



Paediatric inflammatory multisystem syndrome temporally associated with SARS-COV-2 (PIMS-TS)

BACKGROUND

Reports from the UK, Europe, and the USA since late April 2020 have described a number of severely ill children and adolescents with COVID-19 who developed fever and shock frequently associated with abdominal pain and rash. This condition is provisionally named Paediatric Inflammatory Multisystem Syndrome Temporally associated with SARS-COV-2 (PIMS-TS). The United States Centres for Disease Control has named this syndrome Multisystem Inflammatory Syndrome in Children associated with COVID-19 (MIS-C).

The exact link between SARS-CoV-2 and PIMS-TS remains unclear. The epidemiology, particularly the delay in timing between peak SARS-COV-2 infection in the community and PIMS-TS cases, as well as the timing of infection and clinical presentation in individual patients, suggest that this condition may be due to a delayed immune-mediated phenomenon triggered by the virus. Many, but not all, of the reported cases have tested positive for SARS-CoV-2 on PCR and/or serological testing.

The clinical features of PIMS-TS include unexplained persistent fever, acute abdominal pain with diarrhoea or vomiting, muscle pain and general tiredness, hypotension including shock, conjunctivitis, peripheral oedema, rash, lymphadenopathy and a "Strawberry tongue".⁸⁻¹⁰ Heart failure is common and complications can include respiratory distress, acute kidney injury, coagulopathies, and coronary artery abnormalities.

This study will complement data collection by the Paediatric Active Enhanced Disease Surveillance (PAEDS) using the same case definition and modified case report form. Children managed in hospitals participating in PAEDS (see list) should still be reported to APSU to ensure complete data collection by providing minimal identifiers and hospital location, but the CRF does not need to be completed by the reporting clinician. Children in any other location should be reported to APSU and CRF completed as usual.

STUDY OBJECTIVES

- i. To describe the demographic and clinical features of PIMS-TS in children and adolescents
- ii. To estimate the incidence and further characterise the aetiology of PIMS-TS in Australia, specifically the association of PIMS-TS with SARS-CoV-2 infection.
- iii. To determine the overlapping features of PIMS-TS with Kawasaki disease and COVID-19 in Australian children.
- iv. To collect internationally comparable data for potential future data sharing to enable higher powered analysis of PIMS-TS in children and adolescents.

CASE DEFINITION

Children and adolescents (up to 18 years of age) with fever ≥ 3 days **AND** two of the following:

- a) Rash or bilateral non-purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet).
- b) Age specific hypotension or "shock" within first 24 hours of presentation,
- c) Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP),
- d) Evidence of coagulopathy (by PT, PTT, elevated d-Dimers)

e) Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain).

AND

Elevated markers of inflammation such as ESR, C-reactive protein, or procalcitonin.

AND

Exclusion of other infectious causes of inflammation, including bacterial sepsis, staphylococcal or streptococcal toxic shock syndromes.

AND

Evidence of SARS-CoV-2 infection including one or more of: positive RT-PCR or antigen test or confirmed positive SARS-CoV-2 serology (noting testing may be delayed, particularly serology. If all other criteria are met, collect data pending results)

OR contact with a confirmed COVID-19 case.

PAEDS HOSPITALS

- Sydney Children's Hospital Network
- The Royal Children's Hospital, Melbourne
- Monash Health, Victoria
- Queensland Children's Hospital, Brisbane
- Perth Children's Hospital, Perth
- Women's and Children's Hospital Adelaide
- Royal Darwin Hospital, Darwin

INVESTIGATORS

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SELECTED REFERENCES

Wurzel D, McMinn A, Hoq M, Blyth CC, Burgner D, Tosif S, Buttery J, Carr J, Clark JE, Cheng AC, Dinsmore N. Prospective characterisation of SARS-CoV-2 infections among children presenting to tertiary paediatric hospitals across Australia in 2020: a national cohort study. *BMJ open*. 2021 Nov 1;11(11):e054510.

Fraile Navarro D, Tendal B, Tingay D, Vasilunas N, Anderson L, Best J, Burns P, Cheyne S, Craig SS, Erickson SJ, Fancourt NS. Clinical care of children and adolescents with COVID-19: recommendations from the National COVID-19 Clinical Evidence Taskforce. *Medical Journal of Australia*. 2022 Mar 21;216(5):255-63.

Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. *The Lancet* 2020;395:1607- 1608.

National Centre for Immunisation Research and Surveillance, A statement from the Acute Inflammatory Vasculitis working group and the Paediatric Active Enhanced Disease Surveillance (PAEDS) network, Advice for clinicians: Paediatric Inflammatory Multisystem Syndrome Temporally associated with SARS-COV-2 (PIMS-TS) www.ncirs.org.au/advice-for-clinicians-PIMS-TS