

# Multisystem Inflammatory Syndrome in Children (Mis-C)

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**Abstract:** *In children, COVID-19 is usually mild. However, in rare cases, children can be severely affected, and clinical manifestations may differ from adults. In April of 2020, reports from the United Kingdom documented a presentation in children similar to incomplete Kawasaki disease (KD) or toxic shock syndrome. The condition has been termed multisystem inflammatory syndrome in children (MIS-C). Symptoms of MIS-C typically develop two or more weeks following infection with COVID-19 and involves inflammation of different parts of the body, such as the heart, lungs, kidneys, brain, skin, eyes, or gastrointestinal system. MIS-C can be serious, even deadly, but most children who were diagnosed with this condition have gotten better with medical care. So, adequate information regarding this condition is need of the hour.*

**Keywords:** multisystem inflammatory syndrome in children, Post-SARS-CoV-2 infection

## 1. Introduction

In children, COVID-19 is usually mild. However, in rare cases, children can be severely affected, and clinical manifestations may differ from adults. In April of 2020, reports from the United Kingdom documented a presentation in children similar to incomplete Kawasaki disease (KD) or toxic shock syndrome. Since then, there have been reports of similarly affected children in other parts of the world. The condition has been termed multisystem inflammatory syndrome in children (MIS-C); also referred to as pediatric multisystem inflammatory syndrome [PMIS], pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 [PIMS-TS], pediatric hyper inflammatory syndrome, or pediatric hyper inflammatory shock).<sup>1</sup> MIS-C can be serious, even deadly, but most children who were diagnosed with this condition have gotten better with medical care.<sup>3</sup>

## 2. Background

On April 26, 2020, clinicians in the United Kingdom (UK) recognized increased reports of previously healthy children presenting with a severe inflammatory syndrome with Kawasaki disease-like features. The cases occurred in children testing positive for current or recent infection by SARS-CoV-2, the novel corona virus that causes COVID-19, based on reverse-transcriptase polymerase chain reaction (RT-PCR) or serologic assay, or who had an epidemiologic link to a COVID-19 case. Patients presented with a persistent fever and a constellation of symptoms including hypotension, multiorgan (e.g., cardiac, gastrointestinal, renal, hematologic, dermatologic and neurologic) involvement, and elevated inflammatory markers. Respiratory symptoms were not present in all cases.

Additional reports of children presenting with severe inflammatory syndrome with a laboratory-confirmed case of COVID-19 or an epidemiological link to a COVID-19 case have been reported by authorities in other countries. Lately it

is named as Multisystem inflammatory syndrome in children (MIS-C)<sup>2</sup>

### Definition

Multisystem inflammatory syndrome in children (MIS-C) is a condition where different body parts can become inflamed, including the heart, lungs, kidneys, brain, skin, eyes, or gastrointestinal organs.<sup>3</sup>

### Etiology

- The exact cause of MIS-C is not known
- excessive immune response related to COVID-19
- current infection with the COVID-19 virus
- genetic factors<sup>4,5</sup>

### Risk Factors:

- Black and Latino children have been diagnosed with MIS-C compared with children of other races (studies needed for identifying the reason)
- Child between the ages of 3 and 12 years old<sup>4</sup>

### Pathophysiology:

The pathophysiology of MIS-C is not well understood.

**Immune dysregulation** – It has been suggested that the syndrome results from an abnormal immune response to the virus, with some clinical similarities to Kawasaki disease (KD), macrophage activation syndrome (MAS), and cytokine release syndrome, but MIS-C appears to have an immunophenotype that is distinct from KD and MAS. Preliminary studies suggest that patients with severe MIS-C have persistent immunoglobulin G (IgG) antibodies with enhanced ability to activate monocytes, persistent cytopenias (particularly T cell lymphopenia), and greater activation of CD8+ T cells that differ from findings in acute COVID-19 infection. The certainty of these findings is limited due to the small number of patients in these studies.

Understanding the mechanisms of the exaggerated immune response in MIS-C is an area of active investigation.<sup>1</sup>

### Clinical Features:

Ongoing fever lasts 24 hours or longer

Skin/mucous membrane signs and symptoms: Rash, bloodshot eyes, swollen or red hands and feet, inflamed mucous membranes in the mouth, cracked lips, and a swollen tongue that looks like a strawberry, Enlarged lymph nodes

Symptoms and signs of shock or heart problems, such as cold, clammy skin, very low blood pressure, difficulty breathing, severe shortness of breath with exertion, dizziness or light headedness, and a very high heart rate or irregular heartbeat, Feeling unusually tired

Gastrointestinal symptoms: diarrhea, vomiting, or abdominal pain.

Respiratory symptoms such as cough and shortness of breath.

Neurologic symptoms, such as headache, neck pain, confusion, numbness/tingling in the hands and feet, or seizures.

Not all children will have all the same symptoms.<sup>4,5</sup>

### Emergency warning signs of MIS-C

- Severe stomach pain
- Difficulty breathing
- Pale, gray or blue-colored skin, lips or nail beds — depending on skin tone
- New confusion
- Inability to wake up or stay awake
- Persistent pain or pressure in the chest<sup>4,5</sup>

### Diagnostic Methods

- Blood tests: blood clotting, liver function
- Chest x-ray
- Abdominal ultrasound
- Urine tests
- Electrocardiogram, which measures electrical activity in the heart, and echocardiogram (heart ultrasound)

### Case Definition for Multisystem Inflammatory Syndrome in Children (MIS-C)

- An individual aged <21 years presenting with fever<sup>i</sup>, laboratory evidence of inflammation, and evidence of clinically severe illness requiring hospitalization, with multisystem ( $\geq 2$ ) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurologic); **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

<sup>i</sup>Fever  $\geq 38.0^{\circ}\text{C}$  for  $\geq 24$  hours, or report of subjective fever lasting  $\geq 24$  hours

<sup>ii</sup>Including, but not limited to, one or more of the following: an elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), fibrinogen, procalcitonin, d-dimer, ferritin, lactic acid dehydrogenase (LDH), or interleukin 6 (IL-6), elevated neutrophils, reduced lymphocytes and low albumin.

### Additional comments

- Some individuals may fulfill full or partial criteria for Kawasaki disease but should be reported if they meet the case definition for MIS-C
- Consider MIS-C in any pediatric death with evidence of SARS-CoV-2 infection<sup>2</sup>

### Management:

Children diagnosed with MIS-C need close observation. All need to be admitted to the hospital, and some may need intensive care. Pediatric specialists in rheumatology, critical care, and cardiology can anticipate and address different aspects of the illness.

- IV immunoglobulin
- Anti-inflammatory drugs (corticosteroids, and drugs blocking IL-1 or IL-6).
- Low-dose aspirin to decrease the risk of blood clots.
- Fluids for dehydration
- Oxygen to improve breathing
- Antibiotics to protect against infection

Other treatments may be used depending on the results of laboratory tests. Children need to be followed after discharge with repeat echocardiograms to monitor their heart and coronary arteries. Children who are fully recovered at six months no longer need close follow-up.<sup>5,6</sup>

### 3. Prevention

The best way to prevent MIS-C is for all eligible children ages 5 years and up to get the COVID-19 vaccine. Keep taking steps to help avoid exposure to COVID-19.

- **Keep hands clean.** Wash hands often with soap and water for at least 20 seconds. If soap and water aren't available, use a hand sanitizer that contains at least 60% alcohol.
- **Avoid people who are sick.** In particular, avoid people who are coughing, sneezing or showing other signs that indicate they might be sick and contagious.

- **Practice social distancing.** This means that you and your child should stay at least 6 feet (2 meters) from other people when outside of your home.
- **Wear cloth face masks in public settings.** When in indoor public places or outdoors where there is a high risk of COVID-19 transmission, such as at a crowded event or large gathering, both you and your child — if he or she is at least 2 years old — should wear face masks that cover the nose and mouth. Further mask guidance differs depending on whether you are fully vaccinated or unvaccinated.
- **Avoid touching your nose, eyes and mouth.** Encourage your child to follow your lead and avoid touching his or her face.
- **Cover your mouth with a tissue or your elbow when you sneeze or cough.** You and your child should practice covering your mouths when you sneeze or cough to avoid spreading germs.
- **Clean and disinfect high-touch surfaces every day.** This includes areas of your home such as doorknobs, light switches, remotes, handles, countertops, tables, chairs, desks, keyboards, faucets, sinks and toilets.
- **Wash clothing and other items as needed.** Follow manufacturers' instructions, using the warmest appropriate water setting on your washing machine. Remember to include washable plush toys.<sup>4</sup>

#### 4. Complications

In rare cases, MIS-C could result in permanent damage or even death.<sup>4</sup>

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