

# Multisystem Inflammatory Syndrome in Children (MIS-C) and Covid -19

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## ABSTRACT

Multisystem inflammatory syndrome in children (MIS-C) may be a serious condition that appears to be linked to corona virus disease 2019 (COVID-19). MIS-C is taken into account a syndrome — a gaggle of signs and symptoms, not a disease — because much is unknown about it, including its cause and risk factors. Most of the young children who become infected with the COVID-19 virus have only a light illness. The matter with MIS-C caused by Covid-19 is that it develops into severe inflammation during a few hours requiring admission of the patient into a medical care unit. The signs and symptoms depend upon which areas of the body are affected. The precise explanation for MIS-C isn't known yet. Many specialists consider MIS-C to be a complication of COVID-19. Without early diagnosis and appropriate management and treatment, MIS-C can cause severe problems with vital organs, like the heart, lungs or kidneys. In rare cases, MIS-C could end in permanent damage or may be death.

**KEYWORDS:** *Multisystem inflammatory syndrome, COVID-19, Vital organs, inflammation*

## INTRODUCTION

Multisystem Inflammatory Syndrome was noticed first among children and younger people. The disease was so named MIS-C (multisystem inflammatory syndrome -- in children) where patients are below 21 years of age.<sup>1</sup> Later studies found the same syndrome among adults and it was accordingly named MIS-A (multisystem inflammatory syndrome -- in adults). Since a large number of children and young adults are said to be reporting no respiratory symptoms identified with Covid-19, MIS-C went unnoticed for months.<sup>2</sup> Now, researchers in America have studied the spectrum of symptoms related to Covid-19 and include fever, rashes on the body, abdominal pain, diarrhea, nausea and vomiting among the early signs of MIS-C caused by corona virus infection.<sup>3</sup>

The problem with MIS-C caused by Covid-19 is that it develops into severe inflammation in a few hours requiring admission of the patient into an intensive care unit. A few researches made public by the US Centers for Disease Control and Prevention (CDC) revealed that a majority of young people -- below 21 years of age -- died due to MIS-C.<sup>4</sup>

Multisystem inflammatory syndrome in children (MIS-C) may be a serious condition that appears to be linked to corona virus disease 2019 (COVID-19). Most children who become infected with the COVID-19 virus have only a light illness. But in children who continue to develop MIS-C, some organs and tissues — like the heart, lungs, blood

vessels, kidneys, gastrointestinal system, brain, skin or eyes — become severely inflamed. Signs and symptoms depend on which areas of the body are affected.<sup>3</sup> MIS-C is taken into account a syndrome — a gaggle of signs and symptoms, not a disease — because much is unknown about it, including its cause and risk factors. Identifying and studying more children who have MIS-C may help to eventually find a cause<sup>5</sup>

## INCIDENCE

The association between COVID-19 and Kawasaki-like multisystem inflammatory syndrome in children (MIS-C) isn't well understood.<sup>6</sup>

The incidence of post-COVID inflammatory syndrome is 1 of 1000 children affected by COVID-19.<sup>7</sup>

## CAUSES

The exact cause of MIS-C is not known yet, but it appears to be an excessive immune response related to COVID-19. Many children with MIS-C have a positive antibody test result. This means they've had a recent infection with the COVID-19 virus. Some may have a current infection with the virus.<sup>2</sup>

## RISK FACTORS

### Age

Most children with MIS-C are between the ages of 3 and 12 years old, with an average age of 8 years old. Some cases have also occurred in older children and in babies

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### Race

In the U.S., more Black and Latino children have been diagnosed with MIS-C compared with children of other races and ethnic groups

### Health information

The differences in access to health information and services as well as the possibility of risks related to genetics need to be studied

### PATHOPHYSIOLOGY

The pathophysiology of MIS-C is not well understood. It is thought to result from an abnormal immune response to the virus, with some clinical similarities to KD, macrophage activation syndrome (MAS), and cytokine release syndrome. However, MIS-C appears to have an immunophenotype that is distinct from KD and MAS. Most affected children have positive serology for SARS-CoV-2 with negative polymerase chain reaction (PCR), a finding that further supports the hypothesis that MIS-C is related to immune dysregulation occurring after acute infection has passed. However, some children do have positive PCR testing<sup>3</sup>

### CLINICAL FEATURES

Signs and symptoms of multisystem inflammatory syndrome in children (MIS-C) include those below, though not all children have the same symptoms.<sup>2</sup>

- Fever that lasts 24 hours or longer
- Vomiting
- Diarrhea
- Pain in the stomach
- Skin rash
- Feeling unusually tired
- Fast heartbeat
- Rapid breathing
- Red eyes
- Redness or swelling of the lips and tongue
- Redness or swelling of the hands or feet
- Headache, dizziness or lightheadedness
- Enlarged lymph nodes

### Emergency warning signs of MIS-C

- Severe stomach pain
- Difficulty breathing
- Bluish lips or face
- New confusion
- Inability to wake up or stay awake

### DIAGNOSIS

WHO has developed a preliminary case definition and case report form for **multisystem inflammatory disorder in children and adolescents**. The preliminary case definition reflects the clinical and laboratory features observed in children reported to date, and serves to identify suspected or confirmed cases both for the purpose of providing treatment and for provisional reporting and surveillance. The case definition will be revised as more data become available.<sup>1</sup>

### Preliminary case definition[a]

Children and adolescents 0–19 years of age with fever  $\geq 3$  days

**AND** two of the following:

1. Rash or bilateral non-purulent conjunctivitis or mucocutaneous inflammation signs (oral, hands or feet).

2. Hypotension or shock.
3. Features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated Troponin/NT-proBNP),
4. Evidence of coagulopathy (by PT, PTT, elevated d-Dimers).
5. Acute gastrointestinal problems (diarrhoea, vomiting, or abdominal pain).

### AND

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

### AND

No other obvious microbial cause of inflammation, including bacterial sepsis, staphylococcal or streptococcal shock syndromes.

### AND

Evidence of COVID-19 (RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19.

### Differentiating MIS-C and Kawasaki disease

There is considerable phenotypic overlap with MIS-C and KD. Key distinctions between MIS-C and KD include:

- MIS-C commonly affects older children and adolescents, whereas classic KD typically affects infants and young children
- In MIS-C, black and Hispanic children appear to be disproportionately affected and Asian children account for only a small number of cases. By contrast, classic KD has a higher incidence in East Asia and in children of Asian descent
- Gastrointestinal symptoms (particularly abdominal pain) are very common in MIS-C, whereas these symptoms are less prominent in classic KD.
- Myocardial dysfunction and shock occur more commonly in MIS-C compared with classic KD
- Inflammatory markers (especially CRP, ferritin, and D-dimer) tend to be more elevated in MIS-C compared with classic KD<sup>3</sup>

### DIFFERENTIAL DIAGNOSIS

- Bacterial sepsis
- Kawasaki disease
- Toxic shock syndrome
- Appendicitis
- Other viral infections
- Hemophagocytic lymphohistiocytosis (HLH)/macrophage activation syndrome (MAS)
- Systemic lupus erythematosus (SLE)
- Vasculitis<sup>3</sup>

### COMPLICATIONS

Many specialists consider MIS-C to be a complication of COVID-19. Without early diagnosis and appropriate management and treatment, MIS-C can lead to severe problems with vital organs, such as the heart, lungs or kidneys. In rare cases, MIS-C could result in permanent damage or even death<sup>3</sup>.

### MANAGEMENT

- Most children who have been treated as for kawasaki disease have recovered

- Supportive care is a mainstay of therapy for mild or moderate disease
- Major complications may respond well to more aggressive supportive care
- Cardiac and respiratory support may benefit children who present predominantly with shock
- Administration of anti-inflammatory medications
- Treatment of shock
- Prevention of thrombosis
- Immunomodulatory treatment
- IV immunoglobulins
- Cytokine blockers
- Inotropic or vasoactive agents are often used for children with cardiac dysfunction and hypotension
- Anticoagulants have been used.
- Aspirin low-dose has been used
- Treatment strategies are being considered to prevent serious long-term complications such as coronary artery aneurysms (the main complication of Kawasaki disease).
- Close outpatient follow-up by a paediatric cardiology team has been recommended<sup>7</sup>.

### PREVENTION

The best way to help prevent your child from getting MIS-C is to take action to avoid exposure to the COVID-19 virus and teach your child how to do the same. Follow the guidelines of the U.S. Centers for Disease Control and Prevention:

- **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 it's difficult to practice social distancing, 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.
- **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.

### CONCLUSION

The best way to prevent MIS-C is to control the interaction of children with infected or suspected COVID-19 patients. And

should follow all the precautionary measures such as repeatedly washing hands for at least 20 seconds, avoid people who are sick, 6 ft distance between the child and other individuals outside, wear a mask, regularly clean, and disinfect the high touch surfaces on daily basis<sup>8</sup>

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