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Socioeconomic and Racial/Ethnic Disparities in Multisystem Inflammatory Syndrome

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Abbreviations: BCH: Boston Children's Hospital; BMC: Boston Medical Center; CDC: Centers for Disease Control and Prevention; CI: Confidence Interval; COVID-19: Coronavirus disease 2019; ICU: Intensive care unit; IQR: Interquartile range; KD: Kawasaki disease; MA: Massachusetts; MGH: Massachusetts General Hospital; MIS-C: Multisystem inflammatory syndrome in children; RT-PCR: Reverse transcriptase polymerase chain reaction; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; SES: Socioeconomic Status; SVI: Social vulnerability index; US: United States

Table of Contents Summary: This multi-institutional case-control study describes how lower socioeconomic status, increased social vulnerability, and minority racial/ethnic background increase the risk of multisystem inflammatory syndrome in children.

What's Known on This Subject: The pandemic has highlighted racial and socioeconomic disparities in children affected by COVID-19. Data suggests that children from Black or Hispanic racial and/or ethnic backgrounds are also at increased risk for development of multisystem inflammatory syndrome in children (MIS-C).

What This Study Adds: In this multi-institutional case control study, children from minority racial and/or ethnic backgrounds were found to be disproportionately at risk for development of MIS-C, and this finding could not be entirely accounted for by socioeconomic status or social vulnerability index.

Contributors Statements

Dr. Javalkar and Dr. Robson contributed to study design, collected data, contributed to data interpretation, drafted the initial manuscript, and reviewed and revised the manuscript.

Dr. Gaffney contributed to data interpretation, and reviewed and revised the manuscript.

Ms. Bohling, Dr. Arya, Dr. Servattalab, Dr. Sekhavat, and Dr. Kobayashi collected data and reviewed and revised the manuscript.

Dr. Roberts and Dr. Campell collected data, contributed to data interpretation, and reviewed and revised the manuscript.

Dr. Newburger, Dr. de Ferranti, Ms. Baker, Dr. Lee, Ms. Day-Lewis, Dr. Bucholz, Dr. Son, Dr. Henderson, and Dr. Kheir contributed to data interpretation and reviewed and revised the manuscript.

Dr. Friedman conceptualized and designed the study, and reviewed and revised the manuscript. Dr. Dionne conceptualized and designed the study, coordinated and supervised data collection, carried out the data analysis, and reviewed and revised the manuscript.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Abstract

Objective: To characterize the socioeconomic and racial/ethnic disparities impacting the diagnosis and outcomes of multisystem inflammatory syndrome in children (MIS-C).

Methods: This multicenter retrospective case-control study was conducted at 3 academic centers from January 1 to September 1, 2020. MIS-C cases were compared to 5 separate control groups: children with COVID-19, evaluated for MIS-C who did not meet case criteria, hospitalized with febrile illness, with Kawasaki disease and in Massachusetts based on 2010 US census data. Neighborhood socioeconomic status (SES) and social vulnerability index (SVI) were measured via a census-based scoring system. Multivariable logistic regression was utilized to examine associations between SES, SVI, race and ethnicity, with MIS-C diagnosis and clinical severity as outcomes.

Results: Amongst 43 patients diagnosed with MIS-C, 19 (44%) were Hispanic, 11 (26%) were Black, 12 (28%) were White; 22 (51%) were in the lowest quartile for SES and 23 (53%) were in the highest quartile for SVI. SES and SVI were similar between patients with MIS-C and COVID-19. In multivariable analysis, lowest SES quartile (odds ratio 2.2 [95% confidence interval 1.1, 4.4]), highest SVI quartile (odds ratio 2.8 [95% confidence interval 1.5, 5.1]), and racial/ethnic minority were associated with MIS-C diagnosis. Neither SES, SVI, race, nor ethnicity were associated with disease severity.

Conclusions and Relevance: Lower SES or higher SVI, Hispanic ethnicity, and Black race independently increased risk for MIS-C. Additional studies are required in order to target interventions toward improving health equity for children and evaluate the impact of SES on patient outcome.

Introduction

Early in the COVID-19 pandemic, which first emerged in December 2019, most children appeared to only develop mild, if any, clinical manifestations of SARS-CoV-2 infection.[1–3] However, cases soon began to emerge of a hyperinflammatory condition occurring in children 3-4 weeks after COVID-19 infection that has since been termed Multisystem Inflammatory Syndrome in Children (MIS-C).[4–8] MIS-C is characterized by fever, elevated inflammatory markers, multisystem organ involvement and evidence of COVID-19 infection (current or prior)

or confirmed contact with COVID-19.[9,10] MIS-C shares features of Kawasaki disease (KD), including fever, elevated inflammatory markers, rash, mucocutaneous findings and coronary artery complications. However, reports have also found significant differences in patient demographics and laboratory values between MIS-C and KD.[6,11,12]

The pandemic has highlighted several racial, ethnic, and socioeconomic disparities among individuals with COVID-19. National data from the Centers for Disease Control and Prevention (CDC) show that Black and Hispanic/Latinx individuals have disproportionately higher rates of infection and death from COVID-19 compared to White individuals.[13] County- and neighborhood-level studies demonstrate disproportionately higher rates of SARS-CoV-2 infection, morbidity, and/or death in areas that have a greater percentage of minorities or are socioeconomically disadvantaged.[14–17]

In the pediatric population, racial and/or ethnic minority background and lower SES (measured by median family income) have been shown to independently increase risk for SARS-CoV-2 infection.[18] Early case series reported that MIS-C, like SARS-CoV-2 infection, may also disproportionately affect minority populations.[7,19] As of January 2021, 37% of MIS-C cases reported to the CDC were in children who are Hispanic/Latinx and 34% were in Non-Hispanic Black children, compared to 19% in White children.[4] However, the impact of socioeconomic disparities on MIS-C has not been investigated. Prior research has demonstrated that socioeconomic status (SES) has an important impact on health outcomes in several pediatric

diseases.[20–26] It is essential, therefore, to further characterize the impact of social and economic determinants of health and racial disparities in MIS-C.

Methods

Population: This retrospective case-control study included patients diagnosed with MIS-C between January 1st and September 1st, 2020 in Massachusetts. Patients treated at Boston Children's Hospital (BCH), Massachusetts General Hospital (MGH) and Boston Medical Center (BMC) were included.

To better evaluate the impact of SES on MIS-C, we compared children with MIS-C to the following groups (Supplemental Table 1):

1. Children with COVID-19 infection (excluding patients with MIS-C), including both symptomatic and asymptomatic cases, between January 1st and July 1st, 2020;
2. MIS-C "rule-out" group of children evaluated for MIS-C at BCH who ultimately did not meet CDC criteria for MIS-C diagnosis, between January 1st and September 1st, 2020;
3. Children hospitalized for a febrile illness (excluding KD, COVID-19 and MIS-C) at BCH between January 1st and September 1st, 2020;
4. Children diagnosed with KD at BCH between 2010-2016[27] and
5. Children in Massachusetts based on the 2010 US census.

Exclusion criteria included age >21 years, a non-Massachusetts address and congenital heart disease, except for bicommissural aortic valve, mitral valve prolapse, and hemodynamically

insignificant ventricular septal defects. This study was approved or exempted by the institutional review board of each institution and patient consent was obtained when applicable.

Data collection and definitions: Electronic medical records were reviewed to obtain patients' demographics and clinical course. MIS-C was defined using the CDC case definition as an individual aged < 21 years presenting with fever, laboratory evidence of inflammation, clinically severe illness requiring hospitalization, with multisystem (≥2) organ involvement; no alternative plausible diagnosis; and positive for current or recent SARS-CoV-2 infection by RT-PCR, serology or antigen test, or COVID-19 exposure within the 4 weeks prior to the onset of symptoms.[10] All cases of MIS-C (and MIS-C rule out) were adjudicated by a multidisciplinary of experts, including rheumatologists, cardiologists, infectious disease specialists and hematologists. Relevant clinical information, including age, past medical history, clinical symptoms at presentation, laboratory and diagnostic testing results (excluding socio-demographic data) were included in a form sent to the expert team, who were asked whether or not the patient met the CDC definition for MIS-C. The final adjudication was based on the majority vote, and any tied cases were discussed as a group to reach a consensus.

Patients' race and ethnicity were self-reported by patients or parents at time of hospital admission. Understanding that race and ethnicity are complex socio-political constructs, patients were grouped into categories according to the US census and Office of Management and Budget.[28] Race was classified as White, Black, Asian or other (including American Indian or Alaska Native, and Native Hawaiian or other Pacific Islander). Patients of mixed race were

classified as other. Ethnicity was classified as Hispanic (i.e. Cuban, Mexican, Puerto Rican, South or Central American, or other Spanish culture or origin regardless of race) or non-Hispanic. Ventricular dysfunction was defined as a left ventricular ejection fraction <55%. Coronary artery Z-scores were calculated for the left main coronary artery, proximal right coronary artery and proximal left anterior descending artery using the Boston formula.[27] Coronary artery dilation was defined as a coronary artery Z-score ≥2 but <2.5 and coronary artery aneurysms were defined as having a coronary artery Z-score ≥2.5.[27]

A neighborhood SES summary score and social vulnerability index (SVI) were calculated using the 2010 US census based on patient address.[29,30] The variables for the neighborhood SES summary score included: (1) log of median household income; (2) log of median value of housing units; (3) percentage of households receiving interest, dividend or net rental income; (4) percentage of adults 25 years of age or older in the household who had completed high school; (5) percentage of adults 25 years of age or older in the household who had completed college; and (6) percentage of employed persons 16 years of age or older in the household in executive, managerial, or professional specialty occupations.[29] The SVI was calculated using 15 variables classified in 4 themes: (1) socioeconomic status; (2) housing composition/disability; (3) minority status & language and (4) housing/transportation (Supplemental Figure 1).[30] Neighborhood SES summary scores were reported as Z-scores for each of the variables using all census tracts in Massachusetts, and then summed to determine the overall neighborhood SES summary score. SVI was reported as a percentage; higher SVI denotes increased vulnerability of a community. For children in Massachusetts, the neighborhood SES summary score and SVI were calculated

by weight-adjusting the score for each census tract based on the number of children < 18 years of age in each tract.

Outcomes: The primary outcome was the diagnosis of MIS-C and predictor variables included SES, SVI, race and ethnicity. As a secondary aim, we explored the impact of neighborhood SES summary score, SVI, race and ethnicity on treatment needs and disease severity (days of fever, hospital length of stay, intensive care unit [ICU] admission and length of stay, inotrope requirement, positive pressure ventilation, intubation, and cardiac involvement).

Statistical Analyses: In the descriptive analysis, continuous variables were summarized with median and interquartile range (IQR), and categorical variables were summarized as frequencies and percentages. Neighborhood SES summary score and SVI were compared across groups using the Kruskal-Wallis test with pairwise comparisons. The proportion of patients in the lowest SES quartile, highest SVI and race/ethnicity in each group was compared using the Fisher's exact test. Univariable and multivariable logistic regression were used to examine the impact of neighborhood SES or SVI and race/ethnicity on diagnosis of MIS-C (versus children in Massachusetts without MIS-C). The outcome of patients with MIS-C in the lowest SES quartile and highest SVI quartile were compared to those in the other quartiles using the Kruskal-Wallis test and Fisher's exact test. All analyses were performed with Rstudio: Integrated Development Environment for R (Rstudio, Inc., Boston, MA). A two-tailed adjusted P value < 0.05 was deemed statistically significant. The P values were adjusted for false discovery rate using the Benjamini Y and Hochberg Y method.

Results

Sample Characteristics: During the study period, a total of 43 patients (25 male, 58%) were diagnosed with MIS-C, including 29 patients from BCH, 12 from MGH and 2 from BMC. Median age was 9.7 years [IQR 6.5, 16.3] at time of diagnosis. With regards to race/ethnicity, 19 (44%) were Hispanic (White n=5, Black n=4, Other n=10); and of the non-Hispanic patients, 7 (16%) were White, 7 (16%) Black, 2 (5%) Asian and 3 (7%) Other. Overall, 19 patients (44%) had pre-existing comorbidities, with the most common being obesity (n=17, 40%) and asthma (n=6, 14%). ICU admission was required for 19 patients (44%); for fluid resuscitation and monitoring in 7 (16%) patients, vasopressors/vasoactive support in 8 (19%), non-invasive positive pressure ventilation in 5 (12%), and mechanical ventilation in 4 (9%). Cardiac involvement was found in 33 (77%) patients, including elevated BNP in 25 (63%), elevated troponin in 13 (32%), ventricular dysfunction in 21 (49%) and coronary artery dilation/aneurysm in 10 (23%). The majority of patients with MIS-C had positive antibodies to SARS-CoV-2 (n=29, 67%). RT-PCR for SARS-CoV-2 was positive for 20 patients (47%), and 15 patients (35%) had a COVID-19 exposure but negative RT-PCR and antibodies. The majority of patients were treated with intravenous immunoglobulin (n=34, 79%); other treatment used included steroids for 30 (70%) patients and Anakinra for 9 (21%) patients. Six patients (14%) received no immunomodulatory treatment.

Association of SES, SVI, and Race/Ethnicity with MIS-C Diagnosis: Table 1 summarizes the neighborhood SES summary score, SVI, race and ethnicity across the comparison groups. Table 2 shows expanded results with the specific variables and themes included in both measures of SES. There was no significant difference in the neighborhood SES summary score and the SVI

between each of the 3 hospitals' MIS-C groups. In patients with MIS-C, the neighborhood SES summary Z score ranged from -12.0 to 10.2, with a median of -3.5 [IQR -6.7, 0.3]. The neighborhood SES summary score was significantly lower for patients with MIS-C than children in Massachusetts (p=0.0009), children hospitalized with febrile illness (p=0.0009), children with MIS-C rule out (p=0.02), and children with KD (p<0.0001); but similar to patients with COVID-19 (p=0.23) (Figure 1, Table 2). Over half of children with MIS-C were in the lowest SES quartile (n=22, 51%). SVI score, in which higher score denotes increased vulnerability, ranged from 5.8% to 98.9 %, with a median of 76.5 [IQR 57.6, 91.8] in patients with MIS-C. SVI was significantly higher for patients with MIS-C than children in Massachusetts (p<0.0001), children hospitalized with febrile illness (p=0.0006), children with MIS-C rule out (p=0.04), and children with KD (p=0.0001); but similar to patients with COVID-19 (p=0.78) (Figure 1, Table 2). This association was found for the overall SVI, but also all individual categories (SES, housing composition & disability, minority status & language, housing & transportation; Table 2). Over half of children with MIS-C were in the highest SVI quartile (n=23, 53%). Patients with MIS-C and COVID-19 were more likely to be from racial/ethnic minority groups (Black and Hispanic) compared to children hospitalized with febrile illness, MIS-C rule out, KD or children in Massachusetts (Table 1).

Neighborhood SES summary score, SVI, race and ethnicity were all associated with MIS-C diagnosis in univariable analysis (Table 3). In multivariable analysis (with inclusion of SES and SVI in separate models), measures of socioeconomic status and race/ethnicity independently conferred higher risk for MIS-C diagnosis (Table 3). Specifically, Black and Hispanic children

as well as children in the lowest SES quartile and highest SVI quartile had significantly increased odds of developing MIS-C.

Association of SES, SVI, and race/ethnicity with MIS-C Outcomes: There was no significant difference in demographics, hospital course or cardiac complications in patients with MIS-C between patients in the lowest SES quartiles vs. others, or in the highest SVI quartile vs. others (Table 4). There was also no difference in hospital course or cardiac complications based on race or ethnicity.

Discussion

In this retrospective case-control study, we found that patients diagnosed with MIS-C had lower SES, increased social vulnerability and were more likely to be Black and/or Hispanic compared to the general population of Massachusetts children.

Previous studies have shown that that higher rates of SARS-CoV-2 infection are found in neighborhoods with lower income and educational attainment, both of which are factors that are incorporated into the neighborhood SES summary score used in this study.[29] Goyal *et al.* most recently showed that SARS-CoV-2 infection rates among children in particular were associated with lower median family income.[18] Furthermore, the SVI was used in this study to characterize factors beyond education and income that could contribute to disparities. In Massachusetts, neighborhood proportion of foreign-born citizens, mean household size, and proportion of food service workers were associated with increased COVID-19 rate.[31] Individuals more likely to

work in essential occupations, be unable to work from home, and need to use public transportation have likely increased exposure to the virus.[32,33] Our findings showed lower neighborhood household income and educational attainment, and greater neighborhood social vulnerability with regards to housing, transportation, minority status, and language among both the MIS-C and COVID-19 groups. It is therefore plausible that the elevated risk of MIS-C in the lower SES and greater SVI neighborhoods is a result of increased exposure to COVID-19.

While SES and race/ethnicity are strongly correlated,[34] there appears to be an independent risk of MIS-C in Black and Hispanic patients. Our findings are consistent with data from the CDC that found the highest rates of childhood COVID-19 in children of Hispanic/Latinx ethnicity.[13] Two recent studies demonstrate that Black children have higher rates of COVID-19 infection than White children, similar to the disparities seen in adult COVID-19 cases.[18,35] However, the increased risk in patients from minority racial/ethnic groups appears to extend beyond their SES based on our findings showing association of race/ethnicity with MIS-C even after adjusting for SES via two measures. While the neighborhood SES summary score is limited to an assessment of income and education to quantify SES, the use of the SVI enabled an even more complex representation of contributing socioeconomic factors by including an array of measures ranging from housing composition to language to transportation, which were also found to be associated with MIS-C in our study.[30] The effect of race and ethnicity on health disparities can be related to a multitude of alternate complex factors including increased risk of comorbidities, differential access to care, provider bias, and the effects of ongoing racism/discrimination and subsequent chronic stress.[14,36–38] These factors can cause racial and ethnic disparities independent of SES, and could be targets for interventions to improve outcomes.[36,38]

While our study looked at race and ethnicity, the role of host and environmental factors underlying differential MIS-C rates remains unclear. Despite being an early "hot spot" with a high incidence of patients with SARS-CoV-2 infection, China, Japan and South Korea have not reported patients with MIS-C or similar KD-like presentations.[39,40] The cause of this variation remains unclear, and may be related to genetic or environmental predisposition.[41–43] Genetic polymorphisms and environmental factors have been implicated in the development of KD, and could play a similar role in MIS-C.[44–46] The artificial nature of racial and ethnic grouping as a social and political construct limits conclusions regarding the role of population genetics in our findings.[47,48] It is, however, well documented that inequities in environmental exposure exist based on race/ethnicity and SES.[49,50] Future studies exploring genetic sequencing and environmental factors will be key to better understanding their role in MIS-C.

Our findings provide insight into avenues for interventions to reduce racial and socioeconomic disparities in MIS-C and children's health during and beyond this pandemic. Steps to ameliorate risk for exposure to COVID-19 are key to limiting incidence of MIS-C. Identifying neighborhoods in which children are most likely to have COVID-19 exposure can inform public health efforts and may allow proactive protection of at-risk populations. This may include increasing available testing, prioritizing vulnerable neighborhoods for vaccination, and ensuring that families can access health care resources without barriers due to language or insurance status[14,51–53]. Pediatricians also may support ongoing advocacy efforts to combat systemic racism, discrimination, and implicit bias, which can contribute to race- and ethnicity-related health disparities irrespective of SES.[54–57]

Limitations of our study include the small sample size of patients with MIS-C in a single state, and potential lack of generalizability to other states with different demographics. The inclusion of 3 large pediatric centers that cared for pediatric patients during the pandemic ensured that we captured most patients in Massachusetts admitted with MIS-C (43/54 reported to Department of Public Health). The control groups consisted of patients treated at BCH, whereas the patients with MIS-C were diagnosed across 3 academic centers. We did not find significant differences in SES between patients with MIS-C treated at the 3 centers, and compared patients with MIS-C to children in Massachusetts to minimize that possible bias. While we did not find any significant association between SES or race/ethnicity with treatment course or outcomes, statistical power was limited by the small number of patients and this question would be more effectively answered through large, multi-center registries. Patients reporting their race and ethnicity also may not have been given options within the confines of the Electronic Medical Record or verbal questioning to accurately self-identify. While all MIS-C case adjudication was performed using forms including only relevant clinical information, experts were not specifically blinded and known socio-demographic information from participating in the patients' clinical care may have influenced their decision. Lastly, this study relied on the 2010 census, and neighborhoods may have changing SES characteristics over the last decade.

In conclusion, measures of lower SES or higher social vulnerability, non-White race, and Hispanic ethnicity were independent risk factors for MIS-C in children in Massachusetts. The disproportionate number of cases of MIS-C in minority and socioeconomically disadvantaged pediatric populations may be due to increased risk of SARS-CoV-2 infection. Future studies should explore the underlying social, structural, economic, environmental and genetic risk

factors to allow for targeted interventions to support vulnerable pediatric populations most affected by MIS-C and improve health equity.

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Table 1: Distribution of neighborhood socioeconomic status, social vulnerability index, and race and/or ethnicity in children with MIS-C, children with COVID-19, and children in Massachusetts

	MIS-C (n=43)	COVID-19 (n=67)	Massachusetts	P value	P value MIS-C vs COVID-19	P value MIS-C vs MA
Neighborhood SES summary score, median [IQR][A]	-3.5 [-6.7, 0.3]	-2.4 [-5.4, 1.8]	0.2 [-3.3, 3.5]	<0.001	0.15	<0.001
Lowest quartile, n(%)	22 (51)	28 (42)	(24)	<0.001	0.44	<0.001
Social Vulnerability Index, median [IQR][B]	76.5 [57.6, 91.8]	73.4 [46.7, 92.2]	47.6 [22.2,75.3]	<0.001	0.73	<0.001
Lowest quartile, n(%)	23 (53)	31 (46)	(25)	<0.001	0.59	<0.001
Race/Ethnicity						
White, Non-Hispanic, n(%)	7 (16)	12 (18)	(77)	<0.001	0.99	<0.001
White, Hispanic, n(%)	5 (12)	1 (1)	(5)	0.04	0.03	0.04
Black, Non-Hispanic, n(%)	7 (16)	11 (16)	(6)	<0.001	0.99	0.02
Black, Hispanic, n(%)	4 (10)	3 (4)	(1)	<0.001	0.43	<0.001
Asian, n(%)	2 (5)	3 (4)	(5)	0.99	0.99	0.99

Other, Non-Hispanic, n(%)	3 (7)	5 (7)	(0.1)	<0.001	0.99	<0.001
Other, Hispanic, n(%)	10 (23)	18 (27)	(1)	<0.001	0.82	<0.001

[A]Neighborhood SES summary scores are reported as Z scores. [B]Social Vulnerability Index is a percentage, with higher percentage denoting increased vulnerability. MIS-C: Multisystem inflammatory syndrome in children; COVID-19: Coronavirus disease 2019; IQR: interquartile range; MA: Massachusetts

Table 2: Distribution of neighborhood socioeconomic status and social vulnerability index in MIS-C versus all comparison groups

	MIS-C (n=43)	COVID-19 (n=67)	MISC rule out (n=52)	Febrile illness (n=96)	Kawasaki disease (n=297)	Massachusetts	P value
Neighborhood summary score, median [IQR][A]	-3.5 [-6.7, 0.3]	-2.4 [-5.4, 1.8]	-0.1 [-3.9, 2.5]	0.4 [-3.0, 4.2]	0.8 [-2.5, 5.1]	0.2 [-3.3, 3.5]	<0.001
Household income, median [IQR]	-0.6 [-1.2, 0.3]	-0.2 [-0.9, 0.5]	0.1 [-0.7, 0.5]	0.1 [-0.4, 0.7]	0.3 [-0.3, 0.8]	0.3 [-0.4, 0.8]	<0.001
Household value, median [IQR]	0 [-0.2, 0.3]	0.1 [-0.3, 0.6]	0.1 [-0.2, 0.5]	0.2 [-0.3, 0.8]	0.2 [-0.2, 0.8]	0 [-0.6, 0.5]	<0.001
% household with income, median [IQR]	-0.6 [-1.2, 0.1]	-0.5 [-1.1, 0.1]	0 [-0.8, 0.3]	-0.2 [-0.7, 0.6]	0 [-0.6, 0.7]	0 [-0.7, 0.6]	<0.001
% adults who completed high school, median [IQR]	-0.6 [-1.5, 0.4]	-0.2 [-1.1, 0.5]	0.4 [-0.5, 0.5]	0.3 [-0.5, 0.7]	0.4 [-0.3, 0.8]	0.4 [-0.3, 0.7]	<0.001
% adults who completed college, median [IQR]	-0.7 [-1.3, -0.2]	-0.6 [-1.1, 0.2]	-0.1 [-0.9, 0.3]	-0.1 [-0.8, 0.7]	-0.1 [-0.7, 1.0]	-0.2 [-0.8, 0.6]	<0.001
% employee in executive jobs, median [IQR]	-0.6 [-1.4, 0]	-0.4 [-0.9, 0.2]	-0.3 [-0.8, 0.4]	-0.1 [-0.7, 0.8]	0.1 [-0.6, 1.0]	-0.1 [-0.6, 0.6]	<0.001

Social Vulnerability Index, median [IQR][B]	76.5 [57.6, 91.8]	73.4 [46.7, 92.2]	44.3 [26.1, 84.6]	52.8 [28.7, 75.3]	51.9 [22.7, 74.8]	47.6 [22.2,75.3]	<0.001
Socioeconomic status, median [IQR]	75.8 [52.5, 86.5]	73.8 [26.6, 91.6]	42.6 [25.7, 81.3]	43.0 [20.3, 72.5]	45.0 [19.3, 70.2]	46.5 [22.1, 73.8]	<0.001
Housing composition & disability, median [IQR]	59.0 [47.7, 78.5]	63.2 [38.4, 87.1]	48.7 [24.2, 74.2]	50.5 [32.9, 80.1]	48.4 [28.9. 75.5]	52.5 [30.0, 75.8]	0.04
Minority status & language, median [IQR]	84.8 [70.7, 90.0]	84.1 [39.6, 91.4]	58.0 [28.7, 90.0]	58.9 [32.6, 79.5]	58.0 [31.0, 78.1]	46.5 [22.8, 74.4]	<0.001
Housing & transportation, median [IQR]	63.8 [47.1, 84.1]	66.3 [38.9, 82.4]	58.2 [22.8, 80.3]	52.4 [32.9, 69.3]	49.9 [25.9, 72.3]	46.2 [23.1, 71.1]	<0.001

[A]Neighborhood summary scores are reported as Z scores. [B]Social Vulnerability Index is a percentage, with higher percentage denoting increased vulnerability. MIS-C: Multisystem inflammatory syndrome in children; COVID-19: Coronavirus disease 2019; IQR: Interquartile range

Table 3: Association of neighborhood socioeconomic status and race and/or ethnicity with MIS-C diagnosis

	Univariable analysis		**Multivariable analysis**	
	OR [95% CI]	P value	OR [95% CI]	P value
Neighborhood SES Summary Score[A]				
Lowest SES quartile	3.2 [1.8, 5.9]	<0.001	2.2 [1.1, 4.4]	0.02
Race				
White, Non-Hispanic	1			
White, Hispanic	12.1 [3.6, 38.0]	<0.001	8.7 [2.5, 28.2]	<0.001
Black, Non-Hispanic	12.0 [4.1, 37.0]	<0.001	10.8 [3.7, 31.8]	<0.001
Black, Hispanic	84.0 [22.0, 278.4]	<0.001	49.8 [12.4, 176.8]	<0.001
Asian	4.6 [0.7, 19.2]	0.06	5.4 [0.7, 40.8]	0.05
Other, Non-Hispanic	21.4 [4.6, 77.2]	<0.001	14.8 [3.1, 55.3]	<0.001
Other, Hispanic	19.2 [3.6, 38.0]	<0.001	18.8 [7.2, 51.8]	<0.001
Social Vulnerability Index[B]				
Highest SVI quartile	3.4 [1.9, 6.3]	<0.001	2.8 [1.5, 5.1]	0.02
Race				
White, Non-Hispanic	1			
White, Hispanic	12.1 [3.6, 38.0]	<0.001	8.8 [2.5, 28.5]	<0.001
Black, Non-Hispanic	12.0 [4.1, 37.0]	<0.001	10.3 [3.5, 30.3]	<0.001

Black, Hispanic	84.0 [22.0, 278.4]	<0.001	51.4 [12.8, 182.3]	<0.001
Asian	4.6 [0.7, 19.2]	0.06	4.5 [0.7, 18.8]	0.06
Other, Non-Hispanic	21.4 [4.6, 77.2]	<0.001	15.4 [3.2, 57.3]	<0.001
Other, Hispanic	19.2 [3.6, 38.0]	<0.001	19.3 [7.4, 53.1]	<0.001

[A]Neighborhood summary scores are reported as Z scores. [B]Social Vulnerability Index is a percentage, with higher percentage denoting increased vulnerability. Comparisons were made between patients with MIS-C as compared to the general Massachusetts population. MIS-C: Multisystem inflammatory syndrome in children; SES: socioeconomic status; SVI: Social Vulnerability Index; CI: confidence interval

Table 4: Associations between socioeconomic status with demographics and clinical outcomes in patients with MIS-C

	Neighborhood SES Summary Score[A]			Social Vulnerability Index[B]		
	Lowest quartile (n=22)	**Top 3 quartiles (n=21)**	**P value**	**Highest quartile (n=23)**	**Bottom 3 quartiles (n=20)**	**P value**
Demographics						
Age, median [IQR]	9.6 [6.3, 13.3]	10.3 [7.0, 16.6]	0.58	9.7 [6.5, 14.9]	9.3 [6.3, 16.6]	0.88
Male, n(%)	13 (61)	12 (57)	0.99	14 (61)	11 (55)	0.76
Weight, median [IQR]	44.1 [27.2, 61.7]	36.0 [22.7, 726.3]	0.58	45.1 [28.5, 74.1]	33.7 [21.6, 72.5]	0.53
BMI, median [IQR]	21.3 [18.4, 26.2]	22.3 [16.7, 27.6]	0.95	24.2 [18.6, 29.8]	19.9 [16.5, 25.2]	0.10
Comorbidities, n(%)	11 (50)	8 (38)	0.54	11 (48)	8 (40)	0.76
Obesity, n(%)	8 (36)	9 (43)	0.76	10 (43)	7 (35)	0.76
Hospital course						
Days of fever, median [IQR]	6.0 [4.0, 7.8]	7.0 [5.0, 7.0]	0.52	7.0 [4.5, 7.5]	6.5 [5.0, 7.3]	0.94
Hospital LOS, median [IQR]	6.5 [4.0, 9.8]	6.0 [3.0, 10.0]	0.78	6.0 [4.0, 9.5]	5.5 [3.0, 10.5]	0.67
ICU admission, n(%)	11 (50)	8 (38)	0.54	12 (52)	7 (35)	0.36

ICU LOS, median [IQR]	4.5 [2.0, 6.6]	4.0 [3.0, 7.0]	0.77	4.5 [2.0, 7.0]	4.0 [3.0, 8.0]	0.56
Inotropes, n(%)	4 (18)	4 (19)	0.99	4 (17)	4 (20)	0.99
PPV, n(%)	3 (14)	2 (10)	0.99	2 (9)	3 (15)	0.65
Intubation, n(%)	2 (9)	2 (10)	0.99	3 (13)	1 (5)	0.61
Cardiac involvement						
Elevated BNP, n(%)	15 (68)	10 (48)	0.33	14 (61)	11 (55)	0.75
Elevated troponin, n(%)	5 (23)	8 (38)	0.733	6 (26)	7 (35)	0.74
Ventricular dysfunction, n(%)	9 (41)	12 (57)	0.37	10 (43)	11 (55)	0.55
Coronary artery dilation, n(%)	8 (36)	2 (10)	0.07	8 (35)	2 (10)	0.08
AV block, n(%)	2 (9)	2 (10)	0.99	2 (9)	2 (10)	0.99
Treatment						
IVIG, n(%)	17 (77)	17 (81)	0.99	19 (83)	15 (75)	0.71
Steroids, n(%)	16 (73)	14 (67)	0.74	17 (74)	13 (65)	0.74
Anakinra, n(%)	6 (27)	3 (14)	0.46	5 (22)	4 (20)	0.99

[A]Neighborhood summary scores are reported as Z scores. [B]Social Vulnerability Index is a percentage, with higher percentage denoting increased vulnerability. MIS-C: Multisystem inflammatory syndrome in children; BMI: body mass index; LOS: length of stay; ICU: intensive care unit; PPV: positive pressure ventilation; BNP: brain natriuretic peptide; AV: atrioventricular; IVIG: intravenous immunoglobulin; IQR: interquartile range

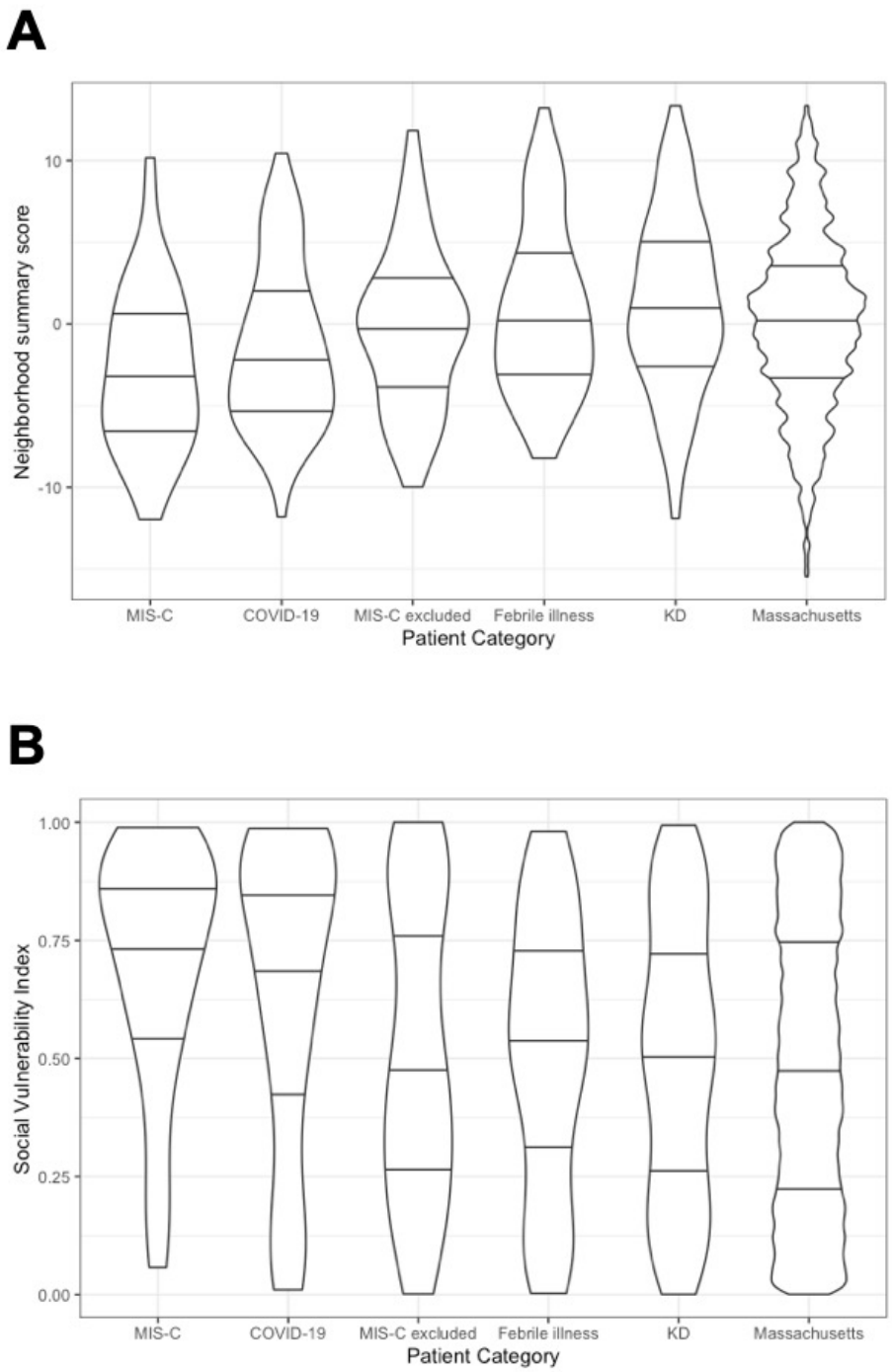
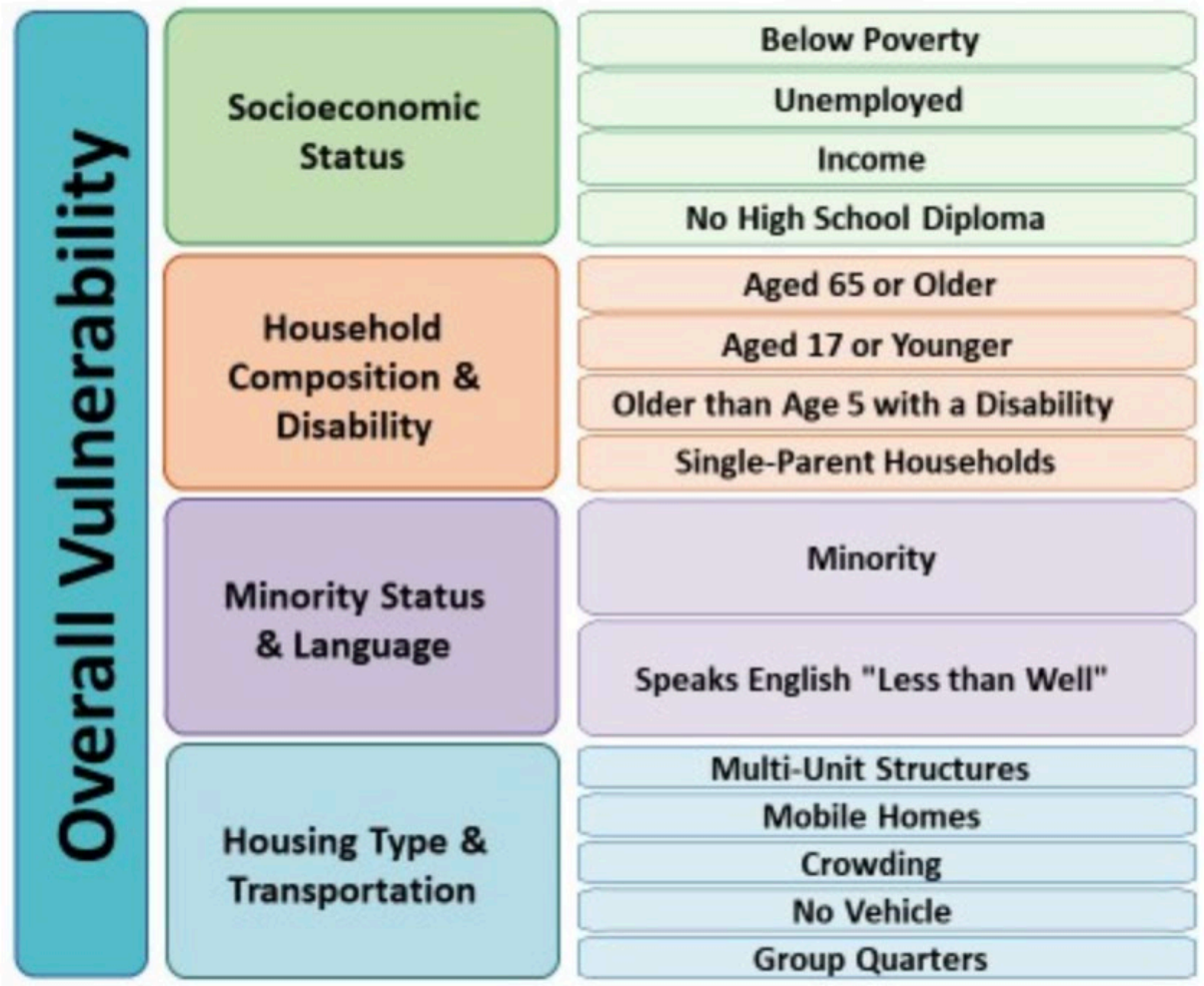


Figure 1: Violin plot of A. Neighborhood SES summary score and B. SVI; including median, 25th, 75th percentile in patients with MIS-C versus children 1) with COVID-19, 2) evaluated for MIS-C who did not meet CDC criteria, 3) hospitalized for febrile illness, 4) with KD, and 5) in Massachusetts.

This figure compares the distribution of Neighborhood SES summary score and SVI between each group studied. The vertical axis corresponds to the neighborhood SES summary score or the SVI, and the width of each curve corresponds to the frequency of patients within the group with that score/index.

Supplemental Table 1: Inclusion criteria for MIS-C and other control groups

	MIS-C (CDC) N=43	COVID-19 N=67	MIS-C Rule-Out N=52	Febrile Illness N=96	Kawasaki Disease (AHA) N=297	Massachusetts
Criteria	Fever Laboratory evidence of inflammation Evidence of clinically severe illness requiring hospitalization Multisystem (≥2) organ involvement (cardiac, renal, respiratory, hematologic, gastrointestinal, dermatologic or neurological) AND No alternative plausible diagnoses; AND Positive for current or recent SARS-CoV-2 infection by RT-PCR, serology, or antigen test; or exposure to a suspected or confirmed COVID-19 case within the 4 weeks prior to the onset of symptoms	Microbiologic evidence of current or past COVID-19 infection (SARS-CoV-2 PCR Positive OR SARS-CoV-2 Antibody Positive) AND No MIS-C diagnosis AND Did not undergo evaluation for MIS-C (no rheumatology consult and no echocardiogram obtained)	Clinical suspicion for MIS-C AND Evaluated by rheumatology AND Echocardiogram performed AND Did not ultimately meet criteria for MIS-C diagnosis after adjudication	Hospitalized for illness presenting with fever AND Negative for SARS-CoV-2 (PCR and antibody) AND No clinical suspicion for MIS-C AND Did not undergo evaluation for MIS-C (no rheumatology consult and no echocardiogram performed)	Hospitalized for complete KD OR Hospitalized for incomplete KD Based upon American Heart Association criteria[27]	Aggregate of data from 2010 census tract, weighted based on population of children in each census tract
Institution	BCH, MGH, BMC	BCH	BCH	BCH	BCH	Census
Time Period	1/1/2020 – 9/1/2020	1/1/2020 – 07/1/2020	1/1/2020 – 9/1/2020	1/1/2020 – 9/1/2020	1/1/2010-12/31/2016	2010



Supplemental Figure: Variables from the American Community Survey included in the calculation of the social vulnerability index.

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