Cardiac Abnormalities Seen in Pediatric Patients During the SARS-CoV2 Pandemic: An International Experience

Running title: Clark et al.; SARS-CoV2 Pediatric Cardiac Abnormalities

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Abstract

**Background:** During the SARS-CoV2 pandemic, there has been increase in hyperinflammatory presentation in previously healthy children with a variety of cardiac manifestations. Our objective is to describe the cardiac manifestations found in an international cohort of 55 pediatric cases with multi-system inflammatory syndrome (MIS-C) during the SARS-CoV2 pandemic.

**Methods and Results:** We reviewed data on previously healthy pediatric patients (≤18 years) with structurally normal hearts who presented at hospitals in the United States, United Kingdom, Spain and Pakistan with MIS-C and had consultation with a pediatric cardiologist. Data collected included demographics, clinical presentation, laboratory values, electrocardiographic abnormalities, echocardiographic findings and initial therapies. A total of 55 patients presented with MIS-C. Thirty-five patients (64%) had evidence of decreased left ventricular function, 17 (31%) had valvulitis, 12 (22%) with pericardial effusion and 11 (20%) with coronary abnormalities. Twenty-seven (49%) required ICU admission and 24 (44%) had evidence of shock. Eleven patients (20%) fulfilled complete Kawasaki disease criteria and had lower NT pro-BNP, D-dimer and ferritin levels compared with those who did not fulfill criteria. Electrophysiologic abnormalities occurred in 6 patients and included complete atrioventricular (AV) block, transient AV block and ventricular tachycardia.

**Conclusions:** We describe the first international cohort of pediatric patients with MIS-C during the SARS-CoV2 pandemic with a range of cardiac manifestations. This paper brings awareness and alertness to the global medical community to recognize these children during the pandemic and understand the need for early cardiology evaluation and follow-up.

**Key words:** pediatric, SARS-CoV2, multi-system inflammatory syndrome (MIS-C), cardiac dysfunction, coronary abnormalities
Nonstandard Abbreviations and Acronyms:

WHO: World Health Organization
MIS-C: multi-system inflammatory syndrome in children
LVEF: left ventricular ejection fraction
KD: Kawasaki disease
AV: atrioventricular
ECMO: extra-corporeal membrane oxygenation
WBC: white blood cell count

Clinical Perspective

What is new?

- We present the first international cohort of patients with multi-system inflammatory syndrome in children and describe the broad range of cardiac findings including a large percentage of cardiac dysfunction, coronary abnormalities, valvulitis and pericardial effusion.

What are the clinical implications?

- Pediatric patients with acute or prior SARS-CoV2 infection can present with a broad range of cardiac findings even in the setting of mild symptoms which demonstrates the need for a high index of suspicion and early cardiology consultation.
In December 2019, a novel coronavirus (SARS-CoV2) was first described in Wuhan, China causing a distinct clinical presentation of pneumonia (COVID-19). By January 2020 the virus had spread throughout the world causing a global pandemic. The virus has typically been described as an adult disease causing primarily respiratory symptoms, with worse outcomes in the elderly and adults with co-morbid conditions\(^1\). Epidemiologic data from China, South Korea, Singapore, Italy and Australia have reported pediatric cases from birth through 19 years with prevalence ranging from 0.6 – 5.2\(^2\)-\(^5\). Compared with their adult counterparts, the majority of pediatric patients have been asymptomatic with milder symptoms including fever, cough, sore throat and nasal congestion\(^6\)-\(^8\), but in mid-April, a center in London, UK noted an increase in the severity of pediatric cases presenting with hyperinflammatory shock\(^9\). Recently, additional cases of pediatric patients from across the globe with a hyperinflammatory syndrome with the potential for multi-organ failure and shock and with temporal association with the SARS-CoV2 viral infection have been described\(^9\)-\(^11\).

The World Health Organization (WHO) has classified the multi-system inflammatory syndrome (MIS-C) associated with COVID-19 as the following: fever \(\geq 3\) days, 2 of the following (rash, non-purulent conjunctivitis, muco-cutaneous inflammation signs, hypotension or shock, myocardial dysfunction, pericarditis, valvulitis, coronary abnormalities, elevated troponin or NT pro-BNP, coagulopathy, acute gastrointestinal problems), evidence of elevated inflammatory markers (ESR, CRP, procalcitonin), no obvious microbial cause and evidence of SARS-CoV2 infection or likely contact with COVID-19 patients\(^12\). Other entities, including the Royal College, have
proposed similar diagnostic criteria including fevers, laboratory evidence of inflammation, organ dysfunction and an absence of additional microbial etiology\textsuperscript{13}.

We present the first international cohort of pediatric patients with MIS-C with the aim to describe the cardiac manifestations encountered during the SARS-CoV2 pandemic.

**Methods**

Because of the sensitive nature of the data collected for this study and the concerns over data-sharing during the SARS-CoV2 pandemic, requests to access the dataset from qualified researchers must be sent to the first author at Children’s Hospital at Montefiore and the request approved by all authors.

An international multi-center retrospective chart review of pediatric patients presenting with MIS-C\textsuperscript{12} who had pediatric cardiology consultation during the SARS-CoV2 pandemic was performed. IRB approval was obtained at the individual centers including Albert Einstein College of Medicine (Bronx, NY, USA), Hospital Sant Joan de Deu (Barcelona, Spain), Royal Brompton and Harefield Hospitals Trust (London, UK), Ochsner Health (New Orleans, LA, USA), Aga Khan University Hospital (Karachi, Pakistan) and National Institute of Cardiovascular Disease (Karachi, Pakistan) and requirement for informed consent was waived. Patients included met the following criteria: age \( \leq 18 \) years, no prior medical history, structurally normal heart and presentation during the SARS-CoV2 pandemic. Only those patients requiring a pediatric cardiology
evaluation were enrolled. Cardiology consultation was initiated by the primary team at the individual centers and the respective cardiology divisions had no impact on which patients received consultation. Data collected included demographic information, clinical presentation, initial management, laboratory testing, electrocardiogram results officially read by a pediatric cardiologist and echocardiographic parameters. Echocardiograms were read by a pediatric cardiologist at their individual sites and data was provided on ejection fraction based on individual center protocols and Z-scores for coronary arteries were based on the Boston scoring system at all participating sites\textsuperscript{14, 15}. Valvulitis was diagnosed based on any valvar regurgitation greater than trivial based on the institutional echocardiogram reader.

**Statistical analysis**

Data was analyzed using SPSS 26.0 software (SPSS Inc., Chicago, Illinois, USA). Descriptive data are presented as the count with percentage and mean ± standard error of the mean and Mann–Whitney test was used to compare quantitative variables.

**Results**

**Overall cohort**

Fifty-five patients met the inclusion criteria (mean age 7 ± 5.2 years): 16 patients from Barcelona, Spain (29%), 14 from London, United Kingdom (26%), 13 from New York City, USA (24%), 9 from Karachi, Pakistan (16%) and 3 from New Orleans, USA (5%). Individual patient data from all centers is presented in Table S1.
Figure 1 demonstrates the continuum of cardiac findings in pediatric patients with MIS-C. Twenty-seven patients required ICU admission (49%), 35 patients (64%) had evidence of myocardial dysfunction with LVEF < 60%, 24 patients (44%) had evidence of shock and 2 (4%) patients did not survive. Among the patients with decreased LVEF, 18 (51%) patients had mildly decreased LVEF (EF 51-60%, mean age 8.3 ± 4.8 years), 11 (32%) patients had moderately decreased LVEF (41-50%, mean age 8.0 ± 4.3 years) and 6 (17%) patients had severely decreased LVEF (<40%, mean age 8.4 ± 5.4 years). Patients who had shock had a significantly higher NT pro-BNP at admission compared to those without (11411 ± 2143 vs 2273 ± 638 pg/mL, p=0.001). Patient symptoms included fever (52/55, 95%), rash (27/55, 49%), gastrointestinal symptoms including abdominal pain, nausea, vomiting or diarrhea, (32/54, 59%), conjunctivitis (18/55, 33%), mucous membrane changes (16/55, 29%), hand or foot swelling (12/54, 22%) and unilateral cervical adenitis (12/53, 23%). Of those patients who had SARS-CoV2 testing, 20/53 (38%) had positive RT-PCR testing and 19/24 (79%) had positive SARS-CoV2 IgG testing; in the total cohort, 36% were positive for RT-PCR and 35% were positive for IgG.

Eleven patients (20%) had features of complete Kawasaki disease (KD) based on established criteria16. Only 2/11 (18%) patients who fulfilled complete KD criteria had evidence of coronary changes. Compared with those patients who did not fulfill criteria, the complete KD group was younger (mean age of 5.4 ± 5.7 years vs 7.5 ± 5.1, p=0.01), had longer length of fever (6.3 ± 1.3 days vs 4.8 ± 2.4 days, p=0.07) and had better left ventricular function (LVEF 58 ± 9% vs 46 ± 18%, p=0.05). None of the patients with complete KD criteria presented with shock or had evidence of valvulitis. Patients who fulfilled criteria for complete KD had statistically significantly lower levels of NT pro-BNP (1606 ± 1089 vs 8522 ± 2143 pg/mL, p=0.007), D-dimer (1.4 ± 0.7
vs. $5.6 \pm 1.0 \text{ ug/mL, } p=0.025$) and ferritin levels ($171 \pm 57 \text{ vs. } 678 \pm 107 \text{ ng/mL, } p=0.008$) compared with those who did not fulfill criteria. Of the patients that fulfilled complete KD criteria, 11/11 (100%) received IVIG, 7/11 (64%) received both steroids and IVIG and 9/11 (82%) received aspirin. All patients that received steroids were also treated with IVIG.

There were 2 mortalities in our cohort, both of which occurred in a low-income country with limited access to resources. Patients were 1 and 5-year old who presented with shock (LV EF 30% in both patients) requiring diuresis and multiple vasoactive agents. Neither patient fulfilled complete KD criteria and both patients were noted to have normal ECGs. Both patients had no evidence of coronary changes or valvulitis and 1 patient had evidence of a pericardial effusion that was not hemodynamically significant by report. NT pro-BNP levels were 2385 and 23750 pg/mL and troponin levels were 0.9 and 1.2 ng/mL respectively. With regards to additional therapies, 1 patient received IV steroids and neither received IVIG.

**Echocardiographic findings**

Patients with abnormal echocardiographic findings and the overall cohort are presented in Table 1. Echocardiographic findings included ventricular dysfunction (n=35, 64%), valvulitis (n=17, 31%), pericardial effusion (n=12, 22%) and coronary artery involvement (n=11, 20%) with overlap between groups (Table 1). Coronary artery abnormalities (Figure 2) included coronary brightness without dilation by Z-score (n=2, 18%), coronary dilation (n=9, 82%) and coronary aneurysms (n=1, 9%). Additional echocardiographic findings of patients in the coronary involvement sub-group included pericardial effusion (5), mitral regurgitation (3), aortic insuffi-
ciency (1), tricuspid regurgitation (1) and left ventricular dilation (1). Only 2 patients had significant coronary dilation (Z-score > 3 with complete KD criteria) with a single patient found to have coronary artery aneurysms (Figure 2 C). This patient was a 4-month-old who presented with 6 days of fever and had evidence of cervical adenopathy but did not fulfill complete KD criteria. Echocardiogram revealed evidence of aneurysms with dilation of both the left main (Z-score +4.8) and right (Z-score +4.7) coronary arteries with normal left ventricular ejection fraction and mild aortic insufficiency. NT pro-BNP was elevated to 3682 pg/mL and troponin was within normal limits (<0.1 ng/mL). The patient received IVIG, steroids, aspirin and clopidogrel therapy.

Electrophysiologic abnormalities
A total of 6 (11%) patients were noted to have an arrhythmia, including complete atrioventricular block (Figure 3A), transient 2nd degree AV block (Figure 3B), sinus pause, ventricular tachycardia and idioventricular rhythm. All patients with arrhythmia had evidence of decreased left ventricular function (LVEF range 27-55%). The single patient with ventricular tachycardia had an LVEF of 30%, QTc prolongation of 530 msec without intra-ventricular conduction delay on the initial ECG and had not received hydroxychloroquine or azithromycin. None of the arrhythmia patients had evidence of coronary brightness or dilation; 1 patient had severe mitral regurgitation and 1 patient had a small pericardial effusion. Overall, 21 patients (38%) were noted to have additional electrocardiographic findings including sinus tachycardia (14), non-specific T wave changes (9), ST changes consistent with pericarditis (4), abnormal QRS axis or voltage criteria for ventricular hypertrophy (2) and 1st degree AV block (1).
Therapy and follow-up

There was a broad range of use of IVIG, steroids, and IVIG + steroids based on institution; medication usage based on cardiac diagnosis can be found in Table 1. IVIG usage based on institution ranged from 22-100%, and was lowest in resource-limited environments, steroids usage was 33-73% and IVIG + steroid combination was 8-64%. Steroids were used alone, without IVIG, in 20% of the overall cohort. While follow-up data is not available for all patients, anecdotally left ventricular systolic function and electrocardiographic abnormalities (including resolution of complete heart block) normalized within 2 weeks of initial presentation but coronary changes including brightness, mild dilation and aneurysms persisted during early follow-up.

Discussion

We present the first international cohort of pediatric patients with MIS-C and cardiac manifestations during the SARS-CoV2 pandemic. We describe a broad range of cardiac involvement including cardiac dysfunction, coronary artery abnormalities, valvulitis, pericardial effusion and electrophysiologic abnormalities. The first description of cardiac involvement in pediatric patients was in 8 patients in the United Kingdom9. All patients had evidence of warm shock, required multiple vasoactive agents and had elevation in either troponin or NT pro-BNP levels. Six out of 8 patients developed evidence of cardiac dysfunction, 2/8 had coronary artery brightness or dilation and a single patient died in the setting of refractory shock and arrhythmia requiring ECMO therapy. Our cohort data further highlights the importance of potential cardiac involvement with MIS-C and early cardiology consultation and work-up, though treatment efficacy remains poorly defined.
There was a high incidence of decreased left ventricular function (64%) and shock (44%) in our cohort of pediatric patients and patients with shock had significantly elevated NT pro-BNP levels compared with the non-shock group. While it is not completely translatable, the adult SARS-CoV2 data has shown a higher mortality rate associated with markers of cardiac injury, especially troponin and NT pro-BNP\textsuperscript{1,18-21}. Though the adult data cannot be directly extrapolated to our pediatric cohort, the finding of elevated NT pro-BNP levels in the decreased function and shock groups does underscore the need for cardiac markers in the evaluation of pediatric patients with suspicion of MIS-C. Additionally, 17 patients developed valvar regurgitation, 12 patients had evidence of pericardial effusion that did not require intervention and 2 patients died in our cohort after presenting with shock. Electrophysiologic abnormalities including AV block and ventricular tachycardia were rare but may have substantial clinical impact and require a high-level of vigilance. While long-term follow-up is limited, early reports are encouraging with improvement in electrophysiologic abnormalities and left ventricular dysfunction, though coronary changes appear to linger.

In our cohort, 11 (20%) patients had evidence of coronary involvement including coronary dilation, coronary brightness or coronary aneurysms. Interestingly, only 2/11 (18%) of the patients with complete KD criteria had evidence of coronary changes which demonstrates that MIS-C is likely a distinct clinical entity from Kawasaki’s disease. While patients who fulfill complete KD criteria will have coronary imaging as a part of the initial echocardiogram protocol, coronary evaluation is paramount in patients with MIS-C, even in the absence of established KD criteria. Additionally, the patients in our cohort who did fulfill the criteria for complete KD tended to be
younger, had a longer duration of fever and had lower NT pro-BNP, D-dimer and ferritin levels. While lymphopenia has been shown to be associated with MIS-C\textsuperscript{13}, our patient cohort did not demonstrate low WBC values. This may represent that patients with a longer duration of fever and symptoms have a less severe course compared to the myocardial dysfunction and shock patients with fulminant presentation.

In our cohort, 20 patients were RT-PCR positive (38\%) and 19 patients had positive IgG testing (35\%). Although the overall number of IgG positivity was low, there was a high positive rate among those that had the test performed (19/24, 79\%). Further, there is a large range of false negative rate of the RT-PCR SARS-CoV2 testing\textsuperscript{22} so a negative test in a patient suspicious for MIS-C does not rule out infection and cardiology evaluation should be based on lab criteria, specifically troponin and NT pro-BNP levels. The antibody test for the virus is not utilized universally\textsuperscript{23} and moreover, the role of IgG and IgM in the disease process is even less well-described.

There are limitations to the manuscript. These cases are described on presentation to enhance the awareness of the cardiac manifestations in children with MIS-C associated with the SARS-CoV2 pandemic. The data is collected from different centers across the world with very different care delivery and economic models which influences the management and laboratory data available on the patients. Coronary Z-scores can be variable based on available scoring systems\textsuperscript{24}, but all institutions in our manuscript utilized the Boston Z-score system so all measurements should be considered consistent. During the early part of the pandemic, the SARS-CoV2 testing rate was low and that does limit our true understanding of the true burden of MIS-C. Further, the cases presented are only those that had consultation with cardiology and there is a potential that
additional patients with MIS-C were undiagnosed and that additional patients with cardiac disease may be been missed. This will likely improve during the course of the pandemic as institutions begin to institute MIS-C protocols based on evolving guidelines. The echocardiographic data is limited due to exposure recommendations during the pandemic and different echocardiography laboratories utilize different protocols for performance and measurements. There is limited follow-up data available, so we are unable to comment on the efficacy of different therapies or the long-term sequela of the cardiac involvement during the SARS-CoV2 pandemic. Three patients were included in our cohort that did not have a documented history of fever with their initial presentation but 2/3 had positive SARS-CoV2 RT-PCR and the third became febrile during the hospital admission. The authors chose to include these patients since they fulfilled other MIS-C criteria, had pediatric cardiology consultation and we understand the subjectivity of parental reporting of fever.

Conclusion

We present the largest international cohort of pediatric patients with symptoms suggestive of MIS-C and cardiovascular manifestations during the SARS-CoV2 pandemic. Ventricular dysfunction was present in 64% of patients with greater than half of those patients with worse than mild dysfunction. A fifth of patients had coronary and pericardial involvement with 11% having clinically relevant arrhythmia or conduction system disease. The clinical picture is distinct from KD but has some overlap with KD diagnostic criteria which is often independent of coronary findings. The range of findings in our cohort, many with mild involvement, emphasizes the need
for continued attention to the potential cardiac involvement in MIS-C and raises the question of the threshold for cardiac investigation in pediatric patients with COVID-19 related illness.

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**Disclosures:** None.

**Supplemental Material:** Table S1.
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Table 1. Demographic, symptoms, laboratory values and initial treatments for overall cohort and patients with cardiac abnormalities; values are presented as number (percentage) or mean ± SEM.

|                              | Overall cohort | Ventricular dysfunction | Coronary abnormalities | Valvulitis | Pericardial effusion |
|------------------------------|----------------|-------------------------|------------------------|------------|---------------------|
| N (%)                        | 55             | 35 (64%)                | 11 (20%)               | 17 (31%)   | 12 (22%)            |
| Age (years)                  | 7 ± 5.2        | 8.4 ± 0.9               | 4.9 ± 1.3              | 8.3 ± 1.2  | 6.8 ±1.5            |
| Weight (kg)                  | 28 ± 3.3       | 33.8 ± 4.8              | 21.3 ± 4.4             | 29.2 ± 4.1 | 26.0 ± 5.3         |
| Length of fever (days)       | 5 ± 0.3        | 4.7 ± 0.4               | 4.5 ± 0.7              | 4.9 ± 0.5  | 4.5 ± 0.5          |
| Fulfill complete KD          | 11 (20%)       | 5 (14%)                 | 2 (18%)                | 0 (0%)     | 5 (45%)            |
| GI symptoms                  | 32 (58%)       | 19 (54%)                | 5 (45%)                | 10 (59%)   | 3 (25%)            |
| WBC (k/uL)                   | 15.0 ± 8.3     | 15.4 ± 1.6              | 21.1 ± 0.3             | 19.0 ± 2.6 | 20.0 ± 3.6         |
| Normal (4.5 – 10.0)          |                |                         |                        |            |                     |
| Platelets (k/uL)             | 281.4 ± 194.2  | 244.4 ± 19.3            | 366.0 ± 80.3           | 213.5 ± 23.0 | 271.9 ± 74.8 |
| Normal (250 – 450)           |                |                         |                        |            |                     |
| NT pro-BNP (pg/mL)           | 284.4 ± 25.8   | 9235 ± 2494             | 5155 ± 3363            | 9235 ± 1703 | 8036 ± 3229     |
| Normal\(^{17}\) (5 – 1,121)|                |                         |                        |            |                     |
|                | 33 (60%) | 18 (51%) | 10 (91%) | 9 (53%) | 7 (58%) |
|----------------|----------|----------|----------|---------|---------|
| IVIG           |          |          |          |         |         |
| Steroids       | 30 (55%) | 19 (54%) | 9 (82%)  | 12 (71%)| 9 (75%) |
| IVIG + steroids| 19 (35%) | 12 (34%) | 8 (73%)  | 6 (35%) | 6 (50%) |

KD: Kawasaki disease, WBC: white blood cell count, IVIG: intra-venous immunoglobulin
Figure Legends:

Figure 1. Cardiac abnormalities in children during the SARS-CoV2 pandemic. WBC: white blood cell count, trop: troponin, CRP: C-reactive protein; GI: gastrointestinal, LVEF: left ventricular ejection fraction, ECG: electrocardiogram, AV: atrioventricular.

Figure 2. Coronary abnormalities in pediatric patients with SARS-CoV2. A) peri-coronary brightness of the left main coronary artery and mild dilation, B) peri-coronary brightness of the right coronary artery, C) aneurysms of the right coronary, left main coronary, circumflex artery and left anterior descending coronary artery in a single patient.

Figure 3. Electrocardiographic findings. A) complete atrioventricular block in a patient with myocardial dysfunction and acute SARS-CoV2 infection (PCR positive) and B) telemetry evidence of transient AV block (Mobitz I) in patient with left ventricular dysfunction and positive SARS-CoV2 PCR.
Cardiac Abnormalities in Children during SARS-CoV2

| Inflammatory Markers          |                      | SARS-CoV2 | PCR + 36% IgG + 35% |
|-------------------------------|----------------------|-----------|---------------------|
| WBC              | 15.000 ± 1.00        |           |                     |
| Lymph %          | 23 ± 3               |           |                     |
| NT-ProBNP        | 7098 ± 1776          |           |                     |
| Trop             | 1.6 ± 0.9            |           |                     |
| CRP              | 21.3 ± 1.9           | SARS-CoV2 |                     |
| Ferritin         | 636 ± 89             |           |                     |

| Symptoms                      |                      |           |
|-------------------------------|----------------------|-----------|
| - Fever                       | 95%                  |           |
| - Rash                        | 49%                  |           |
| - Conjunctivitis              | 33%                  |           |
| - Mucous Membranes            | 29%                  |           |
| - Extremity Swelling          | 22%                  |           |
| - Cervical Adenopathy         | 23%                  |           |
| - GI Symptoms                 | 59%                  |           |

Cardiac Manifestations

- 20% Coronary Vasculitis
- 64% Myocardial dysfunction
- 31% valvulitis
- 22% effusion
- 38% ECG abn
- 11% AV conduction
- Complete Kawasaki
- Heart Failure
- Pericarditis
- Arrhythmia
- Hypotension/Shock (44%)

COVID-19 Pediatric Cardiac Continuum

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SUPPLEMENTAL MATERIAL
| ID | Location | Date of admission | Age | Sex | Ethnicity | Admit t | Presentation | KD criteria | PCR | Ab | LVEF admission | NT-proBN P | Tropo nin | LMC A2-score | RCA Z-score | Echo findings | QTc | ECG comments |
|----|-----------|------------------|-----|-----|-----------|---------|--------------|-------------|-----|----|----------------|------------|-----------|--------------|-------------|---------------|-----|-------------|
| M9 | NYC       | 19-Mar           | 1.5| M   | Black     | ICU     | MIS_C       | 1           | Neg | 60 | 2.3                        | 0.6        | cor invol   | normal       | normal      | normal        |     |             |
| B8 | BCN       | 23-Mar           | 3   | F   | white     | ICU     | MIS_C       | 4           | Neg | 63 | 0.2                        | -1         | normal      | normal       | normal      | normal        |     |             |
| P5 | PAK       | 28-Mar           | 1   | M   | South Asian | ICU     | Heart Failure | 30         | 23750 | 1.2 | 1                         | 0.5        | pEff        | normal       | normal      | normal        |     |             |
| P6 | PAK       | 2-Apr            | 2.5 | F   | South Asian | MIS_C   | 5           | 45         | 1860 | 0.8 | 3.2                        | 2.6        | cor invol, pEff | normal       | normal      | normal        |     |             |
| M10| NYC       | 3-Apr            | 3   | F   | Hispanic  | MIS_C   | 3           | Positive   | 64   | -0.79 | 0.02 | normal       | normal      | normal      | normal       | normal      | normal        |     |             |
| P1 | PAK       | 3-Apr            | 14  | M   | South Asian | ICU     | Heart Failure | 40         | 1898 | 0.117 | 1                         | 1          | 420        | normal       | normal      | normal        |     |             |
| M1 | NYC       | 7-Apr            | 18  | M   | Hispanic  | ICU     | Heart Failure | 0          | Positive | 25 | 887                         | 0.22       | normal      | normal       | normal      | normal        |     |             |
| NO1| NO        | 7-Apr            | 12  | F   | Asian     | ICU     | Heart Failure | 0          | Positive | 27 | 953                         | 38.4       | 0.29       | 0.94         | 417         | CAV Block     |     |             |
| M11| NYC       | 8-Apr            | 6   | M   | Hispanic  | MIS_C   | 4           | Neg        | 59   | 0.11 | 0.16 | normal       | normal      | normal      | normal       | normal      | normal        |     |             |
| B7 | BCN       | 9-Apr            | 1.5 | F   | white     | MIS_C   | 4           | Neg        | 64   | 79   | 0.004 | 2.3                        | 1.3        | cor invol, pEff | normal      | normal      | normal        |     |             |
| B5 | BCN       | 12-Apr           | 11  | F   | white     | MIS_C   | 2           | Positive   | 62   | 2930 | 0.084 | 0.5                       | 0.5        | normal      | normal       | normal      | normal        |     |             |
| B6 | BCN       | 12-Apr           | 11  | F   | white     | MIS_C   | 2           | Positive   | IgG+ | 68   | 5500 | -1.3                      | -0.1       | mild MR/TR | normal       | normal      | normal        |     |             |
| M2 | NYC       | 12-Apr           | 0.2 | M   | Hispanic  | ICU     | Heart Failure | 0          | Positive | 38 | 15000 | 0.16 | 2                        | cor invol, severe MR, LV dilation | 441 | Sinus tachy, flattened T-waves |
| M3 | NYC       | 12-Apr           | 5   | M   | Hispanic  | ICU     | Heart Failure | 0          | Neg *  | 41 | 1354 | 0.01 | pEff                  | 412 | Sinus tachy |
| P7 | PAK       | 14-Apr           | 2   | M   | Pakistan  | ICU     | Heart Failure | 32         | 12536 | 0.2 | 0.5                        | 0.7        | MR         | 360 | normal       |              |             |
| U2 | UK        | 16-Apr           | 4   | M   | Black     | ICU     | Heart Failure | Neg | IgG+ | 55 | 0.25 | pEff, mild MR, TR | Sinus tachy, flattened T-waves | 406 | normal       |
| B4 | BCN       | 19-Apr           | 7   | M   | white     | MIS_C   | 3           | Neg        | IgG+  | 59 | 4730 | -0.7        | -0.2       | 406        | normal       |             |              |             |
| B1 | BCN       | 20-Apr           | 0.3 | M   | Asian     | MIS_C   | 2           | Neg        | IgG+  | 80 | 3682 | 0.001        | 4.8        | 4.7        | cor invol, mild AR | 415 | Sinus tachy, flattened T-waves, ST changes |
| U3 | UK        | 20-Apr           | 0.2 | M   | Asian     | ICU     | Heart Failure | Neg | 0.0168 |             | 0.0168 |             | Sinus tachy |
| B3 | BCN       | 21-Apr           | 3.0 | F   | white     | MIS_C   | 5           | Neg        | IgG+  | 65 | 7990 | 0.2         | -0.9       | normal     |             |              |             |
| M5 | NYC       | 22-Apr           | 7.0 | F   | Arabic   | ICU     | Heart Failure | 0          | Pos   | 48 | 12509 | 0.01 | pEff, mild MR/TR | 400 | Sinus tachy, flattened T-waves |
| B2 | BCN       | 23-Apr           | 1.6 | M   | white     | MIS_C   | 4           | Pos        | IgG+  | 61 | 647  | 1.2         | -0.2       | normal     |             |              |             |
| M4 | NYC       | 23-Apr           | 6   | M   | Black     | ICU     | MIS_C       | 0          | Neg   | 55 | 12827 | 0.01        | 403        | sinuc tachy |             |              |             |
| M6 | NYC       | 23-Apr           | 8   | M   | Hispanic  | ICU     | Heart Failure | 0          | Neg   | 38 | 15000 | 0.13 | Mild MR/TR, mild LV dilation | 462 | Sinus tachy, flattened T-waves, ST changes |
|    |           |                  |     |     |           |         |             |            |       |     |             |            |            |             |              |              |             |

**Table S1. MIS-C SARS – Cov2 Patient Characteristics; UK: United Kingdom, BCN: Barcelona, PAK: Pakistan, NYC: New York City, NO: New Orleans; MIS-C: Multisystem Inflammatory Syndrome in Children temporary associated to COVID-19; ICU: Intensive Care Unit; Neg: negative; cor invol: coronary involvement; pEff: pericardial effusion, MR: mitral regurgitation, TR: tricuspid regurgitation**
| ID  | Gender | Age | Race | Hospital  | Length of Stay | ECG Abnormalities | Testing | Pulmonary Hypertension | Pericardial Effusion | Medications |
|-----|--------|-----|------|-----------|----------------|-------------------|---------|------------------------|------------------|-------------|
| U4  | M      | 23  | White| MIS_C     | 9              | Sinus tachy, flattened T-waves | Pos     | Mild MR/TR             |                  |             |
| B11 | M      | 24  | White| MIS_C     | 3              | Sinus tachy, flattened T-waves | Neg     | Mild MR/TR             |                  |             |
| M7  | F      | 25  | Black| ICU       | 12             | Sinus tachy, flattened T-waves | Neg     | Mild MR/TR             |                  |             |
| U14 | M      | 25  | Black| ICU       | 9              | Sinus tachy, flattened T-waves | Neg     | Mild MR/TR             |                  |             |
| B16 | M      | 26  | White| MIS_C     | 2              | Sinus tachy, flattened T-waves | Neg     | Mild MR/TR             |                  |             |
| P8  | F      | 26  | South Asian| MIS_C | 5              | Sinus tachy, flattened T-waves | Neg     | Mild MR/TR             |                  |             |
| B12 | M      | 27  | White| MIS_C     | 14             | Sinus tachy, flattened T-waves | Neg     | Mild MR/TR             |                  |             |
| U8  | M      | 27  | Black| MIS_C     | 12             | Sinus tachy, flattened T-waves | Neg     | Mild MR/TR             |                  |             |
| U13 | M      | 27  | Black| MIS_C     | 12             | Sinus tachy, flattened T-waves | Neg     | Mild MR/TR             |                  |             |
| B9  | M      | 28  | Arabic| ICU       | 12             | Sinus tachy, flattened T-waves | Neg     | Mild MR/TR             |                  |             |
| B10 | M      | 28  | White| MIS_C     | 3              | Sinus tachy, flattened T-waves | Neg     | Mild MR/TR             |                  |             |
| U9  | M      | 28  | White| MIS_C     | 1.8            | Sinus tachy, flattened T-waves | Neg     | Mild MR/TR             |                  |             |
| U11 | M      | 28  | Black| MIS_C     | 12             | Sinus tachy, flattened T-waves | Neg     | Mild MR/TR             |                  |             |
| U6  | F      | 29  | Asian | MIS_C     | 13             | Sinus tachy, flattened T-waves | Neg     | Mild MR/TR             |                  |             |
| U7  | M      | 29  | White| MIS_C     | 5              | Sinus tachy, flattened T-waves | Neg     | Mild MR/TR             |                  |             |
| U5  | M      | 30  | White| MIS_C     | 2              | Sinus tachy, flattened T-waves | Neg     | Mild MR/TR             |                  |             |
| U10 | F      | 30  | Black| ICU       | 9              | Sinus tachy, flattened T-waves | Neg     | Mild MR/TR             |                  |             |
| U12 | F      | 1-May | Black| ICU       | 7              | Sinus tachy, flattened T-waves | Neg     | Mild MR/TR             |                  |             |
| M12 | F      | 2-May | Black| ICU       | 8              | Sinus tachy, flattened T-waves | Neg     | Mild MR/TR             |                  |             |
| M13 | M      | 3-May | Black| MIS_C     | 5              | Sinus tachy, flattened T-waves | Neg     | Mild MR/TR             |                  |             |
| P2  | M      | 3-May | Black| ICU       | 1.7             | Sinus tachy, flattened T-waves | Neg     | Mild MR/TR             |                  |             |
| P3  | M      | 3-May | Black| ICU       | 6              | Sinus tachy, flattened T-waves | Neg     | Mild MR/TR             |                  |             |
| B13 | M      | 4-May | Black| ICU       | 3              | Sinus tachy, flattened T-waves | Neg     | Mild MR/TR             |                  |             |
| NO2 | M      | 4-May | Black| MIS_C     | 16             | Sinus tachy, flattened T-waves | Neg     | Mild MR/TR             |                  |             |
| NO3 | NO | 4-May | 17 | F  | Black | ICU | MIS_C | 4 | Neg | IgG+ | 5S  | 130 | 3.22 | 0.55 | 0.15 | 426 | first degree AV block |
|-----|----|-------|----|----|-------|-----|-------|---|-----|------|-----|-----|------|------|------|-----|---------------------|
| P9  | PAK| 7-May | 16 | M  | South Asian | 0   | Heart Failure | 35 | 11862 | 0.5   | 1.2 | 1.5 | pEff, mild MR | 420 |