BAPIO Publications

The Physician
Journal of The British Association of Physicians of Indian Origin

COVID-19 in Children & Paediatric Multisystem Inflammatory Syndrome

Sahana Rao MBBS MRCPCH
Oxford University Hospitals NHS Trust, Oxford, UK
Sahana.Rao@ouh.nhs.uk

Keywords; COVID-19, Afro-Caribbean, Paediatric multi-system inflammatory syndrome

cité Rao, S. (2020) COVID-19 in children and paediatric multi-system inflammatory syndrome. The Physician 6(1) ePub 24.05.2020 DOI: 10.38192/1.6.1.13

Full Text

COVID-19 was first reported in Wuhan China and on 9th January 2020, the Chinese CDC reported a novel coronavirus as the causative agent, SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2). The World Health Organization declared the outbreak a Public Health Emergency of International Concern on 30 January, and a pandemic on 11 March.[1]

Children are less affected by COVID-19 as shown by epidemiological studies. According to the European Surveillance System (TESSy), children (aged 0-14years) accounted for only 2.1% of all confirmed COVID-19 cases[2]. TESSy data suggests a U-shaped pattern in the age distribution of the proportion of asymptomatic cases, with 15% aged less than five years; 17% aged 5-9 years and 17% aged 10-14 years. The most commonly reported symptoms include fever and cough [3]. Data from Italian emergency departments found 21% of SARS-CoV-2 positive children to be asymptomatic[4].

Paediatric Multisystem Inflammatory Syndrome

PIM-TS stands for **P**aediatric Multisystem **I**nflammatory **S**yndrome – **T**emporally Associated with **S**ARS-CoV-2. This stands for the hyperinflammatory state seen in children with exposure to SARS-CoV-2. The first case series was described by Riphagen et al and published on May 7th, 2020 in Lancet[5]. Royal College of Paediatrics and Child Health (RCPCH) developed a case definition for PIM-TS[6].

The key features are:

- A child presenting with persistent fever, inflammation (neutrophilia, elevated CRP, and lymphopaenia) with evidence of single or multi-organ dysfunction (shock, cardiac, respiratory, renal, gastrointestinal, or neurological disorder) with additional features. This may include children fulfilling full or partial criteria for Kawasaki Disease.

- Exclusion of any other microbial cause, including bacterial sepsis, staphylococcal or streptococcal shock syndromes, infections associated with myocarditis such as enterovirus.
- SARS-CoV-2 PCR testing may be positive or negative

The Centre for Disease Control, America defined it as Multisystem Inflammatory Syndrome in Children (MIS-C).[7]

- An individual aged <21 years presenting with fever, laboratory evidence of inflammation, and evidence of clinically severe illness requiring hospitalization, with multisystem (>2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological) AND
- No alternative plausible diagnoses AND
- Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or COVID-19 exposure within the 4 weeks prior to the onset of symptoms.

Epidemiology

In a case series from London [2], all children were previously well. Clinical presentations included unrelenting fever (38–40°C), variable rash, conjunctivitis, peripheral oedema, and generalised extremity pain with significant gastrointestinal symptoms. All progressed to warm, vasoplegic shock; refractory to volume resuscitation and required inotropic support. Majority of them did not have any significant respiratory involvement, though seven required mechanical ventilation for cardiovascular stabilisation. Other features included development of small pleural, pericardial, and ascitic effusions. All children had raised inflammatory markers but tested negative for SARS-CoV-2. Echo-bright coronary vessels was a common echocardiographic finding.

The general picture is of children's persistent high-grade fever, limited or no respiratory compromise, fluid refractory shock, extremely high inflammatory markers and frequent cardiac dysfunction.

Parri et al [4] reported from the Bergamo province, Italy where they noted a 30-fold increased incidence of Kawasaki-like disease. The children were older, had a higher rate of cardiac involvement, and 8 (out of ten) had antibodies against SARS-CoV-2.

Clinical features:

Clinical features include a ***persistent fever >38.5°C with Oxygen requirement, Hypotension and some of the following symptoms including a***bdominal pain, confusion, conjunctivitis, cough, diarrhoea, headache ,lymphadenopathy, mucus membrane changes ,neck swelling, rash, respiratory symptoms, sore throat, syncope , vomiting and swollen hands and feet.

Investigations

RCPCH [6] and Don't forget the bubbles [8] recommend the following investigations: FBC, U&E, Glucose, VBG, Lactate, Coagulation, D-dimer, LDH, Triglycerides, Ferritin, Troponin, CK, Vitamin D, ASOT and Viral PCRs. Common findings include [6]:

- Echo and ECG – myocarditis, valvulitis, pericardial effusion, coronary artery dilatation.
- CXR – patchy symmetrical infiltrates, pleural effusion
- Abdo USS – colitis, ileitis, lymphadenopathy, ascites, hepatosplenomegaly
- CT chest may demonstrate coronary artery abnormalities if with contrast

Kawasaki disease:

There are many similarities between the clinical features between PIM-TS and Kawasaki Disease, including fever, rash, conjunctivitis, peripheral oedema and coronary artery involvement on ECHO.[8]

Kawasaki disease is a medium vessel vasculitis which affects children. American Heart Association criteria (2017) defined it as fever for ≥5 days plus four or more clinical criteria, including bilateral bulbar non-exudative conjunctivitis, changes of lips or oral cavity, polymorphic rash, non-suppurative cervical lymphadenopathy (with at least one node ≥ 1.5 cm in diameter), and changes in the hands or feet (erythema, oedema, induration, desquamation). Incomplete types include fever for ≥5 days plus two or three of clinical criteria and raised erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP). Blood tests may reveal presence of anaemia, leucocytosis, thrombocytosis (week 2 of fever), hypoalbuminaemia, and raised transaminases. Echocardiogram may show coronary aneurysms or cardiac dysfunction. Complications of KD include aneurysms of mid-sized arteries, giant coronary artery aneurysms, pericarditis and myocarditis. There are no diagnostic tests for KD.

Management:

RCPCH has published recommendations for the management of PMIS-TS. [6]

- All children should be treated as suspected COVID-19
- For mild to moderate disease supportive care only is recommended.
- Close monitoring with hourly PEWS for signs of respiratory or cardiovascular deterioration and clinical signs of worsening inflammation.
- Standard APLS resuscitation and supportive management.
- Start empiric antibiotics (as per local sepsis protocols).
- Consider IVIG and aspirin early if fulfils criteria for Kawasaki Disease and IVIG if fulfils criteria for toxic shock syndrome
- Immunomodulatory therapy and anti-viral treatment , if needed, after discussion with paediatric ID and/or clinicians with appropriate experience***.***
- ***All stable children should be discussed as soon as possible with specialist services to ensure prompt treatment.***
- ***There should be a low threshold for referral to Paediatric Intensive Care.***

Risk assessment

European Centre for Disease Prevention and Control [2] have summarised that the probability of COVID-19 in children is currently assessed as “low”. The impact of such disease is assessed as “moderate”, therefore the overall risk of COVID-19 in children is assessed as LOW. In summary, the probability of PIMS-TS in children in the EU/EEA is currently assessed as “very low” and the impact of such disease is assessed as “high”, therefore the overall risk of COVID-19-associated PIMS-TS in children is assessed as LOW risk.

Key points:

In the current climate, it is essential that the professionals are aware of PMIS-TS. The children may present to their GPs, Emergency department or Paediatrics with a variety of symptoms. Majority of the children have mild or moderate symptoms, though the small minority may deteriorate quickly.

1. Early recognition and diagnosis of PMIS-TS is important to ensure early treatment and reduce the risk of long-term complications.
2. Clinical features include persistent fever, raised inflammatory markers and with evidence of single or multi-organ dysfunction (shock, cardiac, respiratory, renal, gastrointestinal, or neurological disorder)
3. Awareness and a high level of suspicion in those children presenting with fever, respiratory symptoms and features of Kawasaki disease.
4. Children from BAME backgrounds are more commonly affected.

5. Children with mild to moderate disease require only supportive care. For severe cases, consider retrieval to PICU, antibiotics and immuno-modulatory therapy following discussion with specialists.

References:

1. WHO Director-General's opening remarks at the media briefing on COVID-19—11 March 2020". World Health Organization. 11 March 2020. Retrieved on 23rd May 2020
2. European Centre for Disease Prevention and Control. Paediatric inflammatory multisystem syndrome and SARS-CoV-2 infection in children – 14 May 2020. ECDC: Stockholm; 2020.
3. Castagnoli R, Votto M, Licari A, Brambilla I, Bruno R, Perlini S, et al. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection in Children and Adolescents: A Systematic Review. JAMA pediatrics. 2020
4. Parri N, Lenge M, Buonsenso D. Children with Covid-19 in Pediatric Emergency Departments in Italy. The New England journal of medicine. 2020.
5. Riphagen S et al, Hyperinflammatory shock in children during COVID-19 pandemic. Lancet Published: May 07, 2020.
6. RCPCH https://www.rcpch.ac.uk/sites/default/files/2020-05/COVID-19-Paediatric-multisystem-%20inflammatory%20syndrome-20200501.pdf Accessed 23rd may, 2020.
7. Coronavirus Disease 2019 in Children - United States, February 12-April 2, 2020. MMWR Morbidity and mortality weekly report 2020;69(14):422-6.
8. Paediatric Multisystem Inflammatory Syndrome, Don't Forget the Bubbles, 2020. Available at: http://doi.org/10.31440/DFTB.25760.