Social and Demographic Disparities in the Severity of Multisystem Inflammatory Syndrome in Children

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Abstract: Social constructs are known risk factors for multisystem inflammatory syndrome in children. A review of 206 patients demonstrated that children who were non-Hispanic Black, over the age of 12 years or living in a disadvantaged neighborhood associated with severe multisystem inflammatory syndrome in children (intensive care unit admission, intubation and/or vasopressor use).

Key Words: coronavirus, coronavirus disease 2019, ethnicity, multisystem inflammatory syndrome in children, race, socioeconomic

(*Pediatr Infect Dis J* 2022;41:e256–e258)

Recent reports have confirmed that demographic characteristics are associated with cases, hospitalization and death rates of coronavirus disease 2019 (COVID-19).[1] Specifically, race/ethnicity, age and obesity have been associated with incidence and outcomes of COVID-19 infection,[2–5] as well as a multisystem inflammatory syndrome in children (MIS-C).[6,7] However, the role of social constructs (eg, socioeconomic status and race/ethnicity) on the severity of MIS-C has not been fully explored with sufficient sampling power.

The area deprivation index (ADI) is a validated metric, originally based on measures created by the US Health Resources and Services Administration, that ranks neighborhoods by socioeconomic disadvantage. Factors comprising the tool include housing quality, employment, education and income.[8] Previous studies have demonstrated a relationship between neighborhood deprivation and COVID-19 risk.[9,10] Our goal was to examine the relationship of demographic and socioeconomic disadvantage on the severity of MIS-C.

METHODS

This retrospective study evaluates children diagnosed with MIS-C between May 2020 and September 2021 and admitted to Texas Children's Hospital (TCH). All patients met MIS-C criteria according to the definition set forth by the Centers for Disease Control and Prevention.[11] The institutional review board at TCH approved this study.

Data culled from the electronic medical record included demographics, vaccination status, clinical course, administration of medications and laboratory results. Categories of race and ethnicity were self-determined by the individual/parent and retrieved from the electronic medical record. All laboratory information pertained to the first recorded results upon arrival to TCH. Body mass index (BMI) was converted to an age- and sex-adjusted Z score using Centers for Disease Control and Prevention growth charts.[12] All vaccinated patients in the cohort had both doses by the admission date.

To quantify the severity of MIS-C, we categorized the patients as "severe" if they received vasoactive-inotropic support and/or required mechanical ventilation during their hospitalization. Otherwise, individuals were categorized as "mild." The socioeconomic status of the patients was quantified using the Texas ADI, ranked from 1 to 10 such that a higher ADI rank reflects greater socioeconomic disadvantage. The ADI rank was mapped to the patients from their residential postal codes using the Neighborhood Atlas database.[8]

Comparison of MIS-C severity was conducted via the nonparametric Wilcoxon rank-sum test for continuous variables and Fisher exact test for categorical variables. We examined the association between MIS-C severity, demographics (race/ethnicity, sex, age, BMI), vaccination status and socioeconomic disadvantage (ADI) using multivariable logistic regression. Selection of these variables into the final multivariate model was based on univariate analysis, clinical relevance and goals of this research study. All analyses were performed using Python Statsmodels v0.12.2.

RESULTS

The cohort included 206 patients based in Texas according to their residential postal codes. Despite severity levels, all patients survived hospitalization. The median age was 9.4 years (interquartile range [IQR], 5.5–13.2 years). All patients were under 21 years of age. Overall, 45% (n = 92) of children were female and 42% (n = 86) were overweight. The predominant race/ethnicity was Hispanic (49%), followed by non-Hispanic Black (23%) and non-Hispanic White (20%). Children with severe MIS-C were typically older, overweight and with an elevated ADI.

The median length of hospital stay was 6.7 days (IQR, 4.9–8.5 days), while the median ADI was 5 (IQR, 2–7). Children with severe MIS-C were more likely to have exaggerated levels of brain natriuretic peptide, C-reactive protein, white blood cells, ferritin, procalcitonin, creatinine, blood urea nitrogen, international normalized ratio, protime and reduced amounts of platelets. The median hospital stay for a child with severe MIS-C was 8.1 days compared with 5.6 days for cases with mild MIS-C. The administration of steroids coupled with immunomodulators (eg, anakinra) was higher in children with severe MIS-C (98% vs. 65%). Table 1 provides more details about patient demographics, clinical characteristics and laboratory results classified by MIS-C severity and by socioeconomic category.

Table 2 summarizes the multivariable logistic regression model. This model showed that, when simultaneously controlling

Accepted for publication February 22, 2022

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This project was partially funded by a grant from the National Institutes of Health: R61HD105593.

The authors have no conflicts of interest to disclose.

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ISSN: 0891-3668/22/4106-e256

DOI: 10.1097/INF.0000000000003511

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TABLE 1. Demographic, Clinical Characteristics and Laboratory Results According to MIS-C Severity and Socioeconomic Status

Variables	Entire Cohort	Mild MIS-C	Severe MIS-C	*P*	Low ADI (≤5)	High ADI (>5)	*P*
Overall frequencies, n (%)	206 (100)	118 (57)	88 (43)	NA	118 (57)	88 (43)	NA
Age, n (%)							
<6 yr	56 (27)	43 (36)	13 (15)	<0.001	34 (29)	22 (25)	0.635
6–12 yr	88 (43)	48 (41)	40 (45)	0.569	54 (46)	34 (39)	0.322
>12 yr	62 (30)	27 (23)	35 (40)	0.014	30 (25)	32 (36)	0.094
Sex, n (%)							
Female	92 (45)	54 (46)	38 (43)	0.777	50 (42)	42 (48)	0.480
Male	114 (55)	64 (54)	50 (57)	0.777	68 (58)	46 (52)	0.480
BMI rank, n (%)							
Underweight (BMI <5th)	11 (5)	8 (7)	3 (3)	0.359	8 (7)	3 (3)	0.359
Healthy weight (5th ≤BMI <85th)	109 (53)	69 (58)	40 (45)	0.068	70 (59)	39 (44)	0.035
Overweight (85th ≤BMI)	86 (42)	41 (35)	45 (51)	0.022	40 (34)	46 (52)	0.010
Race/ethnicity, n (%)							
Hispanic	100 (49)	59 (50)	41 (47)	0.674	43 (36)	57 (65)	<0.001
Non-Hispanic White	42 (20)	27 (23)	15 (17)	0.382	33 (28)	9 (10)	0.002
Non-Hispanic Black	47 (23)	20 (17)	27 (31)	0.029	27 (23)	20 (23)	1.000
Non-Hispanic other	17 (8)	12 (10)	5 (6)	0.311	15 (13)	2 (2)	0.009
Insurance type, n (%)							
Commercial	81 (39)	50 (42)	31 (35)	0.316	64 (54)	17 (19)	<0.001
Government	115 (56)	63 (53)	52 (59)	0.479	47 (40)	68 (77)	<0.001
Self-pay	10 (5)	5 (4)	5 (6)	0.747	7 (6)	3 (3)	0.521
ADI, n (%)							
Low (≤5)	118 (57)	78 (66)	40 (45)	0.004	NA	NA	NA
High (>5)	88 (43)	40 (34)	48 (55)	0.004	NA	NA	NA
Vaccination status at admission, n (%)							
Vaccinated	4 (2)	3 (3)	1 (1)	0.637	4 (3)	0 (0)	0.137
Not vaccinated	202 (98)	115 (97)	87 (99)	0.637	114 (97)	88 (100)	0.137
Clinical characteristics							
Prolonged LOS (>6 d), n (%)	118 (57)	46 (39)	72 (82)	<0.001	59 (50)	59 (67)	0.016
ICU admission, n (%)	144 (70)	56 (47)	88 (100)	<0.001	77 (65)	67 (76)	0.124
Mechanical ventilation, n (%)	25 (12)	0 (0)	25 (28)	<0.001	11 (9)	14 (16)	0.196
Inotropic-vasoactive support, n (%)	88 (43)	0 (0)	88 (100)	<0.001	40 (34)	48 (55)	0.004
Steroids alone, n (%)	36 (17)	34 (29)	2 (2)	<0.001	115 (97)	84 (95)	0.463
Steroids + immunomodulator, n (%)	163 (79)	77 (65)	86 (98)	<0.001	91 (77)	72 (82)	0.489
LV EF, %, median (IQR)	59 (51–64)	62 (56–65)	53 (44–60)	<0.001	60 (53–65)	56 (48–63)	0.029
Laboratory results, median (IQR)							
BNP, pg/mL	125 (42–459)	79 (29–252)	296 (96–886)	<0.001	114 (35–459)	141 (51–423)	0.501
Lactate, mmol/L	1.6 (1.6–1.6)	1.6 (1.6–1.6)	1.6 (1.4–2.5)	0.016	1.6 (1.6–1.6)	1.6 (1.5–1.8)	0.813
CRP, mg/dL	17.6 (8.8–23.3)	15.4 (7.5–21.2)	21.4 (15.2–26.5)	<0.001	17.1 (7.9–22.9)	18.9 (14.0–24.6)	0.136
WBC, 10^3/uL	9.3 (6.8–12.4)	8.0 (6.1–11.1)	10.7 (8.5–13.9)	<0.001	9.1 (6.4–11.6)	9.7 (7.5–12.6)	0.089
Ferritin, ng/mL	311 (184–621)	249 (130–463)	418 (267–786)	<0.001	314 (191–636)	311 (176–597)	0.758
Procalcitonin, ng/mL	3.8 (1.5–9.2)	2.2 (1.1–5.4)	7.2 (2.9–15.0)	<0.001	3.9 (1.6–9.6)	3.4 (1.5–9.1)	0.692
Creatinine, mg/dL	0.5 (0.4–0.8)	0.4 (0.3–0.6)	0.7 (0.5–1.1)	<0.001	0.5 (0.3–0.8)	0.5 (0.4–0.8)	0.584
BUN, mg/dL	13 (10–19)	12 (9–16)	17 (12–28)	<0.001	13 (11–19)	13 (9–18)	0.191
INR	1.2 (1.2–1.3)	1.2 (1.1–1.2)	1.3 (1.2–1.4)	<0.001	1.2 (1.1–1.3)	1.2 (1.2–1.3)	0.037
Fibrinogen, mg/dL	556 (496–658)	546 (467–616)	578 (508–717)	0.026	541 (495–623)	590 (511–705)	0.100
D-dimer, ug/mL FEU	3.3 (2.2–4.7)	3.2 (1.9–4.4)	3.5 (2.7–5.1)	0.010	3.4 (2.3–4.6)	3.0 (2.1–4.8)	0.479
Protime, s	15.6 (14.8–16.4)	15.6 (14.6–15.6)	15.9 (15.2–17.2)	<0.001	15.6 (14.7–16.1)	15.6 (15.3–16.7)	0.016
Thrombin time, s	15.6 (15.1–16.1)	15.6 (15.5–16.3)	15.5 (14.7–16.0)	0.011	15.6 (15.4–16.3)	15.6 (14.8–15.9)	0.027
Platelets, 10^3/uL	157 (112–208)	170 (125–230)	143 (102–191)	0.003	156 (113–212)	157 (108–200)	0.570
HGB, g/dL	11.4 (10.4–12.3)	11.2 (10.2–12.3)	11.4 (10.6–12.4)	0.269	11.4 (10.3–12.4)	11.2 (10.5–12.0)	0.574
HCT, %	33.2 (31.0–36.2)	33.1 (31.0–35.8)	33.7 (31.0–36.6)	0.548	33.4 (31.1–36.7)	33.0 (31.0–35.7)	0.602

BNP indicates Brain natriuretic peptide; BUN, blood urea nitrogen; CRP, C-reactive protein; HCT, hematocrit; HGB, hemoglobin; ICU, intensive care unit; INR, international normalized ratio; LOS, length of stay; LV EF, left ventricular ejection fraction; NA, not applicable; WBC, white blood cell.

for sex, BMI and vaccination status, non-Hispanic Black pediatric patients had an increased odds for severe MIS-C in reference to Hispanic patients (odds ratio [OR], 2.30; 95% confidence interval [CI], 1.06–4.99; $P = 0.035$), increasing age of the child associated with the development of severe MIS-C (OR, 1.14 per year; 95% CI, 1.06–1.22; $P < 0.001$) and that increasing ADI also associated with severity of MIS-C (OR, 1.21 per rank; 95% CI, 1.07–1.37; $P = 0.003$).

DISCUSSION

This study highlights the association of socioeconomic disparities and race on severity of illness in a cohort of Texas-based pediatric patients diagnosed with MIS-C. Non-Hispanic Black children, older patients and those living in an area with a high deprivation index were significantly more likely to require intubation and/or vasoactive support. These disparities remained after adjustment for sex, BMI and vaccination status.

Although Hispanic children were more likely to be diagnosed with MIS-C, they had a comparable distribution of mild and severe cases of MIS-C. In contrast, non-Hispanic Black children were disproportionately at higher probability of developing severe MIS-C even when controlling for socioeconomic status. These findings are consistent with other observations by Javalkar et al[6] that Black children had significantly higher odds for MIS-C diagnosis. However, Javalkar et al[6] did not note differences in MIS-C

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TABLE 2. Multivariable Logistic Regression Model for Severe MIS-C

Variables	Coefficient	SE	OR (95% CI)	*P*
Intercept	–2.831	0.591	0.06 (0.02–0.19)	<0.001
Non-Hispanic White (Reference: Hispanic)	0.131	0.437	1.14 (0.48–2.69)	0.764
Non-Hispanic Black (Reference: Hispanic)	0.834	0.395	2.30 (1.06–4.99)	0.035
Non-Hispanic other (Reference: Hispanic)	0.177	0.620	1.19 (0.35–4.03)	0.775
Male (Reference: female)	0.221	0.314	1.25 (0.67–2.31)	0.481
Vaccinated (Reference: not vaccinated)	–1.697	1.225	0.18 (0.02–2.02)	0.166
Texas ADI rank	0.189	0.064	1.21 (1.07–1.37)	0.003
BMI (Z score)	0.007	0.072	1.01 (0.88–1.16)	0.917
Age (yr)	0.130	0.036	1.14 (1.06–1.22)	<0.001

SE indicates standard error.

severity (intensive care unit admission, intubation or inotrope requirement). Our study included 5 times the number of MIS-C cases and was, therefore, better powered to assess disparities in MIS-C severity.

Our analysis also found an increase in odds of severe MIS-C by 21% for each rank increase in ADI. The role of neighborhood deprivation indices on COVID-19 in Louisiana showed similar findings.[10] Although we do not fully understand why non-Hispanic Black children had higher rates of severe MIS-C, we do have a few hypotheses: (1) reduced access to healthcare, (2) differences in ADI may be manifested by crowded homes/neighborhoods, (3) provider bias/racism, (4) distrust of the US medical system given the history of mistreatment and (5) there may be an immunogenomic component.[7,13]

Strengths of our study include the number of patients, the granularity of the data and the correlation of MIS-C severity to clinical outcomes and laboratory markers. Although our work was derived from a single site, it is among the largest MIS-C cohorts in the nation and TCH is a significant referral center for the entire state. Our study did not examine the biological differences that may be inherent in race or ethnicity; instead, we describe these terms as social constructs. Another limitation to our work is the small number of children (n = 4) that received a COVID-19 vaccine. A larger sample is needed to accurately estimate the effect of the vaccination status on MIS-C severity and its relationship with other social and demographic variables.

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