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Multisystem Inflammatory Syndrome in American Indian/Alaska Native Children, March 2020–May 2022

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Abstract

We describe characteristics, clinical features and outcomes of multisystem inflammatory syndrome in children (MIS-C) among American Indian and Alaska Native (AI/AN) persons compared with non-Hispanic white (NHW) persons. AI/AN patients with MIS-C were younger, more often obese, and from areas of higher social vulnerability. A greater proportion of AI/AN patients had severe respiratory involvement and shock.

Keywords

Multisystem Inflammatory Syndrome in Children (MIS-C); American Indian/Alaska Native Health & Epidemiology; COVID-19

INTRODUCTION

Multisystem inflammatory syndrome in children (MIS-C), a severe complication of severe acute respiratory virus syndrome coronavirus-2 (SARS-CoV-2) infection, is characterized by systemic inflammation and multisystem organ involvement in persons aged <21 years.[1,2] Among U.S. cases during February 2020–July 2022, approximately 60% occurred in Hispanic/Latino or Non-Hispanic Black children.[1,3] Lower socioeconomic status and higher social vulnerability index (SVI) have been reported as associated with increased risk for MIS-C.[4] American Indian/Alaska Native (AI/AN) adults have been disproportionately

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Author contribution statement:

Drs Bornstein, Weiser and Apostolou conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript.

Drs Campbell, Zambrano, Yousaf and Ms Miller conceptualized and designed the study, coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content.

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affected by the coronavirus (COVID-19) pandemic, with incidence 3.5 times that among White persons and higher age-adjusted mortality.[5] Among AI/AN persons aged <25 years, persistently higher disparities in COVID-19 incidence have been reported.[6] We describe characteristics, clinical features, and outcomes of MIS-C among AI/AN patients compared with non-Hispanic White (NHW) patients.

METHODS

Health departments reported suspected cases to the Centers for Disease Control and Prevention (CDC)'s using a standardized case report form. Patients' illnesses were evaluated to confirm they met the CDC MIS-C case definition (Supplement 1): (1) clinically severe illness requiring hospitalization in persons aged <21 years, (2) fever ≥38°C for ≥24 hours or report of subjective fever for ≥24 hours, (3) laboratory evidence of inflammation, (4) multisystem (≥2) organ involvement, (5) laboratory evidence of acute or previous SARS-CoV-2 infection by reverse transcription polymerase chain reaction (RT-PCR), serology, or antigen test, or known COVID-19 exposure within 4 weeks of symptom onset, and (6) no alternative plausible diagnosis. Patients reported between February 19, 2020, and June 7, 2022, who met the case definition were included in this analysis. Author team clinicians reviewed comorbidity and organ system involvement free text data to augment clinical results where possible. We used previously established definitions to characterize severe organ system involvement (Supplement 2).[1] Race and ethnicity categorization used a modified method whereby AI/AN patients were classified as such, regardless of reported ethnicity, due to small sample size.[7] White patients without reported ethnicity were included in the NHW comparative group. SVI scores were determined using the CDC SVI 2018 database which utilizes U.S. census data to identify communities that might need additional support during emergencies, including the COVID-19 pandemic[8]. We calculated SVI scores using reported zip code. Waves of MIS-C were defined by nadirs between peaks in reported cases.[1]

Using SAS version 9.4 (SAS Institute, Cary, NC) we compared characteristics among AI/AN versus NHW patients using Kruskal-Wallis test for continuous variables and chi-square tests for categorical variables. Two-sided P values of $\alpha<0.05$ were considered significant.

This activity was reviewed by CDC, determined to meet the requirements of public health surveillance, and conducted consistent with applicable federal law and CDC policy (45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq).

RESULTS

Of 8,561 MIS-C cases reported from 56 jurisdictions, 8,070 had complete race and ethnicity documentation (Table). Of these, 69 (0.9%) patients were identified as AI (n=28), AN (n=8), or both (n=33); 2,798 were identified as NHW. Median age was 7 years (interquartile range (IQR), 4–12) for AI/AN patients and 9 years (IQR, 5–13) for NHW patients (p=0.045). A higher percentage of AI/AN patients were reported from the West (p<0.001) and during the

first MIS-C pandemic wave (p<0.001) than NHW patients. A higher percentage of AI/AN patients were obese (p=0.002) and resided in high SVI areas (p<0.001).

Compared with NHW patients, AI/AN patients more frequently experienced shock (p=0.035) and severe respiratory involvement (p=0.006), including pneumonia (p=0.009) and receipt of high-flow supplemental oxygen (p=0.003). Length of stay was borderline significantly shorter in NHW (5 days [IQR 4-8]) than AI/AN patients (5 days [IQR 3-7]; p=0.049); no statistically significant differences were identified in intensive-care unit (ICU)-level care (p=0.469) or death (p=0.112).

DISCUSSION

AI/AN patients with MIS-C were younger, more often obese, and from areas of higher social vulnerability compared with NHW patients. Previous studies have demonstrated that among hotspot counties, areas with the highest SVI had significantly higher incidence of COVID-19.[9] Tribal geographic regions have higher SVI specifically in the categories of poverty, unemployment, lower per capita income, access to transportation, and crowded housing.[10,11] AI/AN patients from higher SVI areas experienced increased COVID-19 transmission and thus higher risk for developing MIS-C. Most clinical features were similar between the groups, but a greater proportion of AI/AN patients had severe respiratory involvement (49.3% among AI/AN compared to 35% among NHW patients) and cardiovascular shock (49.3% among AI/AN compared to 36.9% among NHW patients) requiring interventions such as high-flow nasal cannula and vasopressors. Despite these differences, treatment type and outcomes did not significantly differ between groups. The shorter IQR for hospital length of stay in NHW compared with AI/AN just below the level of statistical significance is not likely of clinical relevance. Limited sample size precluded robust explorations of hospital and ICU length of stay and death.

The higher proportion of AI/AN patients exhibiting respiratory complications relative to NHW patients may be partly attributable to potential misclassification of severe acute COVID-19 patients as MIS-C patients, especially since AI/AN patients were disproportionately reported earlier in the pandemic when diagnostic algorithms may have been less clear. Although these cases were identified from a large national surveillance dataset, a limitation was the relatively small size of this AI/AN MIS-C cohort, which inhibited detailed subgroup analyses. Race/ethnicity was obtained from the medical record and may be subject to misclassification.[12] To improve ascertainment of AI/AN patients, a comparison with Indian Health Service (IHS) MIS-C data was considered. Preliminary review of MIS-C diagnoses in IHS data systems showed that few of the cases contained in this surveillance system were identified from facilities reporting to IHS. Further investigation is needed in this area to ensure completeness and accuracy of reported AI/AN MIS-C cases.

COVID-19 vaccination has been reported to be protective in preventing MIS-C.[13] Over 75% of AI/AN patients in this analysis were <12 years old, reflecting a younger age distribution of MIS-C among the U.S. populations of AI/AN versus NHW. Efforts to expand pediatric access to COVID-19 vaccination have strategically utilized SVI to maximize coverage and

demonstrated that while first dose coverage rates in high SVI areas were initially low, they improved.[14] Our findings support the rationale for improving COVID-19 immunization of AI/AN children, particularly among younger age groups who reside in high SVI areas.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Disclosures:

The authors have no conflicts of interest to disclose. The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the US Centers for Disease Control and Prevention or the Indian Health Service.

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Table.

Characteristics of American Indian and Alaska Native patients with MIS-C compared with non-Hispanic Whites — United States, February 2020 to June 2022

Characteristic	American Indian and Alaska Native† (n = 69)	Non-Hispanic Whites (n = 2,798)	p value[a]
	No. (%)	No. (%)	
Age group, years[b]			
0-4	23 (33.3)	655 (23.4)	0.055
5-11	30 (43.5)	1,320 (47.2)	0.543
12-20	16 (23.2)	823 (29.4)	0.262
Age, years, median (IQR)	7 (4–12)	9 (5–13)	0.045
Sex[c]			
Male	44 (63.8)	1,756 (62.8)	0.867
Female	25 (36.2)	1,041 (37.2)	0.867
U.S. Census Region[d]			
Northeast	6 (8.7)	429 (15.3)	0.129
Midwest	15 (21.7)	841 (30.1)	0.136
South	18 (26.1)	1,003 (35.8)	0.094
West	30 (43.5)	525 (18.8)	<0.001
Pandemic MIS-C wave[e]			
Wave 1 (Feb 19 - Jun 28, 2020)	9 (13.0)	84 (3.0)	<0.001
Wave 2 (Jun 29 - Oct 17, 2020)	7 (10.1)	153 (5.5)	0.095
Wave 3 (Oct 18, 2020 - Jul 8, 2021)	27 (39.1)	1,302 (46.5)	0.223
Wave 4 (Jul 9, 2021 – Jun 7, 2022)	26 (37.7)	1,258 (45.0)	0.230
Comorbidities			
Obesity[f]	23 (37.7)	553 (21.4)	0.002
Chronic lung disease including asthma	5 (7.2)	159 (5.7)	0.594
Social Vulnerability Index (SVI)[§]			
Low (score: 0-0.32)	11 (18.0)	896 (35.5)	0.005
Moderate (score: 0.33-0.66)	25 (41.0)	1,344 (53.3)	0.053
High (score: 0.67-1.00)	25 (41.0)	283 (11.2)	<0.001
SVI, median (IQR)	0.58 (0.45-0.87)	0.42 (0.26-0.54)	<0.001
Cardiovascular involvement			
Severe cardiovascular involvement	58 (84.1)	2,052 (73.3)	0.046
Arrhythmia	5 (7.2)	152 (5.4)	0.426
Congestive heart failure	2 (2.9)	92 (3.3)	1.000
Elevated troponin	35 (50.7)	1,366 (48.8)	0.808
Shock/receipt of vasopressors	34 (49.3)	1,032 (36.9)	0.035

Characteristic	American Indian and Alaska Native[f] (n = 69)	Non-Hispanic Whites (n = 2,798)	p value[a]
	No. (%)	No. (%)	
BNP or NT-pro BNP ≥ 1000 pg/mL	34 (49.3)	919 (32.8)	0.004
Cardiac dysfunction[g]	19 (30.6)	653 (25.4)	0.350
Pericardial effusion/pericarditis	10 (14.5)	501 (17.9)	0.464
Coronary artery aneurysm/dilatation[h]	7 (11.3)	310 (12.1)	0.854
Myocarditis[i]	9 (13.0)	296 (10.6)	0.512
ECMO	1 (1.4)	34 (1.2)	0.861
Hematologic involvement			
Severe hematologic involvement	46 (66.7)	1,651 (57.6)	0.201
Thrombocytopenia[j]	33 (47.8)	1,116 (39.9)	0.184
Lymphopenia[k]	28 (40.6)	1,028 (36.7)	0.514
Respiratory involvement			
Severe respiratory involvement	34 (49.3)	978 (35.0)	0.014
Pneumonia[l]	21 (30.4)	548 (19.1)	0.026
Pleural effusion	13 (18.8)	479 (17.1)	0.708
Oxygen, high flow nasal cannula	17 (24.6)	351 (12.5)	0.003
Invasive mechanical ventilation	8 (11.6)	165 (5.9)	0.050
Acute respiratory distress syndrome	5 (7.2)	122 (4.4)	0.231
Gastrointestinal involvement			
Severe gastrointestinal involvement[m]	12 (17.4)	627 (22.4)	0.323
Mesenteric adenitis	5/25 (20.0)	363/1,078 (33.7)	0.199
Free fluid	4/25 (16.0)	248/1,078 (23.0)	0.629
Renal involvement			
Severe renal involvement	14 (20.3)	433 (15.5)	0.276
Acute kidney injury	13 (18.8)	417 (14.9)	0.366
Renal failure	2 (2.9)	48 (1.7)	0.340
Hemodialysis	0	23 (0.8)	n/a[n]
Neurologic involvement			
Severe neurologic involvement	7 (10.1)	219 (7.8)	0.483
Meningitis	4 (5.8)	150 (5.4)	0.786
Encephalopathy	2 (2.9)	77 (2.9)	1.000
CVA	1 (1.4)	14 (0.5)	0.307
Any mucocutaneous involvement	47 (68.1)	2,055 (73.4)	0.322
Treatment			
IVIG	57 (82.6)	2,339 (81.6)	0.827
Steroids	57 (83.8)	2,247 (83.8)	0.993

Characteristic	American Indian and Alaska Native[†] (n = 69)	Non-Hispanic Whites (n = 2,798)	p value[a]
	No. (%)	No. (%)	
Outcomes			
Total days in hospital, median (IQR)[o]	5 (4–8)	5 (3–7)	0.049
ICU-level care[p]	40 (58.0)	1,499 (53.6)	0.469
Days in ICU, median (IQR)[q]	4 (2–6)	3 (2–5)	0.124
Death	2 (2.9)	22 (0.8)	0.112

Race and ethnicity reported in 8,070 of 8,561. Racial and ethnic classifications followed CDC's Office of Minority Health and Health Equity (OMHHE) guidance. Non-Hispanic ethnicity was assumed if Hispanic ethnicity was not noted. Hispanic ethnicity was top-coded over White, Black, and Asian race. Because of small sample sizes, American Indian/Alaskan and Native Hawaiian/Pacific Islander patients were reported as such, regardless of ethnicity

[†] Alone or in combination with other races and ethnicities

[a] P values from chi square test and Fisher's exact test (n ≤5) for categorical variables and Kruskal-Wallis trend test for continuous variables.

[b] Percentages calculated among 2,867 persons with known age.

[c] Percentages calculated among 2,866 persons with known sex.

[d] Percentages calculated among 2,867 persons with known census region.

[e] Percentages calculated among 2,867 persons with known date of diagnosis.

[f] By either clinician diagnosis of obesity or body mass index-based obesity; calculated only in children >2 years. Percentages calculated among 2,648 persons.

[§] Percentages calculated among 2,523 persons with known SVI. CDC/ATSDR SVI documentation is available at https://www.atsdr.cdc.gov/placeandhealth/svi/index.html. Median SVI for case-patients and controls are based on U.S. 2018 SVI data.

[g] Includes specified left ventricular dysfunction and right ventricular dysfunction); percentages calculated among 2,632 persons with an echocardiogram performed.

[h] Percentages calculated among 2,632 persons with an echocardiogram performed.

[i] Indicated on case report form.

[j] Information about thrombocytopenia was collected on the case report form under signs and symptoms or calculated from laboratory results as platelets <150,000 cells/μl

[k] Lymphopenia was defined as lymphocyte count <4,500 cells/μl if age <8 months or <1,500 cells/μl if age ≥8 months

[l] Information about pneumonia was collected on the case report form under signs and symptoms, complications, or chest imaging.

[m] Percentages calculated among 1,103 persons with an abdominal imaging performed.

[n] P value n/a because no comparisons were performed for these columns.

[o] Percentages calculated among 2,728 patients with known hospitalization duration.

[p] ICU-level care was defined as having a documented date of ICU admission or known length of ICU stay or having received, ICU-level care including mechanical ventilation, vasopressor support, or extracorporeal membranous oxygenation (ECMO).

[q] Percentages calculated among 1,133 patients with known ICU duration.