# Cardiac Affection in Multisystem Inflammatory Syndrome in Children: The Egyptian Experience

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#### ABSTRACT

**Background:** Multisystem inflammatory syndrome in children (MIS-C) is an uncommon condition linked to SARS-CoV-2, the virus responsible for COVID-19. Typically emerging 2-6 weeks after a child contracts the virus, MIS-C leads to inflammation in various organs, including the heart, kidneys, lungs, brain, skin, and gastrointestinal tract.

**Objective:** To assess the cardiac affection, management and outcome in MIS-C patients.

**Patients and methods:** This analytical cross-sectional study was carried out in Cairo University Children Hospital and included 28 patients, diagnosed with MIS-C post COVID. All patients were subjected to complete history taking, through general, cardiac examination and echocardiographic assessment.

**Results:** Males were the most commonly presented gender accounting for 71.4%, while females were 28.6%. Fever was the most commonly presented symptom (96.4%). Cardiac affection was found in 22 (78.6%) patients by cardiac echocardiography and coronary dilatation was the most common finding by echocardiography in 18 (64.3%) patients. The most common was left coronary artery dilatation in 16 (57.1%) patients, followed by right coronary artery in 8 (28.6%) patients while only 2 (7.1%) had coronary artery aneurysm. All patients in the current study received intravenous immunoglobulin G (IVIG) for 2 days while 14 (50%) patients received pulse steroids followed by oral steroids after IVIG course.

**Conclusion:** Cardiac affection is common in MIS-C patients and must be looked for. The most common presentation is coronary artery dilatation; mostly left coronary artery so early and appropriate intervention is essential to avoid complications.

Keywords: Multisystem inflammatory syndrome in children; COVID-19; Cardiac Affection.

#### BACKGROUND

Coronavirus disease 2019 (COVID-19), a highly contagious viral illness caused by SARS-CoV-2, has profoundly impacted global populations <sup>[1]</sup>. The true incidence of the disease in children is unclear due to a lack of community-based studies. However, it has been observed that over 90% of infants with COVID-19 experience mild, moderate, or no symptoms, although reports of hyperinflammatory states have emerged <sup>[2]</sup>.

Children presenting with multiorgan involvement and hyperinflammatory conditions have been diagnosed with multisystem inflammatory syndrome in children (MIS-C) or pediatric inflammatory multisystem syndrome (PIMS)<sup>[3]</sup>.

Early reports of MIS-C described a wide range of clinical symptoms at initial presentation, often including shock, cardiac dysfunction, gastrointestinal issues, significantly elevated inflammatory markers, cardiac damage, and positive serology for SARS-CoV-2<sup>[4]</sup>. The nonspecific nature of the case definition and the absence of confirmatory laboratory tests make it challenging to distinguish MIS-C from other conditions with similar clinical features, such as severe acute COVID-19<sup>[5]</sup>.

Cardiac involvement is more frequent in MIS-C than in Kawasaki disease (KD), affecting 67–80% of patients. Cardiac manifestations in MIS-C include

coronary artery aneurysms, ventricular dysfunction, abnormal conduction, and arrhythmias. The severity of cardiac symptoms varies, with many patients presenting with cardiovascular impairment and, in some cases, rapid and severe shock <sup>[6]</sup>.

Therefore, this study aimed to assess the cardiac affection, management and outcome in MIS-C patients.

#### PATIENTS AND METHODS

This cross-sectional study was conducted at Cairo University Children's Hospital and included 28 pediatric patients diagnosed with multisystem inflammatory syndrome in children (MIS-C) between October 2021 and March 2022.

# The diagnosis was made according to the World Health Organization (WHO) criteria for MIS-C<sup>[7]</sup>, which include the following:

Patients aged 0 to 19 years with a fever lasting three days or more were included. Clinical signs of multisystem involvement were required, with at least two following: the rash, bilateral nonpurulent of conjunctivitis. or mucocutaneous inflammation (involving the oral cavity, hands, or feet); hypotension or shock; cardiac dysfunction, pericarditis, vasculitis, or coronary abnormalities (as detected by echocardiography or elevated troponin/ Brain natriuretic peptide levels);

evidence of coagulopathy (such as prolonged PT or PTT and elevated D-dimer); and acute gastrointestinal symptoms like diarrhea, vomiting, or abdominal pain.

Additionally, the patients had elevated markers of inflammation, including ESR, CRP, or procalcitonin, with no other clear microbial cause for inflammation, such as bacterial sepsis or staphylococcal/streptococcal toxic shock syndromes. Evidence of SARS-CoV-2 infection was confirmed by positive SARS-CoV-2 RT-PCR, serology, antigen test, or known contact with an individual diagnosed with COVID-19.

MIS- $\overline{C}$  patients of both sexes with age ranged from 2 to 14 years old were included in the study. Patients whose diagnosis of MIS-C was not confirmed were excluded from the study.

Data were obtained through direct interviews with all patients and their legal guardians, as well as a study of medical records from Cairo University Children Hospital's pediatric intensive care unit and general departments. Data from labs and clinical settings were documented during the initial presentation. Clinical data that were gathered included medication therapy, symptoms, preceding illnesses, and demographics. All patients were subjected to through general and cardiac examination including heart sounds either normal, accentuated or muffled, tachycardia, murmur, congestive heart failure, hypotension and shock, The collected laboratory studies were extracted data from patient's files and included complete blood count, serum electrolytes, liver, kidney function tests, CRP, ESR, D-dimer, ferritin and fibrinogen, coagulation profile, COVID PCR or serology (IgG and IgM). Echocardiographic assessment of cardiac function, state of coronaries (coronary artery dilatation) and other findings (e.g., aneurysm, pericardial effusion) were recorded.

Management data included admission either in general department or intensive care unit (ICU), duration of ICU, hemodynamic stability and need of inotropes, need of respiratory support or mechanical ventilation, need for plasmapheresis or dialysis and the received treatment (e.g., IV immunoglobulins (IVIG), steroids, aspirin or any other treatment as anticonvulsants, anticoagulant, biological treatment as tocilizumab (anti IL-6) or anakinra (anti IL-1). Outcome of patient was also recorded.

## Treatment data:

All patients received 1 g/kg/day intravenous immunoglobulin (IVIG) for 2 days. In cases of persistent elevation of inflammatory markers, pulse steroids

(methylprednisolone 10-30 mg/kg/day) were given followed by oral steroids (1-2 mg/kg/day) after IVIG course. In case of coronary dilatation, aspirin was given at 30 mg/kg/day for 1 week followed by 5 mg/kg/day maintenance dose.

#### **Ethical considerations:**

Before being enrolled in the study, the patients or their legal guardians provided their informed consent. Throughout the study, the investigators were the only ones with access to coded data and the identity of the informants. The Cairo University Ethical Committee accepted the study protocol with permission number MS-100-2022., according to the Institutional Committee for the Protection of Human Subjects and following the 18<sup>th</sup> World Medical Assembly, Helsinki, Finland.

#### Statistical methods

Data were collected, reviewed, coded, and entered into the Statistical Package for the Social Sciences (SPSS) version 26 (IBM, Armonk, New York, United States). Qualitative data were expressed as numbers and percentages, while quantitative data were presented as mean, standard deviations, and ranges for parametric data, and as median with interquartile range (IQR) for nonparametric data.

## RESULTS

Our study included 28 MIS-C patients with median age 4.25 (0.25-13) years. Males were the most commonly presented gender accounting for 71.4%, while females were 28.6%.

Among the 28 MIS-C patients (78.6%) had history of household contacts with symptoms suspecting COVID or tested positive for COVID, while (96.4%) of patients had history of COVID infection. COVID-19 PCR was positive in 10.70%, while IgM COVID-19 antibody was positive in 14.30%, and 100% of the included patients were positive for COVID-19 IgG antibodies.

Fever was the most common presenting symptom (96.40%) with mean degree 38.96 degrees and mean duration of 10 days followed by palpitation (85.7%), sore throat (53.6%) and abdominal pain (53.6%), while skin rash presented in 42.9% of patients.

Regarding the clinical examination of different systems, we found that (92.9%) of patients had 2-3 organs involved and tachycardia was the most common presenting sign in 21 (75%) of patients followed by other less frequent signs as demonstrated in table 1.

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Clinical Examination	No. = 28	%
General Examination		70
Conjunctivitis	10	35.7%
Skin peeling	7	25.0%
Erythema of lips	6	21.4%
Cracking of lips	4	14.3%
Strawberry tongue	5	17.9%
Oral ulcers	8	28.6%
Erythema of oral mucosa	5	17.9%
Erythema of palms and soles	5	17.9%
Hypotension	5	17.9%
Shock	4	14.3%
Skin Rash	10	35.7%
Petechial rash	4	14.3%
Ecchymosis	4	14.3%
Edema	13	46.4%
Lymph nodes enlargement	7	25.0%
Cervical lymph node enlargement > 1.5	4	14.3%
Chest Exam	ination	
Diminished sin entry		
Diminished air entry	9	32.1%
Additional sounds:		
Wheezes	4	14.3%
Crepitations	1	3.6%
Wheezes+Crepitations	3	10.7%
Tachypnea	9	32.1%
Respiratory distress	9	32.1%
Degree of respiratory distress		
Grade I	4	14.3%
Grade II	3	10.7%
Grade III	1	3.6%
Grade IV	1	3.6%
Cardiac Exam		T T
Muffled heart sounds	7	25.0%
Tachycardia	21	75.0%
Murmur	6	21.4%
Congestive heart failure	2	7.1%
Any Organo	vlenom	
Hepatomegaly Any Organo	6	21.4%
Splenomegaly	3	10.7%
opicitomegary	3	10.7%

Regarding the laboratory data, mean total leucocytic count (TLC) was 11,880/mm<sup>3</sup> with elevated lymphocytic count in 13 (46.4%) patients and elevated staff count in 4 (14.3%) patients. Thrombocytopenia was found in 6 (21.4%) patients while thrombocytosis in 12 patients (42.9%). The inflammatory markers such as CRP and ESR were elevated in our patients with a mean CRP of 62.15 mg/dL and mean ESR of 61 mm. Liver enzymes were elevated with high levels of ALT in 14 patients (50%) and high AST levels in 18 patients (64.3%). Renal functions were also elevated with high BUN levels in 8 patients (28.6%) and high creatinine levels in 6 patients (21.4%).

Urine analysis showed hematuria in 2 patients and proteinuria in 3 patients. D-Dimer level was elevated in 26 (92.9%) patients, ferritin was elevated in 14 (51.1%) patients, and fibrinogen was elevated in 11 (40.7%) patients while triglycerides were elevated in 5 (17.9%) patients.

Cardiac affection was found in 22 (78.6 %) patients by cardiac echocardiography. Coronary dilatation was the most common finding by echocardiography in 18 (64.3%) patients and coronary dilatation affected multiple branches in some patients. The most common coronary artery dilatation was left coronary artery (LCA) in 16 (57.1%) patients, followed by right coronary artery (RCA) in 8 (28.6%) patients while only 2 (7.1%) had coronary artery aneurysm as shown in table 2.

Table (1).	<b>Faberardia</b>	her finding	of studied succes
Table $(2)$ :	Echocardiograp	ony maings	of studied group.

Echocardiography finding	No. = 28, N (%)
Fractional shortening (FS) mean ± SD	$32.50 \pm 7.09$
FS (Affected)	8 (28.6%)
Cardiac affection:	22 (78.6%)
Coronary dilatation	18 (64.3%)
Coronary artery aneurysm	2 (7.1%)
Dilated LCA	16 (57.1%)
Dilated RCA	8 (28.6%)
Dilated LAD	3 (10.7%)
Dilated LCX	2 (7.1%)
Increased perivascular enhancement	6 (21.4%)
Pericardial effusion	2 (7.1%)
Valvular affection	6 (21.4%)
Myocarditis	1 (3.6%)
Pericarditis	1 (3.6%)
LV dysfunction	8 (28.6%)
Pulmonary hypertension	1 (3.6%)
Dilated cardiomyopathy	1 (3.6%)
Restrictive cardiomyopathy	1 (3.6%)

Left coronary artery (LCA); right coronary artery (RCA); left anterior descending (LAD); left circumflex artery (LCX).

Regarding management of the studied patients, the mean duration of admission was  $20.4\pm 12.2$  days, 15 patients (53.6%) were admitted into general pediatric departments, while 13 (46.4%) patients were indicated for ICU admission at certain point of admission as they were hemodynamically unstable. All patients received immunoglobulin, one dose was sufficient in 24 (85.7%) patients while 4 (14.3%) needed a second dose. Steroids was added to treatment of 26 patients due to persistent elevation of inflammatory markers, where 14 patients received pulse IV steroids at first then continued with oral steroid and 12 patients started with oral steroids. The rest of management plan is illustrated in table 3.

Management	<b>No. = 28</b> (No %)
Admission in general department	15 (53.6%)
Admission in ICU	13 (46.4%)
Hemodynamic instability	13 (46.4%)
Need of inotropes	5 (17.9%)
Need of respiratory support	7 (25.0%)
Need of mechanical ventilation	1 (3.6%)
IVIG	28 (100.0%)
Number of doses of IVIG: Once	24 (85.7%)
Twice	4 (14.3%)
Steroids Pulse steroids	14 (50.0%)
Oral steroids	26 (92.9%)
Aspirin	23 (82.1%)
Anticoagulant (low-molecular-weight heparin)	5 (17.9%)
Actemra	1 (3.6%)
Anakinra	0 (0.0%)
Need of plasmapheresis	1 (3.6%)
Need of dialysis	1 (3.6%)

IVIG: intravenous immunoglobulin.

Regarding clinical outcomes, all patients clinically improved while cardiac function improved in 6 out of 8 affected patients. Regarding dilatation of coronaries out of 18 patients, 17 patients improved and 1 patient showed progression of coronary dilatation. Complications developed in 4 patients in the form of pericardial effusion in one patient, LV dysfunction developed in 2 patients, dilated cardiomyopathy in one patient as shown in table 4.

Imj	provement	No.	%
Clinical improvement		28	100.0%
Cardiac function improvement		6	21.4%
Coronary dilatation	Improvement of dilatation	17	60.7%
	Progression of dilatation	1	3.6%
Development of complications	Complications:	4	14.3%
	Pericardial effusion	1	3.6%
	Valvular affection	0	0.0%
	LV dysfunction:	2	7.1%
	LV hypertrophy	0	0.0%
	Dilated cardiomyopathy	0	0.0%
	LV dysfunction + Dilated cardiomyopathy	1	3.6%
Outcome	Alive	28	100.0%
	Dead	0	0.0%

#### DISCUSSION

Cardiac affection was reported in 22 (78.6%) children in the current study based on Echo findings. In 2020, two studies indicated lower incidence of cardiac affection: **Verdoni** *et al.* <sup>[8]</sup> research, where 60% of patients had cardiac involvement in the form of abnormalities on Echo, and **Toubiana** *et al.* <sup>[3]</sup> study, where 70% of patients had myocarditis. Although **Ramcharan** *et al.* <sup>[9]</sup> study in 2020, reported higher incidence of cardiac affection because all of the patients showed signs of cardiac involvement in their biochemical, electrocardiogram, and Echo.

In our study, coronary dilatation was the most common echocardiographic finding, observed in 18 patients (64.3%). The left coronary artery (LCA) was the most frequently affected, with dilatation occurring in 16 patients (57.1%), followed by the right coronary artery (RCA) in 8 patients (28.6%). Only 2 patients (7.1%) had coronary artery aneurysms. These findings are consistent with other studies that have reported coronary artery abnormalities (CAAs) in 9–24% of patients with MIS-C [<sup>3, 10, 11]</sup>. CAAs typically present as dilatation or smallsized aneurysms in most cases. Furthermore, 15 patients (8%), according to **Feldstein** *et al.*'s <sup>[6]</sup> report, had coronary-artery aneurysms (z scores  $\geq$ 2.5) in either the right or left coronary artery. **Davies** *et al.* <sup>[12]</sup> also reported in 2020 that 28 patients (36%) had coronary artery anomalies (18 patients had aneurysms and 10 showed increased echogenicity).

According to the present study, valvular affection was reported in 6 (21.4%) children. In contrast to our results, the **Ramcharan** *et al.* <sup>[9]</sup> study from 2020 found that 13 patients (87%) had mitral and/or tricuspid valve regurgitation. The patients' significant improvement at the median of 1-2 days suggested that the condition was a temporary valvulitis.

Left ventricular (LV) dysfunction and decreased fractional shortening were found in 8 (28.6%) children in our study. This was comparable with **Sethy** *et al.* <sup>[13]</sup> study where myocardial dysfunction was found in 8 (38.1%). Higher incidences of LV dysfunction were reported by **Ramcharan** *et al.* <sup>[9]</sup>; **Chattopadhyay** *et al.* <sup>[14]</sup> they reported that about 80% had myocardial dysfunction and fractional shortening was reduced in 53.3% of patients. Moreover, **Verdoni** *et al.* <sup>[8]</sup> **and Toubiana** *et al.* <sup>[3]</sup> studies found that 50%, 71% of patients respectively had abnormal left ventricular ejection fraction (LVEF).

In our study only one patient had myocarditis by electrocardiogram (ECHO). However, higher incidence of myocarditis was reported in **Pal** *et al.*<sup>[15]</sup> study in 2022 in 41 patients (57.7%) in the form of disproportionate tachycardia, electrocardiogram changes and echocardiographic changes.

In our study, 4 children (14.3%) presented with shock, which is lower than the 48% reported by **Sethy** *et* 

*al.* <sup>[13]</sup>, where many children required inotropic support and volume resuscitation. Case reports from France <sup>[4]</sup> and UK <sup>[12]</sup> described even more acute presentations, with shock exhibiting features similar to streptococcal toxic shock syndrome. The difference can be attributed to that data from other studies were reported from intensive care unit admissions rather than the general pediatric population.

In our study, fever was the most common presenting symptom, occurring in 96.4% of patients, followed by palpitations (85.7%), sore throat (53.6%), and abdominal pain (53.6%). Skin rash was observed in 42.9% of patients. These findings are similar to those reported by **Mamishi** *et al.* <sup>[16]</sup> in a cohort of 45 children with MIS-C in Iran, where fever was the most prevalent symptom, and 51% of patients presented with rash, conjunctivitis, and abdominal discomfort. In a meta-analysis of 39 studies, **Ahmed** *et al.* <sup>[17]</sup> also identified fever (100%), abdominal pain/diarrhea (73.7%), and vomiting (68.3%) as the most common symptoms, with lower frequencies of conjunctivitis (51.8%) and rash (56.2%).

In our study, 9 patients (32.18%) experienced respiratory distress, with one (3.6%) suffering from grade IV respiratory distress. This is comparable to the findings of **Sethy** *et al.* <sup>[13]</sup>, who reported that 9 patients (42.8%) experienced respiratory distress during admission, with eight showing signs of pulmonary edema or shock, and one presenting with acute respiratory distress syndrome (ARDS). **Godfred-Cato** *et al.* <sup>[18]</sup> from the USA reported a higher incidence of significant respiratory involvement (63%) in MIS-C, which exceeds the findings of our study.

Mean TLC in the present study was 11,880/mm<sup>3</sup> with elevated lymphocytic count in 13 (46.4%) patients and elevated staff count in 4 (14.3%) patients, which is similar to the study by **Sethy** *et al.* <sup>[13]</sup> with a mean TLC of 13,800/mm<sup>3</sup> and mean neutrophil and lymphocyte counts of 72% and 22%, respectively. **Lagunas-Range** *et al.* <sup>[19]</sup> conducted a meta-analysis that identified a correlation between high white cell count, low lymphocyte count, low platelet count, elevated CRP levels, and increased disease severity.

Four (14.3%) patients in the present study had neutrophilia, while neutrophilia was seen 70.6% of **Chattopadhyay** *et al.* <sup>[14]</sup> cases. Thrombocytopenia was found in 6 (21.4%) patients in the present study. Similar to our finding, thrombocytopenia was found in 3 (14.2%) patients in **Sethy** *et al.* <sup>[13]</sup> study, however, none of them had extremely low platelet counts, which may help differentiate this illness from dengue or severe sepsis.

Our patients had increased levels of inflammatory markers, including CRP (62.15 mg/dL) and ESR (61 mm). Similarly, the **Sethy** *et al.* <sup>[13]</sup> study revealed a mean ESR of 76.4 mm and a mean CRP of 52.2 mg/dL. Furthermore, **Ramcharan** *et al.* <sup>[9]</sup> reported median CRP

levels (mg/L) of 154 mg/L while it was 210 mg/L in **Chattopadhyay** *et al.* <sup>[14]</sup> cases.

Ferritin in the current study was elevated in 14 (51.1%) patients. In line with our study, **Pouletty** *et al.* <sup>[10]</sup> study reported that ferritin was highly elevated (>500  $\mu$ g/L) in 50% of cases. Moreover, **Mamishi** *et al.* <sup>[16]</sup> reported highly elevated ferritin in 47% of cases.

We noticed that only 3 (10.7%) of our MIS-C patients were positive for COVID PCR while IgM COVID-19 antibody was positive in 14.30%, and 100% of the included patients were positive for COVID-19 IgG antibodies, which suggests an association with these patients' prior COVID illnesses. Similar to this, the majority of patients in the **Sethy** *et al.* <sup>[13]</sup> research from 2021 had positive IgG to SARS-CoV-2, and 4 (19.4%) of them had positive COVID PCR results. Nevertheless, it was impossible to overlook the epidemiological link with prior COVID-19 infection.

Data from Public Health England show that beginning around April 16, 2020-approximately four weeks after a significant increase in COVID-19 cases in the UK—there was a sharp rise in MIS-C cases <sup>[20]</sup>. Most MIS-C patients tested positive for antibodies, indicating a prior infection, while only about one-third tested positive for SARS-CoV-2 via PCR. The low PCR positivity rate, combined with the high antibody positivity and the delayed onset of the condition relative to the pandemic curve, suggests that MIS-C is likely driven by the development of acquired immune responses to SARS-CoV-2 rather than by direct viral invasion. Furthermore, comparable patterns were found in studies conducted in France by **Belot** et al. <sup>[21]</sup> and the USA by **Feldstein** et al. <sup>[6]</sup>. Children frequently exhibit past SARS-CoV-2 infection rather than present infection.

Among patients in the current study, 13 (46.4%) patients were indicated for ICU admission mainly for the need of respiratory support (25.0%). This need for intensive care was comparable to Verdoni et al. [8] study, as 50% of patients needed ICU admission. However, a different study found a greater frequency of ICU admission, with of the patients 8 needing respiratory support and 67% of patients requiring intensive care monitoring and therapy due to their cardiovascular instability. Furthermore, 70% of the patients in the Toubiana et al. [3] study needed intensive care admission. On the other hand, all Chattopadhvav et al. <sup>[14]</sup> patients required intensive care unit admissions, pointing to high severity of illness of their cohort, probably due to delayed presentation to health care facility in India.

The key to a successful outcome is early detection of shock, appropriate fluid resuscitation, immediate administration of inotropes and vasopressors and good timing. According to the present study, 5 (17.9%) children needed inotropes. In the **Sethy** *et al.* <sup>[13]</sup> study, the need for inotropes was higher; even after receiving adequate fluid resuscitation, 47.6% of the patients needed inotropic support. Additionally, the prevalence of systemic hypotension was higher in the **Ramcharan** *et al.*<sup>[9]</sup> study, with 67% of patients requiring fluid resuscitation, inotropic support, and vasopressor support, compared to 50% of patients in the **Verdoni** *et al.*<sup>[8]</sup> study.

In the current study, 7 (25.0%) patients needed respiratory support where 1 (3.6%) patient only needed mechanical ventilation. Similar to our study, mechanical ventilation was required in 5% of children due to respiratory distress in **Sethy** *et al.* <sup>[13]</sup> study. Of the 570 MIS-C cases in the **LaRovere** *et al.* <sup>[22]</sup> study in USA, 38.1% required some sort of respiratory support, whereas 39.1% of the cases in the **Jain** *et al.* <sup>[23]</sup> study from Mumbai needed invasive respiratory support, Furthermore, **Ramcharan** *et al.* <sup>[9]</sup> found that 53% of patients required respiratory support; of these, half needed a high-flow nasal cannula and the other half needed mechanical ventilation.

All patients in the current study received 1 gm IVIG for 2 days while 14 (50%) patients received pulse steroids followed by oral steroids after IVIG course. **Henderson** *et al.* <sup>[24]</sup> **and Hennon** *et al.* <sup>[25]</sup> have recommended IVIG as the first option in the treatment of MIS-C, which is in line with our results.

Additionally, Whittaker et al. [11] observed that 61% of patients with fever and inflammation alone, 72% of patients with shock, and 100% of patients with presentations similar to Kawasaki disease were treated with IVIG. However, in the Sethy et al. <sup>[13]</sup> study, the clinical presentation, its severity, and degree of cardiac involvement were taken into consideration when deciding whether to administer IVIG, a steroid, or both. As a result, a greater proportion of patients in the Sethy et al. <sup>[13]</sup> research received steroids while just 42.8% of patients received IVIG. Additionally, in the Ramcharan et al. [9] trial, 33.3% of patients got IV methylprednisolone, which was followed by an oral prednisolone weaning course, whereas 66.6% of patients received IVIG. There is insufficient data to determine which treatments are better in treating MIS-C patients because there is such variance in these practices.

Low dose aspirin was given to 23 (82.10%) patients in the present study and low-molecular-weight heparin (LMWH) as anticoagulant were prescribed in 5 (17.90%) patients. It's still unclear if MIS-C patients and acute COVID patients have comparable thrombosis risks. But according to **Henderson** *et al.* <sup>[24]</sup>, it makes sense to begin LMWH for MIS-C in these patients because they have high D-dimer levels and multiorgan failure that calls for critical care treatment.

All children clinically improved by the end of the current study. Similarly, all patients in **Kok** *et al.* <sup>[26]</sup> study in 2021 clinically improved by the end of the study.

In the current study, out of the 22 patients who developed cardiac affection, 2 (21.4%) out of 8 children had residual LV dysfunction on discharge. On the contrary, all the cases with myocardial dysfunction in **Sethy** *et al.*, <sup>[13]</sup> study responded to the supportive treatment.

In the present study, out of the 18 patients who developed coronary dilatation, state of dilatation of coronaries improved in 17 (60.7%) patients, while progression of dilatation was only reported in 1 (4.54%) patient. Similar to **Feldstein** *et al.* <sup>[27]</sup> study from 2021, which found coronary aneurysms in 57 patients (13.4%), 53 (93.0%) had mild ones, 4 (7.0%) had moderate ones, and none had massive or giant ones. In 79.1% of patients, aneurysms reverted to normal by 30 days, and in 100% by 90 days. On the contrary, all of patients in **Nelson** *et al.* <sup>[28]</sup>, study in 2021 developed either primary or worsening of dilation after initial treatment with IVIG.

In our study no mortality cases occurred although 9 % mortality was reported in **Sethy** *et al.* <sup>[13]</sup> study in 2020. The limitations of this study include its relatively small sample size, which may limit the generalizability of the findings. Additionally, the study's cross-sectional design prevents the establishment of causality between the observed factors and outcomes. The reliance on retrospective data collection could also introduce bias, and the absence of long-term follow-up limits the ability to assess the persistence or evolution of the observed clinical features. Finally, the study's findings may be influenced by the specific population and healthcare setting, which may not be representative of broader or more diverse populations.

#### CONCLUSION

Cardiac affection is common in MIS-C patients and must be looked for. The most common presentation is coronary artery dilatation, mostly left coronary artery so early and appropriate intervention is essential to avoid complications.

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#### REFERENCES

- **1. Biryukov J, Boydston J, Dunning R** *et al.* (2020): Increasing temperature and relative humidity accelerates inactivation of SARS-CoV-2 on surfaces. mSphere., 5:4.
- **2.** Dong Y, Mo X, Hu Y *et al.* (2020): Epidemiology of COVID-19 among children in China. Pediatrics,145:6.
- **3. Toubiana J, Poirault C, Corsia A** *et al.* (2020): Kawasakilike multisystem inflammatory syndrome in children during the covid-19 pandemic in Paris, France: prospective observational study. BMJ., 369:m2094.

- **4. Belhadjer Z, Méot M, Bajolle F** *et al.* (2020): Acute heart failure in multisystem inflammatory syndrome in children in the context of global SARS-CoV-2 pandemic. Circulation, 142:429-36.
- **5. Bialek S, Hughes M, McNamara L** *et al.* (2020): Coronavirus disease 2019 in children - United States. MMWR Morb Mortal Wkly Rep., 69:422-6.
- **6. Feldstein L, Rose E, Horwitz S** *et al.* (**2020**): Multisystem inflammatory syndrome in U.S. children and adolescents. N Engl J Med., 383:334-46.
- **7. Acevedo L, Piñeres-Olave B, Niño-Serna L** *et al.* (2021): Mortality and clinical characteristics of multisystem inflammatory syndrome in children (MIS-C) associated with covid-19 in critically ill patients: an observational multicenter study (MISCO study). BMC Pediatr., 21:516.
- 8. Verdoni L, Mazza A, Gervasoni A *et al.* (2020): An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. Lancet, 395:1771-8.
- **9. Ramcharan T, Nolan O, Lai C** *et al.* (2020): Paediatric inflammatory multisystem syndrome: Temporally associated with SARS-CoV-2 (PIMS-TS): Cardiac features, management and short-term outcomes at a UK tertiary paediatric hospital. Pediatr Cardiol., 41:1391-401.
- **10.** Pouletty M, Borocco C, Ouldali N *et al.* (2020): Paediatric multisystem inflammatory syndrome temporally associated with SARS-CoV-2 mimicking Kawasaki disease (Kawa-COVID-19): a multicentre cohort. Ann Rheum Dis., 79:999-1006.
- **11. Whittaker E, Bamford A, Kenny J** *et al.* (2020): Clinical characteristics of 58 children with a pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2. JAMA., 324:259-69.
- **12.** Davies P, Evans C, Kanthimathinathan H *et al.* (2020): Intensive care admissions of children with paediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) in the UK: a multicentre observational study. Lancet Child Adolesc Health, 4:669-77.
- **13. Sethy G, Mishra B, Jain M** *et al.* (2021): Clinical profile and immediate outcome of multisystem inflammatory syndrome in children associated with COVID-19: A multicentric study. J Glob Infect Dis., 13:159-63.
- **14. Chattopadhyay A, Saigal Kalra K, Saikia D** *et al.* (2022): Severe multi-inflammatory syndrome in children temporally related to COVID 19-clinical course, laboratory profile and outcomes from a North Indian PICU. J Intensive Care Med., 37:1229-37.
- **15.** Pal P, Bathia J, Ganguly M *et al.* (2022): Cardiac evaluation in multisystem inflammatory syndrome in children (MIS-C) associated with COVID-19. Indian Pediatr., 59:339-40.

- **16. Mamishi S, Movahedi Z, Mohammadi M** *et al.* (2020): Multisystem inflammatory syndrome associated with SARS-CoV-2 infection in 45 children: a first report from Iran. Epidemiol Infect., 148:e196.
- **17.** Ahmed M, Advani S, Moreira A *et al.* (2020): Multisystem inflammatory syndrome in children: A systematic review. E Clinical Medicine, 26:100527.
- **18. Godfred-Cato S, Bryant B, Leung J** *et al.* (2020): COVID-19-associated multisystem inflammatory syndrome in children - United States, MMWR Morb Mortal Wkly Rep., 69:1074-80.
- **19. Lagunas-Rangel F (2020)**: Neutrophil-to-lymphocyte ratio and lymphocyte-to-C-reactive protein ratio in patients with severe coronavirus disease 2019 (COVID-19): A meta-analysis. J Med Virol., 92:1733-4.
- **20. Jiang L, Tang K, Levin M** *et al.* (**2020**): COVID-19 and multisystem inflammatory syndrome in children and adolescents. Lancet Infect Dis., 20:e276-e88.
- **21. Belot A, Antona D, Renolleau S** *et al.* (**2020**): SARS-CoV-2-related paediatric inflammatory multisystem syndrome, an epidemiological study, France, 1 March to 17 May 2020. Euro Surveill, 25(22):2001010.
- **22. LaRovere K, Riggs B, Poussaint T** *et al.* (2021): Neurologic involvement in children and adolescents hospitalized in the United States for COVID-19 or multisystem inflammatory syndrome. JAMA Neurol., 78:536-47.
- **23. Jain S, Sen S, Lakshmivenkateshiah S** *et al.* (2020): Multisystem inflammatory syndrome in children with COVID-19 in Mumbai, India. Indian Pediatr., 57:1015-9.
- 24. Henderson L, Canna S, Friedman K *et al.* (2020): American College of Rheumatology Clinical Guidance for Multisystem Inflammatory Syndrome in Children Associated With SARS-CoV-2 and Hyperinflammation in Pediatric COVID-19: Version 1. Arthritis Rheumatol., 72:1791-805.
- **25. Hennon T, Penque M, Abdul-Aziz R** *et al.* (2020): COVID-19 associated Multisystem Inflammatory Syndrome in Children (MIS-C) guidelines; a Western New York approach. Prog Pediatr Cardiol., 23:101232.
- **26.** Kok E, Srivaths L, Grimes A *et al.* (2021): Immune thrombocytopenia following multisystem inflammatory syndrome in children (MIS-C) a case series. Pediatr Hematol Oncol., 38:663-8.
- **27. Feldstein L, Tenforde M, Friedman K** *et al.* (2021): Characteristics and outcomes of US children and adolescents with multisystem inflammatory syndrome in children (MIS-C) Compared with severe acute COVID-19. JAMA., 325:1074-87.
- **28.** Nelson M, Mrosak J, Hashemi S *et al.* (2022): Delayed coronary dilation with multisystem inflammatory syndrome in children. CASE (Phila), 6(1):31-5.