitals, AND
- Previously included in the COPP/COPP-IMM study between 1st of March 2020 and 1st of September 2022, with consent to be approached for subsequent studies, AND
- Informed consent for the reinfection substudy

Exclusion criteria

Age 18 years or older
No COVID-19 or MIS-C
No informed consent
For blood sampling: body weight under 3 kg

Exclusion criteria for the substudy on reinfections
A potential subject who meets any of the following criteria will be excluded from
- No consent from guardians and/or patient

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled

Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	28-05-2021
Enrollment:	200
Type:	Actual

Ethics review

Approved WMO

Date:	20-05-2021
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	17-11-2021
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	18-02-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	08-06-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Not approved

Date:	28-12-2022
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	16-02-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL76177.058.21