Clinical Guidance

Paediatric Critical Care: PIMS-TS
Paediatric Multisystem Inflammatory Syndrome temporally associated with SARS-CoV2

Summary
This is to provide guidance regarding the diagnosis and management of Paediatric Multisystem Inflammatory Syndrome temporally associated with SARS-CoV-2. Please see STRS app or PIMS-TS: Referral pathway and clinical management guideline on GTi for immunomodulation dosing as being modified frequently.

This clinical guideline has been produced by the South Thames Retrieval Service (STRS) at Evelina London for nurses, doctors and ambulance staff to refer to in the emergency care of critically ill children. This guideline represents the views of STRS and was produced after careful consideration of available evidence in conjunction with clinical expertise and experience. The guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient.

<table>
<thead>
<tr>
<th>Change History</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date</td>
</tr>
<tr>
<td>December 20</td>
</tr>
</tbody>
</table>

Keywords
SARS, CoV-2, COVID-19, Hyperinflammation, Multisystem, Inflammatory, Cardiac, Kawasaki, Evelina, child, Paediatric, STRS, critical care, PICU, PIMS, TS, MISC, MIS-C,
Paediatric Critical Care

Paediatric Multisystem Inflammatory Syndrome temporally associated with SARS-CoV-2

The Covid-19 pandemic has been temporally associated with the emergence of a paediatric presentation of severe inflammation and shock. This syndrome has clinical similarities to Kawasaki shock and toxic shock and it can be difficult to differentiate at presentation thus management must include antibiotics and cardiac assessment. Very few patients have had coronavirus detected by PCR on throat/nasal swabs, however serological evidence of SARS-CoV-2 infection is present in the majority. The spectrum of disease is wide; children who are cardiovascularly stable can be managed locally with advice from paediatric ID team. Please refer to STRS if signs of shock, deterioration or planned for transfer.

**Clinical features**

May include one or more of the following:
- Persistent Fever > 39 C
- Lethargy and Myalgia
- Abdominal Symptoms: Pain, Diarrhoea and Vomiting
- Rash/Conjunctivitis
- Hypotension (Wide pulse pressure), tachycardia +/- Shock

**Laboratory features**

- Hyponatraemia
- Raised Ferritin (>500)
- Raised Fibrinogen
- Raised D-Dimer
- Renal dysfunction
- Raised CRP
- Raised Troponin and B-NP
- Lymphopenia / neutrophilia
- Platelets initially low or normal

**Significant similarity in presentation with other paediatric conditions**

Septic shock - may require higher volume fluid resuscitation and source control: senior clinical review
Peritonitis -negative laparotomy reported in some cases: cautious specialist surgical review with appropriate radiology

**Initial management**

Examination:
- Exclude potential septic foci and careful cardiac assessment (liver, JVP, cardiac / thoracic ratio on CXR)

Resuscitation:
- If signs of shock – fluid resuscitation (10ml/kg aliquots) with re-evaluation after each bolus and discuss with STRS
- If no improvement with fluid, start inotropes: Dopamine@ 5 - 10mcg/kg/min, until central access (consider noradrenaline)
- Ceftriaxone and Clindamycin as sepsis impossible to exclude
- Anaesthetic team review and discuss with STRS

Severe myocardial dysfunction common:
- If intubation required: cardio-stable induction (ketamine+ draw up emergency drugs)
- Caution on moving ventilated patients - instability observed in severe cardiac dysfunction (extremely preload dependant)
- Monitor for arrhythmias

**Laboratory features**

Core investigations:
- FBC, Full biochemical profile (Na, K, Ur, Cr, Ca, Phos, Mg, LFTs)
- CRP, PCT, ESR
- Ferritin, Triglycerides, Trop-T, D-Dimers, CK, NT-proBNP, LDH
- Coagulation profile (Including Fibrinogen)
- Blood / Urine culture
- Blood film
- INR
- Coagulation profile prior to starting)
- Chest X-ray
- Consider abdominal imaging to exclude abdominal pathology

**Cardiac Manifestations and Management**

Pancarditis may include: bi-ventricular impairment, mitral/ tricuspid valve regurgitation, diastolic dysfunction, arrhythmia, pericardial effusion, coronary artery dilatation / aneurysm
Clinical course unpredictable with rapid deterioration observed in some
- 12 lead ECG – arrhythmias reported
- Urgent echocardiogram
- Low threshold for milrinone infusion
- Severe cases consider levosimendan or argipressin based on clinical picture: cardiac function vs vasoplegia
- VA ECMO for refractory shock – crossmatch blood

**Immunomodulation to be guided by ID and MDT. Consider entry into RECOVERY trial, will influence the following:**

- IVIG 2g/kg (use IBW) (must save serum before giving) monitor for fluid overload during infusion.
- Methylprednisolone 10mg/kg (max 1 gram) daily for 3 days

**Additional immunomodulation may include:**

- Tocilizumab (IL-6 receptor antibody)
- Repeat IVIG dose
- Longer duration of steroids
- Anakinra (IL-1 receptor antagonist)
- Infliximab (monoclonal antibody)

**Significant similarity in presentation with other paediatric conditions**

Septic shock - may require higher volume fluid resuscitation and source control: senior clinical review
Peritonitis -negative laparotomy reported in some cases: cautious specialist surgical review with appropriate radiology

**Initial management**

Examination:
- Exclude potential septic foci and careful cardiac assessment (liver, JVP, cardiac / thoracic ratio on CXR)

Resuscitation:
- If signs of shock – fluid resuscitation (10ml/kg aliquots) with re-evaluation after each bolus and discuss with STRS
- If no improvement with fluid, start inotropes: Dopamine@ 5 - 10mcg/kg/min, until central access (consider noradrenaline)
- Ceftriaxone and Clindamycin as sepsis impossible to exclude
- Anaesthetic team review and discuss with STRS

Severe myocardial dysfunction common:
- If intubation required: cardio-stable induction (ketamine+ draw up emergency drugs)
- Caution on moving ventilated patients - instability observed in severe cardiac dysfunction (extremely preload dependant)
- Monitor for arrhythmias

**Laboratory features**

Core investigations:
- FBC, Full biochemical profile (Na, K, Ur, Cr, Ca, Phos, Mg, LFTs)
- CRP, PCT, ESR
- Ferritin, Triglycerides, Trop-T, D-Dimers, CK, NT-proBNP, LDH
- Coagulation profile (Including Fibrinogen)
- Blood / Urine culture
- Blood film
- INR
- Coagulation profile prior to starting)
- Chest X-ray
- Consider abdominal imaging to exclude abdominal pathology

**Cardiac Manifestations and Management**

Pancarditis may include: bi-ventricular impairment, mitral/ tricuspid valve regurgitation, diastolic dysfunction, arrhythmia, pericardial effusion, coronary artery dilatation / aneurysm
Clinical course unpredictable with rapid deterioration observed in some
- 12 lead ECG – arrhythmias reported
- Urgent echocardiogram
- Low threshold for milrinone infusion
- Severe cases consider levosimendan or argipressin based on clinical picture: cardiac function vs vasoplegia
- VA ECMO for refractory shock – crossmatch blood

**Immunomodulation to be guided by ID and MDT. Consider entry into RECOVERY trial, will influence the following:**

- IVIG 2g/kg (use IBW) (must save serum before giving) monitor for fluid overload during infusion.
- Methylprednisolone 10mg/kg (max 1 gram) daily for 3 days

**Additional immunomodulation may include:**

- Tocilizumab (IL-6 receptor antibody)
- Repeat IVIG dose
- Longer duration of steroids
- Anakinra (IL-1 receptor antagonist)
- Infliximab (monoclonal antibody)