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Cardiac Complications in Children with Acute COVID-19 vs. Multi-system Inflammatory Syndrome in Children (MIS-C)

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An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
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Abstract

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By Matthew Hensley

Background

Multisystem Inflammatory Syndrome in Children (MIS-C) is associated with COVID-19 infection, but not much is understood about its pathophysiology and how outcomes of MIS-C differ from those of acute COVID-19 infection. The specific areas of uncertainty and research need include frequency, determinants, and clinical features of cardiovascular involvement among children diagnosed with acute COVID-19 and MIS-C.

Methods

We conducted a retrospective analysis of data obtained from the clinical records of patients admitted to Children's Healthcare of Atlanta hospitals from March 2020 to August 2021. Study population consisted of those admitted for symptoms of acute-COVID 19 infection or patients meeting the CDC criteria for MIS-C. Cardiovascular involvement was defined by one or more of the following: elevated troponin, elevated brain natriuretic peptide (BNP), reduced ejection fraction (EF), an abnormal EKG reading, requirement of vasoactive medications, and presence of coronary dilation. Multivariable logistic regression was used to analyze associations between cardiovascular involvement and age, race/ethnicity, and comorbidities. For the MIS-C cohort, cardiovascular involvement was broken down into individual factors for analysis. The results of logistic regression analyses were expressed as crude and adjusted odds ratios (OR) and the corresponding 95% confidence intervals (CI).

Results

We analyzed 346 acute COVID-19 patients with median age of 8.9 years and 304 MIS-C patients with a median age of 9.1 years. Cardiovascular involvement was present in 258 MIS-C patients (84.9%) and 36 of acute COVID-19 patients (10.4%). Among acute COVID-19 patients, obesity was statistically significantly associated with cardiovascular involvement. Among MIS-C patients, statistically significant associations included obesity, age >5 years, and non-Hispanic Black race/ethnicity.

Conclusions

There is a striking difference in the likelihood of cardiovascular involvement among patients with MIS-C vs. acute COVID-19 as well as statistically significant associations with obesity, race/ethnicity, and age. These results reinforce our institutional practice of following all patients with MIS-C in cardiology clinic while limiting follow up of acute COVID-19 to those with evidence of cardiovascular involvement.

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Introduction

Starting in December 2019, a new strain of virus, known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV2), has led to a pandemic with high morbidity and mortality.[1] The impact of the resulting disease, coronavirus disease 2019 (Covid-19) has been felt across the world; however, initial reports indicated that severe disease in children was much less common than in adults.[2]

An early study in February 2020 by the Chinese Center for Disease Control indicated only 5.8% of cases in children being classified as severe or critical compared to 18.5% in adult patients.[3,4] Among pediatric patients with severe or critical COVID-19, a majority were under the age of 1 year. This difference in severity by age has continued to be consistently reported in other parts of the world. As of March 2022, the US Centers for Disease Control and Prevention (CDC) estimated that children (age 17 and under) represent only 17.6% of the total known cases despite representing 22.3% of the population.[5] An earlier CDC study reported that the risk of hospitalization among children was 8 per 100,000 population, an estimate that was more than 20 times lower compared to the corresponding risk of 164.5 per 100,000 population among adults.[6]

The etiology behind the difference in severity between age groups is not fully understood. This may be because children had less exposure being more confined within the household. There could also be important age-related differences in how the immune system responds to the virus.[7]

Another important distinction might be in the presence of significant comorbidities that are more common among adults. In a study of 713 pediatric patients hospitalized for COVID-19 in July-August of 2021, two-thirds of participants had one or more underlying medical conditions. Specifically, 83% of patients aged 5-11 and 88% of patients aged 12-17 had

identifiable co-morbidities with the most common underlying condition being obesity (32.4%).[8] We can compare this to a different study on 178 adult patients admitted to the hospital in March 2020 where 89.3% were found to have one or more comorbidities, most commonly hypertension (49.7%) and obesity (48.3%).[9] These data appear to indicate that among hospitalized COVID-19 patients the overall prevalence of comorbidities was comparable across age groups, and obesity was commonly present among both children and adults..

Another key factor associated with hospitalization for COVID-19 is race/ethnicity. Whereas racial/ethnic disparities in COVID-19 hospitalization rates among adults are well documented[10], similar observations are reported for pediatric age groups. In one recent study, the risk of hospitalization among Hispanic or Latino and non-Hispanic black children was 16.4 and 10.5 per 100,000 population respectively; substantially higher than the corresponding risk of 2.1 per 100,000 among non-Hispanic white children.[6] It is important to note, however, that the observed disparities in this study may be attributable to differences in the distributions of comorbidities because racial/ethnic minority children had higher prevalence of comorbidities, 45% among Hispanics and 29.8% among Non-Hispanic Blacks, compared to 14.9% in their non-Hispanic white peers. Another factor that warrants consideration is the potentially higher levels of SARS-CoV2 exposure among Hispanic adults due to greater proportion of individuals engaged in direct-service occupations with decreased opportunities for social distancing, which in turn may lead to more severe disease among children in the same household.[10]

While children with COVID-19 appear to be less likely to have severe acute complications, there is a peculiar syndrome that can develop weeks after an acute infection. In April 2020, clinicians in the United Kingdom began reporting cases of previously healthy children presenting with cardiac shock, fever, and hyperinflammation.[11] The following month the

CDC requested the reporting of cases meeting criteria for a multisystem inflammatory syndrome in children (MIS-C).[12]

As the data on MIS-C accumulates, the case definition of this condition continues to evolve. The current CDC definition includes age <21 years, fever, laboratory evidence of inflammation, clinically severe illness with 2 or more organ systems involved, evidence of current or recent SARS-CoV-2 infection within 4 weeks of onset of symptoms, and no alternative plausible diagnosis.[13] Given such a broad definition, there is still a gap in the understanding of factors that could help to differentiate MIS-C from other diagnoses. Especially limited is the datum that would permit a direct comparison of patients with acute COVID-19 and those who develop MIS-C.

With these knowledge gaps in mind, the purpose of the present study was to compare cardiovascular involvement among pediatric COVID-19 patients hospitalized for the acute disease to those who were admitted with the diagnosis of MIS-C. We hypothesize, based on clinical experience, that patients admitted for MIS-C will be more likely to experience cardiovascular involvement than patients admitted for acute COVID-19.

Methods

This is a retrospective analysis of the data obtained from the clinical records of patients admitted to Children's Healthcare of Atlanta hospitals from March 2020 to August 2021. Patients were considered eligible for inclusion if they were admitted for either acute COVID-19 or MIS-C. The acute COVID-19 cohort included patients admitted with one or more typical symptoms and a positive polymerase chain reaction (PCR) test. Patients with incidental findings

of SARS-CoV-2 but whose primary admission was for another reason were excluded. Patients included in the MIS-C cohort met the previously described CDC case definition.[13]

The data on each eligible cohort member were collected using the Research Electronic Data Capture (REDCap) system. Data collected included demographics, cardiac biomarkers, electrocardiography (EKG) results, use of vasoactive medications, and echocardiogram results. Information on comorbidities including asthma, obesity, congenital heart disease, and presence of a chromosomal or genetic syndrome, was also captured from the electronic medical record.

The presence of cardiovascular involvement was defined as having one or more of the following during hospitalization: elevated troponin, elevated brain natriuretic peptide (BNP), reduced left ventricular ejection fraction (EF), an abnormal EKG reading, requirement of vasoactive medications, and presence of coronary dilation. Elevated troponin was defined as any measurement above 0.015 ng/mL at any point during hospitalization and elevated BNP was defined as any measurement above 400 pg/mL. These cut-offs were chosen for consistency with previous studies.[2, 14] Reduced EF was defined as any measurement of left ventricular ejection fraction below 55% on any echocardiogram during hospitalization. Echocardiogram measurements were also used to determine presence of coronary dilation. The EKG results in both cohorts were reviewed by a single cardiologist for consistency and classified as ‘abnormal’, ‘borderline’, or ‘normal’. Only EKG results denoted as ‘abnormal’ were included in the definition of cardiovascular involvement. Receipt of any vasoactive medications such as epinephrine or norepinephrine for episodes of shock or to maintain blood pressure was also used as evidence of cardiovascular involvement.

Distributions of participant characteristics were examined by calculating counts and percentages for categorical variables and median values and interquartile ranges (IQR) for

continuous variables. Factors associated with cardiovascular involvement were examined by performing two sets of logistic regression analyses. The first logistic regression analysis focused on acute COVID-19 patients and the outcome of interest was defined as any type of cardiovascular involvement. In the second analysis, the sample was limited to MIS-C patients and the outcomes of interest were defined based on the distinctive features of cardiovascular involvement. The results of logistic regression analyses were expressed as crude and adjusted odds ratios (OR) and the corresponding 95% confidence intervals (CI). All data analyses were performed using Statistical Analysis System (SAS) software, version 9.4 (SAS Institute, Cary, NC).

Results

As shown in Table 1, there were 346 patients with a diagnosis of acute COVID-19 and median age of 8.92 years old (IQR 1.56-15.44). The race/ethnicity distribution of acute COVID-19 patients was 86 (24.86%) non-Hispanic White, 168 (48.55%) non-Hispanic Black, 75 (21.67%) Hispanic, and 11 (3.18%) reported as other race/ethnicity. Comorbidities were present in 205 (59.25%) with asthma being the most common at 85 children (24.57%).

There were 304 patients with a diagnosis of MIS-C with a median age of 9.11 years old (IQR 5.93-12.66). Among those, 57 (18.75%) were non-Hispanic White, 188 (61.84%) were non-Hispanic Black, 48 (15.79%) were Hispanic, and 11 (3.62%) were marked as “Other” race/ethnicity. Comorbidities were present in 125 participants (41.12%) with obesity being the most common type, affecting 88 children (28.95%).

Cardiovascular involvement was present in 258 MIS-C patients (84.9%) and 36 of acute COVID-19 patients (10.4%). Elevated troponin was the predominant clinical feature that was

found in 206 of 258 (79.8%) patients with cardiovascular involvement (Table 2). Other clinical features of cardiovascular involvement (in descending order of frequency) included elevated BNP (n=180, 69.8%), reduced EF (160, 62.02%), vasoactive medication requirement (n=126, 48.8%), abnormal EKG (n= 53, 20.5%), and dilated coronaries (n=32, 12.4%). Among patients with cardiovascular involvement in the acute COVID-19 group, 7 (19.4%) had elevated troponin, 5 (13.9%) had elevated BNP, 1 (2.8%) had reduced EF, 8 (22.2%) required vasoactive medications, and 26 (72.2%) had abnormal EKG.

Among acute COVID-19 patients (Table 3), obesity was the only factor statistically significantly associated with cardiovascular involvement with an adjusted OR of 2.56 (95% CI: 1.03-6.36). The results of the crude and adjusted logistic regression analyses evaluating factors associated with different clinical features of cardiovascular involvement in the MIS-C cohort are presented in Tables 4 and 5. Obesity was statistically significantly associated with elevated troponin and reduced EF with adjusted OR (95% CI) estimates of 1.99 (1.09-3.64) and 2.03 (1.19-3.46), respectively (Table 5). Other notable findings included significantly higher odds of elevated BNP (OR=2.28), reduced EF (OR=2.11) and vasoactive medication requirements (OR=2.69) among non-Hispanic Black patients relative to their non-Hispanic white counterparts. Using children under the age of 5 years as the reference category, participants in the oldest age group (≥12 years) were especially likely to have elevated troponin (OR=2.85; 95% CI 1.37-5.91), reduced EF (OR= 2.83; 95% CI 1.38-5.82), and require vasoactive medications (OR=3.6; 95% CI 1.68-7.70). The corresponding results for the 5- to 12-year-old group were generally in the same direction (Table 5).

The breakdown of the various combinations of cardiovascular involvement among patients with MIS-C is depicted in graph 1. The most common combination was having all

factors of cardiovascular involvement except for dilated coronaries at 21.1%. This was followed by having no factors of cardiovascular involvement at 16.5% and BNP>400, elevated troponin, and reduced EF at 10.9%.

Discussion

Using the data on 346 patients diagnosed with acute COVID-19 and 304 patients diagnosed with MIS-C we observed that the two groups demonstrated striking difference in the likelihood of cardiovascular involvement. Almost 85% of MIS-C patients experienced some level of cardiovascular involvement compared to only 10% in the acute COVID-19 group.

While there have been reports of myocarditis in adult acute COVID-19 patients, the development of these inflammation mediated responses is poorly understood.[15, 16] It is also not well understood exactly how COVID-19 is related to the hyperinflammatory response of MIS-C weeks after infection. One study attempted to compare the cytokine storm seen in acute COVID to the hyperinflammatory response in MIS-C and Kawasaki Disease but found that while there was some overlap for MIS-C and Kawasaki disease, both differed from the response seen in acute COVID.[17]

Kawasaki Disease is a vasculitis that appears somewhat similar to MIS-C with respect to both the clinical presentation and the proposed pathophysiological mechanism. It is thought that in both condition there is production of self-reactive antibodies in a hyperinflammatory response shortly after an acute viral infection.[17] Kawasaki Disease has a high incidence in East Asian ancestry so there is thought to be a genetic predisposition, but no such pattern has been discovered yet for MIS-C.

In both cohorts, obesity was found to be an important comorbidity. Among COVID-19 patients, obesity was the only factor significantly associated with cardiovascular involvement, and among MIS-C patients it was fairly consistently related to various clinical features. Previous studies have shown that obesity is a common underlying condition for both COVID-19 and MIS-C.[8, 18] Additionally, obesity has been found to be associated with cardiovascular disease and proinflammatory mediators found to be associated with cardiometabolic dysfunction.[19] This could mean that obese children are already more susceptible to cardiovascular involvement, but more research would need to be done to investigate a possible inflammatory connection.

Whereas race and ethnicity were not associated with cardiovascular involvement in the acute COVID-19 group, there were notable racial, especially Black-White, disparities in relation to clinical findings, such as elevated BNP, reduced EF and need for vasoactive medications, in the MIS-C cohort. Previous studies have shown higher rates of MIS-C among non-Hispanic Black children even after controlling for COVID-19 rates.[20] It is possible that the observed disparities reflect racial-ethnic differences in predisposition like that suggested for Kawasaki disease.

Our results are similar to a previous retrospective study on MIS-C that found statistically significant results with higher odds ratios for decreased cardiac function among non-Hispanic Black vs. non-Hispanic White patients (OR=1.7, 95% CI 1.1–2.8) as well as age groups 6-12 years (OR 1.7, 95% CI 1.2-2.5) and 13-20 years (OR=2.4, 95% CI 1.6–3.7) vs. ages 5 years and under.[21] Their analysis also included the comorbidity of obesity, but results were not statistically significant.

There are several limitations to our study. First, in our institution, assessment for cardiac involvement is part of standard of care for MIS-C, but not for acute COVID-19. Thus,

echocardiogram, electrocardiogram, and cardiac biomarker evaluation were obtained in patients with COVID-19 only if there was clinical suspicion for an abnormality. This could lead to under-ascertainment of cardiac involvement in those with acute COVID-19. However, it was reassuring that the use of vasoactive medications – medicines that are typically dictated by clinical scenario – were likewise not common in those with acute COVID-19 (2.3%, as compared to 41% in those with MIS-C). Secondly, as a tertiary hospital, those with more severe cardiovascular involvement may be referred to our center for care. This could mean that MIS-C patients with less cardiovascular involvement were not seen at our hospital and lead to our sample of MIS-C patients having an erroneously high proportion of cardiovascular involvement. Another limitation is that in a large healthcare center we do not have uniform reading of EKGs, echocardiograms, and decision to use vasoactive medications. Different cardiologists could disagree on whether a certain reading is truly abnormal or if the status of the patient is severe enough to warrant certain vasoactive medications. This is unlikely to be a major contributor as decision making is not always up to a single individual due to institutional guidelines and team conferences, but this could affect generalizability outside of the Children's Healthcare of Atlanta network.

The relatively high likelihood of cardiovascular involvement among MIS-C patients compared to acute COVID-19 patients reinforces our institutional practice of following all patients with MIS-C in cardiology clinic and limiting the follow up of acute COVID-19, to only those with evidence of cardiovascular involvement.[22] Future study is needed to determine how acute COVID-19 and MIS-C may impact long-term cardiovascular health in these patients.

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Tables & Graphs

Table 1: Descriptive characteristics of the study population

Participant Characteristics	**Acute COVID-19** N	%	**MIS-C** N	%
Age group				
<5	143	41.33	59	19.41
5-12	67	19.36	157	51.64
>=12	136	39.31	88	28.95
Race-ethnicity				
Non-Hispanic White	86	24.86	57	18.75
Non-Hispanic Black	168	48.55	188	61.84
Hispanic	75	21.67	48	15.79
Other	11	3.18	11	3.62
Co-morbidities				
Yes	205	59.25	125	41.12
No	141	40.75	179	58.88
Asthma				
Yes	85	24.57	41	13.49
No	261	75.43	263	86.51
Obesity				
Yes	46	13.29	88	28.95
No	300	86.71	216	71.05
Congenital heart disease				
Yes	24	6.94	7	2.3
No	322	93.06	297	97.7
Chromosomal/genetic disorder				
Yes	20	5.78	3	0.99
No	326	94.22	301	99.01
Cardiovascular involvement				
Yes	**36**	**10.4**	**258**	**84.87**
No	310	89.6	46	15.13
Total:	**346**		**304**	

Table 2: Clinical features of patients with cardiovascular involvement

Participant Characteristics	Acute COVID-19		MIS-C	
	N	%*	N	%*
Max BNP>400	5	13.89	180	69.77
Elevated Troponin	7	19.44	206	79.84
Abnormal EKG**	26	72.22	53	20.54
ECHO EF<55%	1	2.78	160	62.02
Dilated coronaries	0	0	32	12.40
Vasoactive medications required	8	22.22	126	48.84
Total	36		258	

*Percent is out of patients within that cohort with cardiovascular involvement

Acronyms and abbreviations: BNP- brain natriuretic peptide, EKG- electrocardiogram, ECHO- echocardiogram, EF- ejection fraction, CI- cardiovascular involvement

Table 3. Factors associated with cardiovascular involvement among acute COVID-19 patients*

Participant Characteristics	Crude		Adjusted	
	OR	95% CI	OR	95% CI
Age group				
<5	1	(reference)	1	(reference)
5-12	1.48	(0.58, 3.81)	1.47	(0.54, 3.99)
>=12	1.67	(0.77, 3.60)	1.29	(0.54, 3.09)
Race-ethnicity				
Non-Hispanic White	1	(reference)	1	(reference)
Non-Hispanic Black	0.912	(0.40, 2.07)	0.85	(0.36, 2.04)
Hispanic	1.17	(0.46, 2.98)	0.90	(0.33, 2.46)
Asthma				
No	1	(reference)	1	(reference)
Yes	0.77	(0.33, 1.77)	0.69	(0.29, 1.65)
Congenital heart disease				
No	1	(reference)	1	(reference)
Yes	2.04	(0.66 - 6.25)	1.93	(0.61, 6.12)
Chromosomal/genetic anomalies				
No	1	(reference)	1	(reference)
Yes	1.80	(0.52, 6.18)	2.07	(0.57, 7.46)
Obesity				
No	1	(reference)	1	(reference)
Yes	2.75	(1.22, 6.19)	2.56	(1.03, 6.36)

*Shaded cells indicate statistically significant results

Table 4. Factors associated with different forms of cardiovascular involvement among MISC patients (crude analyses)*

Participant Characteristics	BNP>400 OR	BNP>400 95% CI	Troponin Elevated OR	Troponin Elevated 95% CI	Reduced EF OR	Reduced EF 95% CI	Vasoactive medications OR	Vasoactive medications 95% CI	Coronary Dilation OR	Coronary Dilation 95% CI
Age group (years)										
<5	1	(reference)	1	(reference)	1	(reference)	1	(reference)	1	(reference)
5-12	1.03	(0.56, 1.91)	2.74	(1.48, 5.09)	1.48	(0.81, 2.71)	1.90	(0.99, 3.66)	1.23	(0.43, 3.51)
≥12	0.73	(0.38, 1.43)	2.61	(1.31, 5.19)	2.68	(1.36, 5.29)	2.81	(1.38, 5.72)	1.56	(0.51, 4.76)
Race-ethnicity										
Non-Hispanic White	1	(reference)	1	(reference)	1	(reference)	1	(reference)	1	(reference)
Non-Hispanic Black	2.43	(1.33, 4.44)	1.67	(0.91, 3.08)	1.83	(1.00, 3.34)	2.41	(1.25, 4.65)	2.04	(0.58, 7.15)
Hispanic	2.29	(1.04, 5.03)	1.77	(0.78, 3.99)	2.07	(0.95, 4.52)	2.00	(0.88, 4.55)	2.57	(0.61, 10.89)
Other	1.65	(0.45, 6.04)	1.94	(0.47, 8.08)	1.23	(0.34, 4.52)	1.60	(0.41, 6.25)	10.29	(1.90, 55.82)
Asthma										
No	1	(reference)	1	(reference)	1	(reference)	1	(reference)	1	(reference)
Yes	0.73	(0.38, 1.43)	0.82	(0.40, 1.67)	0.86	(0.44, 1.70)	1.11	(0.56, 2.18)	0.69	(0.20, 2.40)
Congenital heart disease										
No	1	(reference)	1	(reference)	1	(reference)	1	(reference)	1	(reference)
Yes	0.27	(0.04, 1.66)	0.2	(0.03, 1.21)	1.02	(0.19, 5.54)	<0.001	n/a	<0.001	n/a
Chromosomal/genetic disorder										
No	1	(reference)	1	(reference)	1	(reference)	1	(reference)	1	(reference)
Yes	0.82	(0.06, 12.19)	0.63	(0.04, 9.74)	1.82	(0.13, 26.29)	>1000	n/a	<0.001	n/a
Obesity										
No	1	(reference)	1	(reference)	1	(reference)	1	(reference)	1	(reference)
Yes	1.24	(0.74, 2.07)	1.97	(1.10, 3.51)	2.18	(1.30, 3.65)	1.63	(0.98, 2.70)	0.43	(0.16, 1.16)

*Shaded cells indicate statistically significant results

Acronyms and abbreviations: BNP- brain natriuretic peptide, EKG- electrocardiogram, ECHO- echocardiogram, EF- ejection fraction

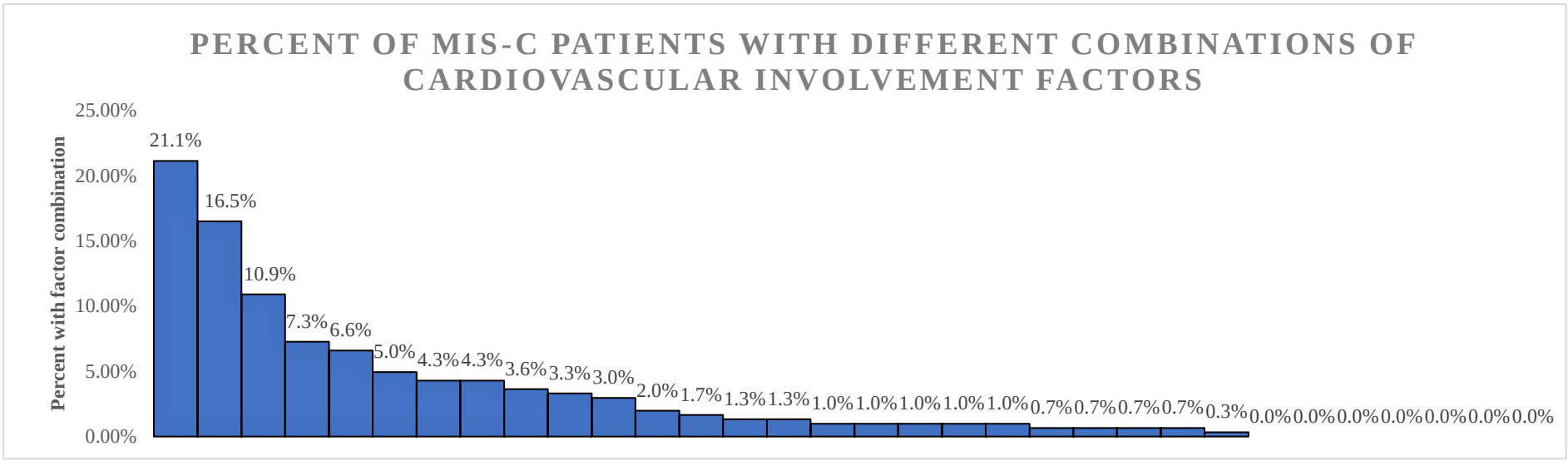
Table 5. Factors associated with different forms of cardiovascular involvement among MISC patients (multivariable analyses)*

Participant	BNP>400		Troponin Elevated		Reduced EF		Vasoactive medications		Coronary Dilation	
Characteristics	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Age group										
<5	1	(reference)	1	(reference)	1	(reference)	1	(reference)	1	(reference)
5-12	1.11	(0.59, 2.08)	3.08	(1.63, 5.83)	1.5	(0.81, 2.81)	2.21	(1.12, 4.38)	1.18	(0.41, 3.45)
>=12	0.81	(0.40, 1.63)	2.85	(1.37, 5.91)	2.83	(1.38, 5.82)	3.6	(1.68, 7.70)	1.7	(0.53, 5.42)
Race-ethnicity										
Non-Hispanic White	1	(reference)	1	(reference)	1	(reference)	1	(reference)	1	(reference)
Non-Hispanic Black	2.28	(1.23, 4.22)	1.72	(0.90, 3.28)	2.11	(1.12, 3.98)	2.69	(1.35, 5.33)	2.01	(0.56, 7.15)
Hispanic	2.18	(0.98, 4.87)	1.62	(0.68, 3.82)	1.88	(0.83, 4.25)	2.01	(0.85, 4.77)	1.01	(-0.46, 2.48)
Other	1.59	(0.43, 5.92)	1.74	(0.40, 7.59)	1.18	(0.31, 4.53)	1.48	(0.37, 6.03)	8.45	(1.5, 47.42)
Asthma										
No	1	(reference)	1	(reference)	1	(reference)	1	(reference)	1	(reference)
Yes	0.79	(0.39, 1.59)	0.77	(0.37, 1.62)	0.75	(0.37, 1.54)	0.98	(0.48, 2.01)	0.79	(0.22, 2.85)
Congenital heart disease										
No	1	(reference)	1	(reference)	1	(reference)	1	(reference)	1	(reference)
Yes	0.35	(0.05, 2.24)	0.19	(0.03, 1.23)	0.94	(0.16, 5.51)	n/a	n/a	n/a	n/a
Chromosomal/genetic disorder										
No	1	(reference)	1	(reference)	1	(reference)	1	(reference)	1	(reference)
Yes	0.65	(0.04, 10.47)	0.73	(0.04, 12.98)	2.68	(0.18, 41.08)	n/a	n/a	n/a	n/a
Obesity										
No	1	(reference)	1	(reference)	1	(reference)	1	(reference)	1	(reference)
Yes	1.28	(0.76, 2.19)	1.99	(1.09, 3.64)	2.03	(1.19, 3.46)	1.53	(0.90, 2.61)	0.4	(0.14, 1.10)

*Shaded cells indicate statistically significant results

Acronyms and abbreviations: BNP- brain natriuretic peptide, EKG- electrocardiogram, ECHO- echocardiogram, EF- ejection fraction

Graph 1: Distribution of cardiovascular involvement factors among patients with MIS-C



BNP>400	Y	N	Y	N	Y	Y	N	Y	Y	N	Y	N	N	N	Y	N	N	Y	Y	Y	N	N	N	Y	N	N	N	N	Y	Y	Y	Y
Troponin Elevated	Y	N	Y	Y	Y	Y	Y	N	Y	Y	N	N	N	Y	N	N	Y	N	Y	Y	N	N	Y	Y	Y	N	N	Y	N	N	N	N
Reduced EF	Y	N	Y	N	N	N	Y	N	Y	Y	Y	Y	N	N	Y	N	Y	N	N	N	Y	Y	N	Y	N	N	Y	Y	N	N	Y	Y
Vasopressors	Y	N	N	N	N	Y	N	N	Y	Y	N	N	Y	Y	Y	N	Y	Y	Y	N	Y	N	Y	N	N	Y	Y	N	Y	N	Y	N
Coronary Dilation	N	N	N	N	N	N	N	N	Y	N	N	N	N	Y	N	Y	Y	N	Y	Y	N	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y