Cardiac involvement in children with multisystem inflammatory syndrome (MIS-C) following infection with different SARS-CoV-2 variants

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Revised Abstract

Background: MIS-C is a hyper inflammatory condition following SARS-CoV-2 infection. Although COVID-19 infection rates and severity have varied based on circulating SARS-CoV-2 variants, it is unclear if cardiac involvement in MIS-C varies following infection with different SARS-CoV-2 variants. Objective: The objective of this study is to describe the severity of cardiac involvement in children with MIS-C following three different waves of SARS-CoV-2 infections.

Methods: Children hospitalized with a diagnosis of MIS-C were enrolled in a prospective observational study. Demographic, clinical, laboratory (troponin I and B-type natriuretic peptide (BNP)), electrocardiogram (EKG) and echocardiogram (ECHO) data for children diagnosed between 4/20 and 12/21 and followed at 1- and 6-months was analyzed. The cohort was divided into 3 groups to represent cases that followed infection with the Wuhan (4/20-10/20, group 1), Alpha (B.1.1.7, 11/20-7/21, group 2) and Delta (B.1. 617.2, 8/21-12/21, group 3) variants. Cardiac involvement during hospitalization and follow-up was compared between the groups.

Results: The cohort includes 131 children with MIS-C, divided into three groups to reflect infections caused by Wuhan, Alpha and Delta strains of SARS-CoV-2. The median age was 10 years and the majority affected were male (66.4%) and Black (49.6%). At MIS-C diagnosis, elevated troponin and brain type natriuretic peptide (BNP) were detected in 52% and 82% of children. Abnormal electrocardiogram (EKG) and decreased left ventricular (LV) function were evident in 25% of the cohort (EKG - 28/112, 25%; LV – 33/131, 25%) with no significant differences between the three groups (p = 0.14 for EKG and p = 0.79 for LV function). Coronary artery (CA) dilatation (Z score > 2.5) was detected in 3/131 (2.35%) during hospitalization. BNP and troponin I were normal in all children with short and mid-term follow up. EKGs obtained at short and mid-term follow up were normal in a majority. ECHO was normal in 103 children with short-term and 47 children with mid-term follow up.

The cohort includes 131 children with MIS-C (32, 61 and 38 in groups 1, 2 and 3, respectively) with a median age of 10 years. Two-thirds were male (66.4%) and 49.6% were Black. Elevated BNP and troponin I levels were seen in 82% and 52.7% of children at initial diagnosis. A third of the cohort had at least one abnormal EKG finding. The proportion of children with abnormal laboratory and EKG findings was not different between the groups. Decreased left ventricular function on ECHO was seen in 25% (33/131) of the cohort with similar distribution among the three groups (p = 0.79). Trivial-small pericardial effusions were detected in 22% (29/131). Coronary artery abnormalities were detected in 11.45% (15/131), a majority in group 1 (25%; 8/32). At 1- and 6-monthfollow-up visits, BNP and Troponin I were normal in all children. At the 6-month follow-up visit, EKG was normal in all and ECHO was normal in 37/41 children with trivial to mild valvular regurgitation in four children.

Conclusion: In this prospective cohort study, favorable short- and mid-term cardiac outcomes were observed in children with MIS-C, irrespective of infection following different SARS-CoV-2 variants (Wuhan vs Alpha vs Delta).

Introduction

- Multisystem inflammatory syndrome in children (MIS-C) is a hyper inflammatory condition temporally associated with SARS-CoV-2 infection with a significant overlap with other entities like Kawasaki disease (KD) and toxic shock syndrome (TSS) with clinical presentation and treatment.
- COVID-19 infection rates and severity vary depending on SARS-CoV-2 variant, and COVID-19 vaccination status
- Cardiac involvement has remained a prominent feature of MIS-C but the impact of SARS-CoV-2 variants on extent and severity of cardiac involvement in MIS-C remains to be explored
- Determining the extent of cardiac involvement and outcomes in MIS-C following infection with different variants to-date will help with appropriate planning for future waves of MIS-C and understanding the pathogenesis of this entity.

Objective

The objective of this study is to describe acute cardiac involvement and short-, and mid-term cardiac outcomes in children with MIS-C that followed three different waves of the SARS-CoV-2 infection during the first two years of the Pandemic.

Materials and Methods

Study population: Early during the SARS-CoV-2 pandemic, a multi-disciplinary clinic was established to monitor children with MIS-C hospitalized at Children's of Alabama (COA)/University of Alabama at Birmingham (UAB). Children, 0-21 years at hospital admission that met the CDC diagnostic criteria for MIS-C and admitted to COA/UAB between April 2020 and December 2021were included in this study.

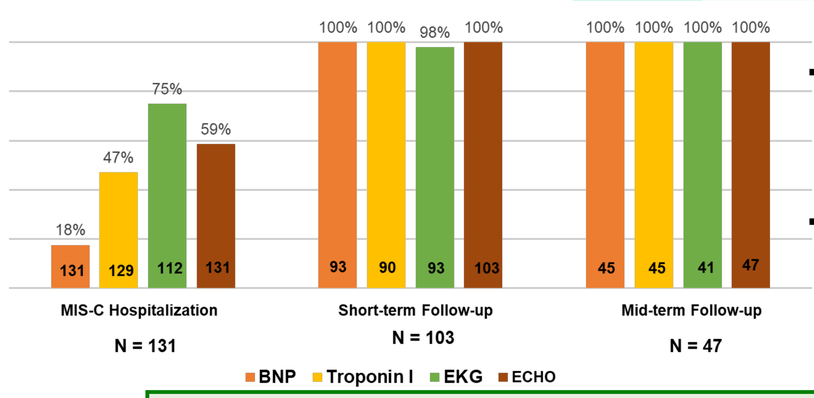
Follow-up: Children diagnosed with MIS-C at admission were monitored as outpatients at 4-6 weeks (short-term) and six months (mid-term) after initial diagnosis with serial laboratory, electrocardiogram (EKG) and echocardiograms (ECHO) at these visits in a multi-disciplinary clinic.

Methods: Laboratory, EKG and ECHO findings were collected at the diagnosis and follow-up visits. Troponin I > 0.04 ng/ml and BNP > 100 pg/ml were considered to be outside of normal range. EKG data was coded as normal/abnormal (non-specific ST and T wave changes (NS ST-T changes), prolonged QT interval and right and/or left bundle branch blocks (RBBB/LBBB). Data on following ECO parameters was collected - 1) qualitative left ventricular (LV) systolic function (normal or decreased – mild, moderate and severe) 2) quantitative LV systolic function (ejection fraction (EF) normal (> 54%), mild decrease (45-54%), moderate decrease (35-44%) and severe (< 35%), 3) pericardial effusion (present/absent),4) coronary artery involvement [normal vs dilatation (Z score > 2.5)]. The cohort is divided into three groups for comparison depending on predominant SARS-CoV-2 variant during the Pandemic: 1) Group 1 includes children with MIS-C diagnosed between April, 2020 and Oct, 2020 (Wuhan strain), 2) Group 2 includes MIS-C diagnosed between Nov, 2020 and July, 2021 (Alpha – B.1.1.7) and 3) Group 3 includes those children diagnosed between August, 2021 and Dec, 2021 (Delta – B.1. 617.2).

Results

- 131 children met the CDC criteria for MIS-C
- Groups 1, 2 and 3 included 32, 61 and 38 children respectively to reflect MIS-C that followed infections caused by the Wuhan, Alpha and Delta variants
- Median Age: 10 years (CI: 8.8 -12 years)
- Predominant Sex: Male (66.4%)
- Predominant Race and Ethnicity: Black non-Hispanic (49.6%)
- Median hospitalization duration: 4 days (3-6 days)
- At MIS-C diagnosis:
  - ~ 53% with elevated troponin
  - 82% with BNP elevation
  - 25% (28/112) with EKG abnormalities
  - 41% (54/131) with ECHO abnormalities
  - 2.3% with dilated coronary arteries (CA)

Timelines for Cohorts	Entire Cohort	Group 1 (4/20 – 10/20)	Group 2 (11/20- 7/21)	Group 3 (8/21- 12/21)	P value
N	131	32	61	38	-
Laboratory Analysis					
SARS-CoV-2 PCR+	33/131 (25.2%)	9/32 (28.1%)	23/61 (37.7%)	1/38 (2.6%)	0.7
SARS-CoV-2 IgG +	123 (93.9%)	25/32 (78%)	59/61 (96.7%)	38/38 (100%)	0.9
Elevated Troponin	68/129 (52.7%)	20/32 (62.5%)	30/59 (50.84%)	18/38 (47.4%)	0.4
Elevated BNP	108 (82.4%)	27/32 (84.4%)	50/61 (81.9%)	31/38 (81.6%)	0.94
Electrocardiogram (EKG)					
Abnormal EKG	28/112 (25%)	7/29 (24%)	16/48 (33.3%)	5/35 (14.3%)	0.14
NS ST-T wave	26	6	15	5	
1º AV block	1	1	0	0	
RBBB	1	0	1	0	
Echocardiogram (ECHO)					
Abnormal ECHO	54/131 (41.2%)	16/32 (50%)	24/61 (39.3%)	14/38 (36.8%)	0.5
Left Ventricular Dysfunction	33/131 (25.2%)	8/32 (25%)	14/61 (22.9%)	11/38 (28.9%)	0.79
Mild	21	5	9	7	
Moderate	9	2	4	3	
Severe	3	1	1	1	
Pericardial Effusion	29/131 (22.1%)	10/32 (31.2%)	13/61 (21.3%)	6/38 (15.8%)	0.29
Dilated CA Z score > 2.5	3/131 (2.3%)	2/32 (6.2%)	0/61 (0%)	1/38 (2.6%)	-



- 103 children with short-term follow-up
  - 100% with normal BNP and troponin I
  - 98.9% with normal EKG findings
  - 100% normal ECHO findings
- 47 children with mid-term follow-up
  - 100% with normal BNP and troponin I levels
  - 100% with normal EKG findings
  - 100% with normal ECHO findings

Conclusions

In this single center prospective cohort study of children with MIS-C,

- We demonstrate demonstrate favorable short- and mid-term cardiac outcomes in children with MIS-C
- No observed differences in the frequency and severity of cardiac involvement during the acute phase and at short and mid-term follow-up, irrespective of infecting SARS-CoV-2 variant (Wuhan vs Alpha vs Delta).

References

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