Cardiac findings in multisystem inflammatory syndrome in children: Short term follow up in a large Indian series

Sejal Suresh Shah[1], Praveen Kumar K. Naidu[1], Sumithra Selvam[2], Rakshay Shetty[3], Chandrika S. Bhat[3], Sunita Maheshwari[1]

[1]Hands on Heart, RxDx Healthcare, Bengaluru, Karnataka, India, [2]St. John's Research Institute, Bengaluru, Karnataka, India, [3]Rainbow Children's Hospitals, Bengaluru, Karnataka, India

ABSTRACT

Background : **We present a large Indian series of Multisystem inflammatory syndrome in children (MIS-C) associated with coronavirus disease 2019 (COVID-19) infection. The aim of the study is to present the incidence and pattern of cardiac involvement in children with MIS-C and their short-term follow-up.**

Methods and Results : **Consecutive 144 children younger than 18 years of age diagnosed with MIS-C referred for cardiac evaluation between June 1 and November 30, 2021, were included and were followed up till February 2022. In addition to the demographics, details of COVID-19 infection, and biomarkers, their cardiovascular assessment (echocardiogram and electrocardiogram) was documented at baseline and on follow-up. The median age of children with MIS-C was 60 (24–104) months. Abnormal cardiac imaging was noted in 59% of children. Ventricular dysfunction was noted in 13.9% and coronary abnormalities were noted in 25.7% of children. The median duration when the first cardiac abnormality was reported was 7 (5–10) days. The distribution of age categories between children with and without cardiac abnormality was comparable. Children with cardiac abnormalities were followed up for a median duration of 47 (30–58) days. Complete resolution was documented in 92% of children after a median duration of 20 (9–38) days. There were no readmissions or deaths during follow-up.**

Conclusion : **Cardiac involvement in children with MIS-C is frequent with coronary abnormalities and ventricular dysfunction being the most common manifestations. Most children exhibit complete clinical and myocardial recovery with appropriate anti-inflammatory therapy. Studies on long-term outcome of these children are needed.**

Keywords : Cardiac abnormalities, coronavirus, coronavirus disease 2019, multisystem inflammatory syndrome in children, MIS-C

INTRODUCTION

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2 virus) causing Coronavirus disease 2019 (COVID-19) rapidly spread worldwide in the early 2020 when the World Health Organization (WHO)

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Address for correspondence: Dr. Sejal Suresh Shah, Hands on Heart (Pediatric Cardiology Group), RxDx Healthcare and Teleradiology Solutions, Kundanhalli Main Road, Opposite Graphite India, EPIP Zone, Bengaluru - 560 048, Karnataka, India.
E-mail: sejalshahsuresh@yahoo.com

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declared a global pandemic. Early reports indicated a favorable prognosis in the pediatric population compared to adults. Children were less affected, more often asymptomatic, or mildly symptomatic and had documented rapid recovery.[1-4] However, by April 2020, health-care professionals noted a rise in children presenting with multisystem inflammatory illness, including Kawasaki-like disease with a temporal association with COVID-19.[5,6] As more cases started appearing, the Centers for Disease Control and Prevention (CDC) and WHO issued an alert and termed the condition as Multisystem Inflammatory Syndrome in Children (MIS-C).[7-9] The possibility of children's immune system interacting with the virus differently than in adults was suggested as a possible cause for children reacting differently to COVID-19.

Cardiac involvement has been noticed right from the initial studies in a high proportion of children with MIS-C including myocardial and coronary involvement.[5,6,10-12] The understanding regarding how to care for patients with MIS-C has rapidly evolved. However, the long-term impact especially on the cardiovascular system is still unclear. Here, we describe a large cohort of children diagnosed with MIS-C focusing on cardiovascular involvement. The objective of this study is to highlight the incidence and type of cardiac involvement in children with diagnosed MIS-C with their short-term cardiac follow-up. This article puts forth the perspective of a pediatric cardiologist in the management of MIS-C– a disease needing a multidisciplinary approach.

METHODS

Study design

The study was approved by the institutional ethics committee. The study was conducted with CDC Policy waiver of consent.[13] It was a multi-center, prospective study. Information on children diagnosed with MIS-C over a period of 6 months starting from June 1, 2021, was collected. The last date of follow-up for outcomes was February 2022.

Participants

All sequential patients with a diagnosis of MIS-C seen by the authors on the cardiac side were included. All children were <18 years of age. The diagnosis of MIS-C was based on the WHO definition.[14] All the patients are required to have a positive test for SARS-CoV-2 by detection of serum antibodies or nucleic acid from a nasopharyngeal specimen. The cardiac reference was done by the treating pediatricians in view of the presence of shock/life-threatening symptoms or if Tier 1 investigations were positive (based on the Indian Academy of Paediatrics guidelines published in April 2021).[15] Most of the time, the primary evaluation was done when the children were hospitalized for the acute illness. Children were advised to follow up 1–2 weeks and 4–6 weeks after discharge for an echocardiogram, later at 3 and 6 months. The follow-ups were done on an outpatient basis. More aggressive follow-up was advised in case the initial findings were abnormal.

Data collection

Data were collected from the available hospital records. Data included the demographic information of the children, history of COVID-19 infection (confirmed or suggestive symptoms) either in the child or in the family, duration between COVID-19 infection and the current illness, presenting symptoms, laboratory results, echocardiographic findings, electrocardiogram findings, and management. Need for intensive care, features of cardiogenic shock, and use of vasopressors was noted. The primary focus was on the cardiac manifestations including ventricular dysfunction, coronary dilatation, pericarditis, valvulitis, and conduction abnormalities.

Defining the illness

The onset of fever was considered as day 1 of the illness. Among the blood investigations, the values of erythrocyte sedimentation rate, C-reactive protein, serum ferritin, lactate dehydrogenase, D dimer, troponin, and pro-B-type natriuretic peptide (BNP) were noted. Any measurement beyond the reference range was considered abnormal. A child was defined to have abnormal cardiac findings in investigations if the child had any of the following five abnormalities at any of the visits –abnormal electrocardiogram (ECG), left ventricular (LV) dysfunction, pericardial effusion, atrioventricular valve regurgitation and/or coronary dilatation. Each child having more than one echocardiogram was then classified based on the worst finding.

LV ejection fraction (LVEF) was measured in parasternal long axis view by M mode echocardiography and LVEF >55% was categorized as normal. LVEF <55% was considered depressed or based on the qualitative assessment. LVEF of 45%–54% was considered as mild LV dysfunction, LVEF of 35%–44% was considered moderate LV dysfunction and <35% was severe dysfunction.[16] Pericardial effusion was considered mild when it was <5 mm and moderate when it was more than 5 mm. Coronary arteries were considered as normal when the body surface area (BSA) adjusted z scores in the proximal segments were <2. "Dilation only" was considered when the *z* score was 2 to <2.5. Coronary aneurysms were classified as small (*z* score 2.5–5), moderate (*z* score 5–10), and large (*z* score >10 or absolute dimension ≥8 mm).[17] The website used for the calculation of *z* scores was Dallaire and Dahdah-Montreal

JASE 2010. *z* scores were based on the BSA or only the weight when height was not available.

A child was considered "compliant" if he or she had followed up for at least 3 months after the onset of fever and had a definite outcome. Outcome in terms of resolution of LV dysfunction and coronary aneurysm over time was evaluated. Outcome was analyzed in the "compliant" group and was considered to represent the overall "cardiac abnormality" group.

Statistical analysis

Clinical characteristics of the children measured as continuous variables are summarized as median and interquartile range and categorical variables as frequency and percentages. The proportion of children who presented with cardiac abnormality was reported and the clinical characteristics associated with the presence of cardiac abnormality were assessed using Chi-square test, Fisher's exact test, and Mann–Whitney *U*-test, as appropriate. Demographic and clinical characteristics were also compared by children with compliance/noncompliance, and recovery/nonrecovery. Kaplan–Meier analysis was carried out to estimate the median recovery time. $P < 0.05$ was considered statistically significant. All the analyses were performed using IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.

RESULTS

From June 1, 2021, to November 30, 2021, a total of 144 children were referred who met the WHO criteria for the diagnosis of MIS-C. The median age of these children was 60 (24–104) months, with more than half of them being <5 years of age. All children were previously healthy with no documented morbidity including congenital heart disease.

Out of 144 children, 143 children were hospitalized during the illness. Overall, 85 children (59.0%) had any of the defined cardiac abnormalities. The clinical characteristics of children diagnosed with MIS-C (*n* - 144) and children with cardiac abnormality (n-85) are presented in Table 1.

Out of 144 children, 7 children did not have a fever. Most of these children (6/7) were <2 months of age (5/7 were neonates) and had a history of COVID-19 infection in the mother during pregnancy. They predominantly had respiratory symptoms in addition to cardiogenic shock (5/7) and needed intensive care treatment.

The entire cohort underwent an echocardiogram at the first visit. Among 59 (41%) children with no cardiac abnormality, the clinical and echocardiography parameters were completely normal until they had last followed up which was a median duration of 13 days.

No significant association was observed between the presence of cardiac abnormality and gender, age categories, presentations of symptoms, and Troponin levels. However, 95% of children with elevated NT Pro-BNP had a cardiac abnormality ($P = 0.09$).

The type and timing of cardiac abnormality found in these 85 children are summarized in Table 2. The first cardiac abnormality was detected after a median duration of 7 (5–10) days after the onset of fever. The ECG abnormality included atrial and ventricular ectopics, exaggerated sinus arrhythmia, and inappropriate sinus tachycardia and bradycardia. Ventricular dysfunction was noticed among 20 children during the hospital stay and was mild in 16 children, moderate in 2 children, and severe in 2 children. Pericardial effusion was mild to moderate in all. Atrioventricular valve regurgitation was Grade I to II in all patients. Coronary artery dilatation was noticed in the left main coronary artery (LMCA), left anterior descending artery, and the right coronary artery (RCA) and the severity ranged from mild dilatation to moderate aneurysm. No child had a documented large aneurysm. Figure 1a-c shows coronary artery dilatation by site and severity.

The frequency of follow-up varied in 85 children with cardiac abnormality based on the severity of illness and compliance. Amongst the 85 children, 51 children

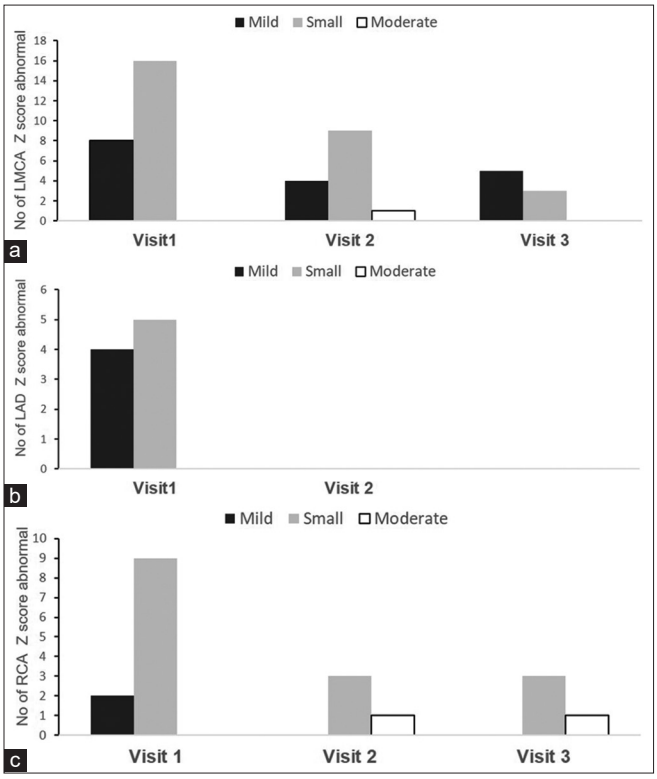


Figure 1: Distribution of Coronary artery disease across visits, the site and severity, (a) Number of children with LMCA dilatation, (b) Number of children with LAD dilatation, (c) Number of children with RCA dilatation

Table 1: Clinical characteristics of children diagnosed with multisystem inflammatory syndrome in children (*n*=144) and children with cardiac abnormality (*n*=85) along with the median values of abnormal biochemical parameters

Variable	Entire study population (*n*=144), *n* (%)	Children with cardiac abnormality (*n*=85), *n* (%)
Age (months)		
<12	17 (11.8)	6 (7.1)
12–60	60 (41.7)	39 (45.9)
60–120	44 (30.6)	25 (29.4)
>120	23 (16.0)	15 (17.6)
Boys	93 (64.6)	56 (65.9)
Girls	51 (35.4)	29 (34.1)
Weight (kg), mean±SD	20.5±14.7	22.5±14.3
Positive test for SARS-CoV-2		
RAT/RTPCR	19 (13.3)	14 (16.7)
On serological assay		
IgM	55 (42.0)/131	63 (77.8)/81
IgG	118 (84.3)/140	35 (47.3)/74
IgG/IgM	137 (95.1)/140	79 (97.5)/81
History of COVID-19 infection in the past		
In the child	23 (16.3)	16 (19.3)
In the family	56 (39.4)	31 (36.9)
Duration between COVID infection and presentation of symptoms (days)*	45 (30–65)	45 (30–83)
Symptoms		
Fever	137 (95.1)	83 (97.6)
GI symptoms	60 (41.7)	38 (44.7)
Respiratory symptoms	25 (17.4)	16 (18.8)
Rashes	53 (36.8)	35 (41.2)
Intensive care admission	76 (52.8)	49 (57.6)
Shock	57 (39.6)	37 (43.5)
Use of inotropes	48 (34.5)	34 (42.0)
Biochemical parameters*		
CRP elevated (mg/L)	114/135 (61 [17–150])	71/82 (69.5 [20–150])
ESR (mm/h)	76/80 (47 [30–73])	45/48 (45.5 [30–77.3])
PCT (ng/mL)	15/18 (5.1 [0.65–14.6])	13/15 (4.68 [0.68–15.0])
D-Dimer (mg/L)	85/98 (2.3 [1.1–4.5])	48/58 (3.5 [1.29–8.60])
LDH (U/L)	72/88 (328 [263–446])	51/59 (363 [269–514])
Ferritin (ng/mL)	47/116 (251 [95–641])	35/72 (313.5 [114.2–831.3])
Troponin (ng/mL)	9/14 (1.5 [0.4–6.2])	5/8 (1.2 [0.10–1.50])
Pro BNP (ng/L)	37/43 (3521 [404–14,095])	21/22 (5920 [3874–2773])

*Median values with 25th and 75th percentile. Reported as *n* (%). For biochemical parameters, data was reported only for available data. RAT: Rapid antigen test, RT-PCR: Reverse transcription polymerase chain reaction, GI: Gastrointestinal, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, LDH: Lactate dehydrogenase, PCT: Procalcitonin, Pro BNP: B-type natriuretic peptide, SD: Standard deviation, SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2, COVID-19: Coronavirus disease 2019, IgG: Immunoglobulin G, IgM: Immunoglobulin M

Table 2: Distribution of number of children with abnormal electrocardiographic and echocardiographic findings in children diagnosed with multisystem inflammatory syndrome in children (*n*=85) across visits

	Total number of children with abnormal findings	Visit 1 (1 week)	Visit 2 (2 weeks)	Visit 3 (4 weeks)	Visit 4 (7 weeks)	Visit 5 (8 weeks)
ECG abnormal	39	39	3	3	0	0
PE	25	22	6	1	1	1
CAD	37	31	24	11	4	3
LV dysfunction	20	20	3	1	0	0
AVVR	33	33	2	3	2	0

Reported are number of children. ECG: Electrocardiogram, PE: Pericardial effusion, CAD: Coronary artery dilatation, LV: Left ventricle, AVVR: Atrioventricular valve regurgitation, ( ) - Median duration of follow up

were compliant throughout the study with a minimum duration of 3 months' follow-up [Flow Chart 1]. Although 34 children were noncompliant, they were discharged with clinical recovery and had a follow-up of <3 months with indefinite cardiac outcomes. A higher proportion of females and children with respiratory symptoms were found to be noncompliant (P = 0.04 and P = 0.0001, respectively) whereas higher number of children with coronary artery dilatation were found to be compliant (P = 0.01). The remaining parameters such as demographics, laboratory, and cardiac characteristics were comparable between compliant and noncompliant groups. Refer to Supplementary Table 1 (available on line) which shows the comparision of demographics and clinical parameters between the compliant and non compliant groups.

Recovery in children with cardiac abnormality was analyzed in the compliant group. These 51 children had a median duration of follow-up for 47 (30–58) days. Recovery was documented in 92% (47/51) of children. Kaplan Meier analysis showed that the median recovery duration was 30 (22–37) days [Figure 2]. Ventricular dysfunction which was noticed in children during their hospital stay resolved and none had cardiac dysfunction at the time of hospital discharge. Pericardial effusion completely resolved in all but one, before discharge. Atrioventricular valve regurgitation correlated with ventricular dysfunction, and it completely disappeared once the LV function improved. Three children continued to have coronary artery dilatation at the end of 8 weeks [Table 2 and Figure 1] which continued till the end of the study.

Table 3 shows the factors associated with nonrecovery. All four children who did not recover from the cardiac abnormalities were between 2 and 5 years of age ($P = 0.059$) and all had gastrointestinal symptoms ($P = 0.059$) during the illness. The initial laboratory parameters were comparable between recovery and nonrecovery groups. None of these four children had LV dysfunction in the initial phase of illness. In the nonrecovery group, one child had RCA moderate aneurysm documented as persisting at 182 days after the onset of illness. Two children, who were diagnosed and treated on days 4 and 7 of illness, had LMCA small aneurysm persisting after 168 and 201 days of illness, respectively. One child who had persistent pericardial effusion until the last follow-up, is being evaluated for other inflammatory causes.

Treatment modalities of the children with MIS-C included intravenous immunoglobulins (IVIG), corticosteroids, and aspirin in addition to supportive care. Immunoglobulins were given to 78/144 children in the dose of 2 g/kg. None of these patients received a second dose of IVIG. Steroids were given in 84/144 children and the dosing was based on the phenotype. Children who presented with shock or went into shock during illness received pulse methylprednisolone at 10 mg/kg/day for 3 days, followed by low-dose steroids, and children who did not have features of shock received low-dose steroids at 2 mg/kg/day, followed by gradual tapering. Oral Aspirin was given to all children. Low molecular weight heparin (2/144 children), Anakinra (4/144 children), and tocilizumab (2/144) were also used. There were no deaths with clinical recovery in 100% of the entire 144 children studied.

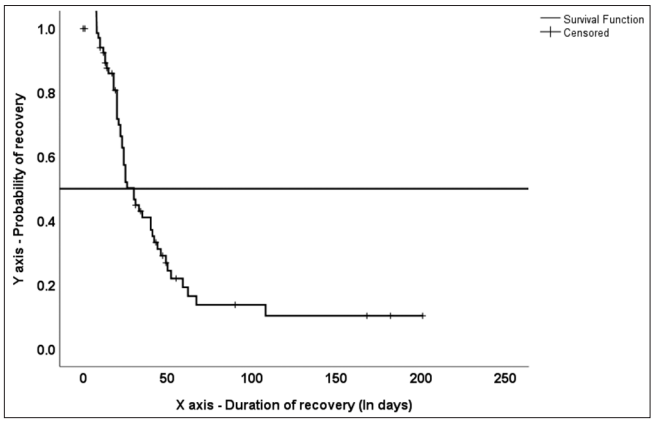


Figure 2: Kaplan–Meier curve showing duration of recovery. X axis: Duration of recovery in days, Y axis: Probability of recovery; ——Line: Indicates 50% probability of recovery

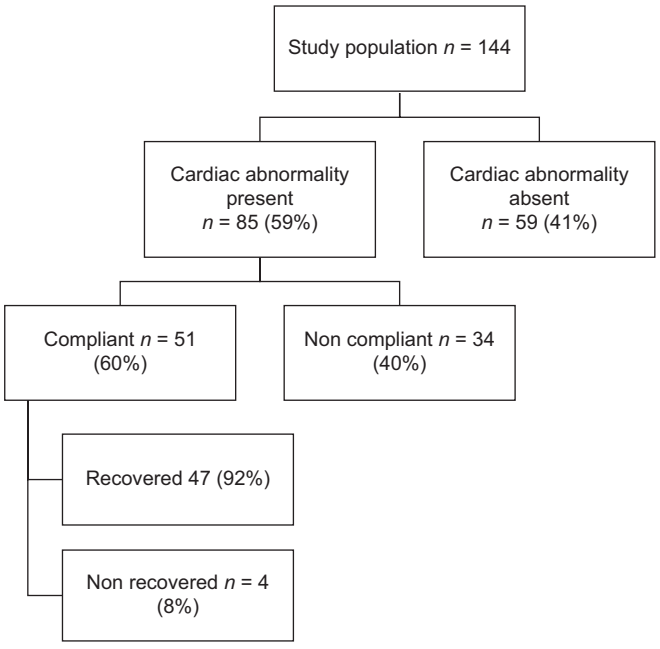
DISCUSSION

In late April 2020, MIS-C was recognized for the first time in the world as a new entity temporally associated

Table 3: Comparison of characteristics between recovery and nonrecovery groups

	Non-recovered (*n*=4), *n* (%)	Recovered (*n*=47), *n* (%)	*P*
Age category (months)			
≤12	0	1 (2.1)	0.06
13–60	4 (100)	18 (38.3)	
61–120	0	17 (36.2)	
>120	0	11 (23.4)	
Gender			
Male	2 (50.0)	36 (76.7)	0.24
Female	2 (50.0)	11 (23.4)	
Fever	4 (100)	46 (97.9)	0.77
Respiratory symptoms	0	3 (6.4)	0.60
Rashes	3 (75.0)	22 (46.8)	0.28
Gastrointestinal symptoms	4 (100)	24 (51.1)	0.06
Intensive care admission	2 (50.0)	27 (57.4)	0.77
Shock	1 (25.0)	21 (44.7)	0.45
Need for inotropes	1 (25.0)	19 (42.2)	0.50

Reported as *n* (%)



Flow Chart 1: Distribution of study population based on compliance and recovery among children with cardiac abnormality

with COVID-19 infection. MIS-C was noted to take place in clusters and at a median of 36 days after the peak incidence of COVID-19 infection in the affected area.[10,18] In India, the surge of MIS-C cases was seen almost a year later, i.e., April 2021 onward. The cause for this gap could be related to a late peak of COVID-19 infection seen in our country and could also have been related to delayed awareness in recognizing the entity.

The pathophysiology of MIS-C is thought to be a hyperimmune response to the virus in a genetically susceptible child.[19] Alsaied *et al.* have summarized the potential etiology of cardiovascular involvement in MIS-C and correlated it with the clinical presentation including the cardiac manifestations. Possible etiologies include cardiomyocyte invasion, dysregulated inflammatory response, endothelial injury, and hypercoagulability.

The median age of these patients was found to be 60 (20–104) months, which was much younger compared to the studies published so far (9 years), most of which are meta-analyses and international studies.[20-23] Fever has been an "essential" criterion for the diagnosis of MIS-C.[7-9] However, we have included seven children without fever, in view of the positive status of SARS-CoV-2 infection, raised inflammatory markers, and the nature of response to treatment.

Common ECG abnormalities have been described including nonspecific ST segment/T wave abnormalities, abnormal PR intervals, and premature atrial or ventricular beats.[12] Atrioventricular conduction abnormalities have been documented with the electrographic abnormalities after 8–9 days from the initial symptoms.[24] Sinus bradycardia and tachyarrhythmia have also been noted.[25] Although high-dose steroids can cause bradycardia, inflammation/edema of the conduction tissue as a part of myocardial injury is thought to be the cause for conduction abnormalities.[24] Carmona *et al.* recommend frequent ECGs to monitor PR prolonging/QTc elongation which could lead to life-threatening arrhythmias. The recovery for atrioventricular conduction abnormalities is considered unpredictable. All ECG changes reverted to normal during follow-up in our cohort.

The majority of the previous studies have documented the cardiac involvement during acute illness. The most common cardiac finding in studies reported has been acute myocardial dysfunction with patients presenting in shock, with elevated cardiac enzymes and requirement for inotropes.[10,26-29] Acute myocarditis was documented to occur <1 week after the onset of fever and gastrointestinal symptoms.[28] All patients have been documented to have full clinical recovery with a median recovery period of 2 days.[10,27] In our study, there was complete clinical and myocardial recovery on echocardiogram in a short span of a few days in 13.9% of children with ventricular dysfunction. Persistent abnormalities in strain and diastolic function have been demonstrated in patients with normal ejection fraction, implying the persistence of subclinical myocardial injury even after LV systolic function appears normal with traditional measures.[30] This emphasizes the need for a long-term follow-up of these children. In children who do not have abnormalities on conventional assessment, the peak left atrial longitudinal strain obtained by atrial deformation analysis has been suggested to potentially be diagnostic of LV diastolic dysfunction in myocarditis in MIS-C.[31]

Coronary artery involvement has been described in MIS-C right from the beginning, the incidence of which has been variable. A large cohort has reported coronary involvement in up to 24% of patients.[27] This incidence was found to be much higher than Kawasaki disease.[6] This correlates with our case series incidence of 25.7%. Coronary artery dilatation is proposed to be related to fever, circulating inflammatory mediators, or inflammation and disruption of the arterial wall.[19] However, Whittaker *et al.* found that the laboratory findings among children who developed coronary artery dilatation or aneurysms were not meaningfully different from those without coronary artery aneurysms.[26] In our series, we did document a near statistically significant correlation of NT Pro-BNP levels with any cardiac abnormality (P = 0.09). The lack of clear clinical and laboratory markers that identify patients who develop coronary artery aneurysms implies the need for echocardiography to detect coronary artery aneurysms, and to monitor either the worsening or resolution of these changes. In terms of the severity of coronary involvement, majority of the children in the past have demonstrated small and moderate aneurysms, similar to the finding in this study. Occasional cases of large aneurysm and late formation of aneurysms have been noted.[6,26] The mild severity and rapid resolution of coronary artery dilatation suggest that coronary dilatation often results from vasodilatation related to proinflammatory milieu rather than from the destruction of arterial wall by inflammatory cells.[32]

The long-term prognosis of MIS-C is not known. Although the ventricular function and arrhythmias are seen to resolve in a short duration of time, the natural history of coronary abnormalities is uncertain.

We found certain limitations of echocardiogram for diagnosing coronary abnormalities. The RCA was sometimes confused with a pericardial fold. It was also difficult to be accurate in the assessment of distal coronary arteries sizes. A cardiac computed tomography scan is expected to provide a more accurate assessment; however, we did not consider it in our children in view of radiation and the fact that the management would not change. The role of cardiac magnetic resonance imaging on follow-up to evaluate the myocardial characteristics

and ventricular function needs to be decided with further studies. One of the major limitations of this study, like other studies on MIS-C would be the definition of the disease, i.e., difficulty in differentiation between the cytokine storm related to acute COVID-19 infection and MIS-C. MIS-C can mimic other diseases and whether the presence of antibodies against COVID-19 is incidental or causal is difficult to decide. There is a possibility that coronary dilatation in the acute febrile illness could be related to nonspecific inflammation causing vasodilatation and not specifically to MIS-C, especially due to the lack of a control panel. Limitations related to the measurement of coronary artery sizes on echo, the subjective variation, and multiplication of error when z score is calculated cannot be overlooked.

CONCLUSIONS

Cardiovascular manifestations are common in children with MIS-C. Most children clinically recover from the acute illness and show significant early and intermediate recovery in terms of normalizing the myocardial and coronary abnormalities. The long-term sequelae especially of coronary involvement need to be explored by follow-up studies. Future research is needed to define the risk factors in children to develop MIS-C after COVID-19 infection and to prognosticate long-term systemic outcomes.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Comparison of demographic and clinical parameters between compliant and noncompliant groups

	Noncomplaint (*n*=34) *n*(%)	Complaint (*n*=51)*n*(%)	*P*
Age category (in years)			
Less than 1	5 (14.7)	1 (2.0)	0.08
2	17 (50.0)	22 (43.1)	
6–10	8 (23.5)	17 (33.3)	
>10	4 (11.8)	11 (21.6)	
Gender			
Male	18 (52.9)	38 (74.5)	0.04
Female	16 (47.1)	13 (25.5)	
IgG/IgM			
Positive	30 (100)	49 (96.1)	0.27
Negative		2 (3.9)	
Symptoms			
Fever	33 (97.1)	50 (98.0)	0.77
Respiratory	13 (38.2)	3 (5.9)	0.0001
GI	10 (29.4)	28 (54.9)	0.02
Biochemical parameters*			
Troponin ng/mL	0.10 (0.78–1.40)	1.11 (0.25–15.7)	0.87
PBNP pg/ml	5840 (3057–15602)	6643 (3874–30,000)	0.60
CRP mg/dL	61 (20–144)	75 (18.9–154.5)	0.56
ESR mm/hr	39 (16.5–68.2)	49 (31.7–82.7)	0.18
Ferritin µg/L	304 (86–1104)	317 (130–721)	0.91
D-Dimer mg/L	2.01 (0.97–9.75)	3.80 (1.90–7.04)	0.45
LDH U/L	434 (255–913)	346 (276–424)	0.35
Cardiac parameters			
AVVR any time			
Absent	18 (52.9)	34 (66.7)	0.43
Grade I	14 (41.2)	16 (31.4)	
Grade II	2 (5.8)	1 (2.0)	
LVD			
Absent	26 (76.5)	39 (76.5)	0.50
Mild	8 (23.5)	9 (17.6)	
Moderate and severe	0	3 (5.9)	
PE			
Absent	21 (61.8)	39 (76.5)	0.25
Mild	12 (35.3)	10 (19.6)	
Moderate to severe	1 (2.9)	2 (4.0)	
CORART			
Absent	25 (73.5)	23 (45.1)	0.01
Present	9 (26.5)	28 (54.9)	
Echo			
No abnormality	5 (14.7)	5 (9.8)	0.49
Abnormality seen	29 (85.3)	46 (90.2)	

IgG: Immunoglobulin G, IgM: Immunoglobulin M, GI: Gastrointestinal, PBNP: Pro BNP: B-type natriuretic peptide, CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, LDH: Lactate dehydrogenase, AVVR: Atrioventricular valve regurgitation, LVD: Left ventricular dysfunction, PE: Pericardial effusion, CORART: Coronary artery dilatation, *Median values with 25th and 75th percentile