

## Multisystem Inflammatory Syndrome in Children (MIS-C): A Case Report

**Dr. Pranita Tambe<sup>1</sup>, Dr. Ganesh Misal<sup>2</sup>, Dr. Suresh Waydande<sup>3</sup>, Prof. Dr. Sunil Natha Mhaske<sup>4</sup>**

<sup>1</sup>Junior Resident, <sup>2</sup>Senior Resident, <sup>3</sup>Professor & Head of department Paediatrics, DVVPF's Medical College & Hospital, Ahmednagar-414111, Maharashtra, India.

<sup>4</sup>Professor Paediatrics & Dean, DVVPF's Medical College & Hospital, Ahmednagar-414111, Maharashtra, India.

### Abstract:

We are in the midst of an unprecedented global pandemic of coronavirus disease (COVID-19), caused by the novel coronavirus SARS-CoV-2. Although, initially thought to affect children less severely, SARS-CoV-2 infection has recently been associated with a novel set of clinical manifestations presently called multisystem inflammatory syndrome in children (MIS-C), which shown a rapid increment in cases across the world among the pediatric population. Here, we bring a case report, followed up in the rural tertiary care hospital.

**Keywords:** MIS-C, SARS-CoV-2, Kawasaki disease

### Introduction:

Beginning in China on December 19th, the coronavirus 2 (SARS-CoV-2)[1], which, at that time, had not yet been identified in human beings, spread quickly across the world. Although the infection (COVID-19) manifests in adult populations with severe acute interstitial pneumonia, according to a study conducted on children under 18 years old, in 29% of the symptomatic cases, this evolution occurred in only 1.7% of cases. This, in addition to the involvement of the respiratory system showing a more benign evolution. However, there are reports of frequent gastrointestinal involvement[2] and, among other symptoms, an incidence increases of Kawasaki or Kawasaki-like syndrome, when associated with SARS-CoV-2[3,4], however, the acceptance of this terminology is not unanimous.

The first case report of a six-month-old child with Kawasaki disease (KD) and COVID-19 was published in the US on April 7, 2020. At the end of that month, the UK's National Health Service (NHS) published a warning about children manifesting Kawasaki syndrome and toxic shock syndrome in association with COVID. Meanwhile, studies and

case reports began to emerge around the world, corroborating the alert.[5] By the end of June 2020, approximately 1000 MIS-C cases had been documented globally.[6]

Classic Kawasaki disease is defined as an acute and self-limited vasculitis which affects medium-sized vessels, occurring almost exclusively in children under five years old, with a peak from nine to 11 months. Unlike this classic age group, MIS-C temporarily associated with SARS-CoV-2 affected children of an older age group, both of which are indicative in smaller sample studies, as in the UK study with 58 children who developed MIS-C associated with SARS-CoV-2, with an average age of nine years; in an Italian study, it was 7.5 years.[7]

Laboratory tests showed neutropenia, lymphopenia, thrombocytopenia and elevated inflammatory markers, both in the group studied in the UK and Italy, with elevated ferritin, hypertriglyceridemia and increased D-dimer, making it more suggestive of MIS-C. The RT-PCR, serology or antigen detection was performed for SARS-CoV-2 detection; however, these tests were negative in some patients.[8]

**Corresponding Author:** Dr. Pranita Tambe

**Email ID:** pranitatambe863@gmail.com

**Address:** Department of Paediatrics, DVVPF's Medical College & Hospital, Ahmednagar-414111, Maharashtra, India

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The treatment of mild cases of MIS-C follows the same course of the classic Kawasaki, with immunoglobulin infusion (IVIG) 2 g/kg; while in some cases, a repeat dose is administered in resistant cases, or even an adjuvant to corticosteroids, cyclosporine and biological agents, such as anti-interleukin 1, are employed to reduce the development of coronary dilation and other cardiovascular changes.

In moderate to severe cases of MIS-C, in addition to IVIG and aspirin, the use of methylprednisolone in the form of pulse therapy is recommended—at a dose of 30 mg/kg/day, for three days, for severe cases, and in moderate cases, 10–20 mg/kg/day for one to three days, followed by a maintenance dose. For refractory cases, following two doses of IVIG and corticosteroids may require biological agents (anti IL-1, anti IL-6 or anti-TNF). The use of anticoagulation is not well established. Mild-to-moderate cases of MIS-C can be managed with a prophylactic dose of enoxaparin and severe cases with a therapeutic dose.[8]

### Case Report:

Patient, female, three months old, with no significant past medical history, admitted to the Children's Emergency Room at Dr. Vithalrao Vikhe Patil Memorial Hospital, with a history of high-grade fever for 3 days, with cold and cough evolving a day after the onset of the fever. Concomitantly, she presented important conjunctival hyperemia with no secretion and also oral mucosa fissures. The child's mother also complained of gastrointestinal symptoms such as vomiting and not accepting feeds.

On admission, patient presented with low-grade fever (38.2°C), lethargic and was hemodynamically unstable, oxygen saturation was 82% SpO<sub>2</sub>, heart rate (HR) was 121 bpm, respiratory rate was 46 breaths per minute with subcostal retractions, peripheries were cold, pulses were weak, GCS was 8/15, B/L coarse crepitation on respiratory auscultation with normal cardiac examination (Pic-1)

### Investigations:

Initially, Hb 9.1 gm/dL, Ht 28.6%, leukocytes 9400/microL (neutrophils 39%/ lymphocytes 49%), Absolute Neutrophil Count 3700 per microL, platelets 3,49,000, S. Sodium 135, S.K 5.4, Ca 9.2, P

3.56, urea 28, creatinine 0.7, ESR 37, AST 31, ALT 75, S. LDH 986.75 IU/L, D-Dimer 1.08 microgm/ml, S. SARS COV-2 Antibody Index >10. Furthermore, the chest radiography was suggestive of lobar pneumonia and blood and urine cultures were negative.

### Treatment:

As child was gasping and general condition of child was poor at presentation, child was intubated there itself and was shifted on AMBU to Paediatric Critical Care Unit for further management. On Day one, after initial stabilization of child, all blood investigations were sent along with inflammatory markers and SARS-COVID 19 antibodies. (Due to acute deterioration of patient and prior epidemic, MIS-C was suspected). Empirical antibiotics, ceftriaxone and amikacin were started. On Day three, child was weaned off on CPAP.

All inflammatory markers were raised along with positive index of SARS COVID 19 antibodies and hence IV Methylprednisolone in dose of 10 mg/kg/day for 5 days and IVIG in dose of 1gm/kg were added. Nebulization with budesonide was added. Chest physiotherapy was added. On day four, Enoxaparin was added due to raised D-Dimer levels in dose of 1 mg/kg subcutaneously. Feeds were started with oro-gastric tube. On day 5, child was taken on O<sub>2</sub> by nasal prongs. OGT feeds were increased gradually as per tolerance of child. On day 8, child was weaned off of oxygen and oral feeds were started which the child tolerated very well.(Pic - 2)



**Pic- 1 At the time of admission**



**Pic-2 At the time of discharge**

### **Discussion:**

In view of the current scenario, with new data on the behavior of SARS-CoV-2, the pediatric population has gained prominence for non-respiratory manifestations, despite the lower number of cases in relation to the adult population, and even presenting with fatal outcomes. Most cases of pediatric (MIS-C) temporarily associated with SARS-CoV-2 have so far seen non-fatal outcomes; however, with a greater number of cardiac involvement than classical Kawasaki disease, there is a greater need for care in the Intensive Care Unit (ICU).

In addition to more frequent gastrointestinal symptoms, it presents with laboratory changes that are mainly of inflammatory markers and higher D-dimer than Kawasaki disease. Clinical suspicion can be difficult due to the various spectra of the disease, and laboratory tests are not always positive. Evidently, even at a later time, they can remain negative. Early treatment, given the greater cardiac involvement in MIS-C has become the main pillar in an attempt not to increase the number of acquired heart diseases. Despite the greater number of resistant cases, the majority of MIS-C cases responded well to classic IVIG and aspirin therapy.

The emergence of MIS-C serves as a reminder that children, though largely spared from the most severe outcomes associated with COVID-19, may still experience serious medical consequences related to SARS-CoV-2 infection. Although, current evidence suggests MIS-C is rare among children and adolescents, comprehensive surveillance data are

limited, and a few reports have suggested the low incidence observed thus far may, in part, be influenced by reduced exposure to SARS-CoV-2 due to schools not being in session or fully open for in-person instruction.[9] Because recent re-initiations of in-person education may increase extra-household contact frequency and duration for many children, additional strict vigilance is warranted to assess potential impact on pediatric incidence rates of both COVID-19 and MIS-C.

While causality (and the complete causal mechanism) is yet far from established, current findings are in favor of temporal association between SARS-CoV-2 infection and MIS-C, with MIS-C typically occurring within two to four weeks after infection. Noting this lag in time, and that MIS-C patients more often test positive for SARS-CoV-2 antibodies than the virus, some have proposed that MIS-C may be a post-infectious phenomenon related to antibody-mediated enhancement of disease rather than the result of acute viral infection.[10] Though several hypotheses are being explored, research studies are urgently needed to understand the underlying mechanisms of MIS-C.[10]

While more research is needed to establish risk and prognostic factors for MIS-C, some trends appear to be relatively consistent in the published literature thus far. MIS-C can develop in previously healthy children with no known comorbidities and usually presents within four weeks following SARS-CoV-2 infection, though symptoms consistent with MIS-C may appear before the resolution of COVID-19 symptoms in some cases. Moreover, given that a large subset of SARS-CoV-2-infected children display mild to no symptoms, some children may develop MIS-C with little to no forewarning, and in some cases, caregivers may not even be aware that the child was previously infected with SARS-CoV-2. Therefore, it is important that caregivers are alerted to remain attentive to possible symptoms for several weeks following potential exposure to the virus or a positive SARS-CoV-2 molecular or antigen test. Early visible symptoms include prolonged fever, abominable pain, rash, and red eyes. As GI symptoms often precede other common symptoms of MIS-C, it is important to inform caregivers to watch for symptoms resembling those of common gastrointestinal infections.

**Conclusion:**

Further evidence of the increase in the incidence of pediatric MIS-C, temporarily associated with SARS-CoV-2, appears daily, calling pediatricians' attentions to this new diagnosis with often more fatal outcomes than Kawasaki cases (to date). The diagnosis is very challenging due to the variety of clinical and laboratory presentations, with both positive and negative COVID-19 test results, but one should not delay therapy as soon as the diagnostic suspicion is generated. Follow-up is the most important, as these complications often appear later. We await further studies, given the novelty of the disease to improve the diagnosis and care of the pediatric population.

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