INPATIENT AND OUTPATIENT DIFFERENCES IN PEDIATRIC PATIENTS WITH LABORATORY-CONFIRMED COVID-19

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Abstract: Among 30,286 pediatric inpatient and outpatient encounters with laboratory-confirmed COVID-19 seen at one of 40 US healthcare organizations, 1586 (5.2%) were inpatient. Encounter types varied by age and sex; the proportion of Black/African American inpatients was significantly higher than outpatients, and Hispanic/Latinx children made up nearly one-fourth of patients.

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Studies indicate most children experience less severe coronavirus disease 2019 (COVID-19) illness than adults,1 but rates of pediatric COVID-19 related hospitalizations increased in recent months.2 Factors associated with hospital admission compared with outpatient encounters among children with COVID-19 are poorly understood. While 1 other study to date compared pediatric inpatients to those seen in outpatient settings,3 we sought to conduct this study using a stricter definition of COVID-19, including requiring a positive test, and a larger time frame to better understand the risk factors for the hospital admission.

METHODS

We conducted a retrospective cohort study of 10,285,590 inpatient and outpatient encounters from 1/1/2020 to 8/31/2021 among patients ≤18 years old with COVID-19 seen at 1 of 40 healthcare organizations in the United States reporting data to TriNetX, a global health research network with continuously refreshed data for more than 45 million patients in the United States.4 COVID-19 cases were defined by having an International Classification of Diseases (ICD-10) code (U07.1) and a positive severe acute respiratory syndrome coronavirus 2 test 2 weeks before or 3 days after the index encounter. Excluded were patients with an ICD-10 code of B97.89 or ICD-9 079.89 for other viral infections. Outpatient was defined as an encounter in the emergency department or outpatient clinic. Non-COVID-19 encounters were those without the codes defined above for cases. Comorbidities were defined using ICD-10 codes documented before or at the index encounter. Treatments given the day of up to 5 days after the index event were included. Descriptive statistics, t-test and χ² tests were computed using SAS Enterprise Guide v7.1 (SAS Institute, Inc., Cary, NC). This study was deemed exempt by our organization’s Institutional Review Board.

RESULTS

As of August 31, 2021, 30,286 encounters among patients ≤18 years old with laboratory-confirmed COVID-19 were included in the study population; 1586 (5.2%) were inpatient encounters. The cohort was racially/ethnically diverse with 24% of patients Hispanic/Latinx and 23% Black/African American among patients with these data reported. The distributions of age groups were similar between inpatient and outpatient encounters but differed when further analyzed by sex, with inpatient encounters among patients <13 years of age occurring more often among males and admissions among patients 13–18 years of age occurring more often among females. Among those with race reported, Black/African American patients had more frequent inpatient (33%) than outpatient encounters (29%) for COVID-19, and these were both higher than non-COVID-19 encounters among Black/African American patients (22%), whereas white patients were less likely to have inpatient (63%) than outpatient encounters (69%) for COVID-19 and these were both lower than non-COVID-19 encounters among white patients (73%) (Table). In regard to geographic differences, patients in the South were more likely to be admitted to a hospital than to be seen as an outpatient (59% vs. 53%) but these rates were similar to non-COVID-19 encounters in the South (59%) and patients in the West were less likely to have an inpatient admission than an outpatient encounter (3% vs. 16%) but these differed from the rate of non-COVID-19 encounters in the West (8%).

All major comorbidities analyzed were more common among inpatients compared with outpatients and among inpatients compared with non-COVID-19 encounters. Comparing inpatients, outpatients and non-COVID-19 encounters, notable differences were higher rates of metabolic disorders: 27% vs. 7% vs. 7%; diabetes: 6% vs. 1% vs. 0.5% and overweight/obesity: 10% vs. 6% vs. 4%; anemia: 12% vs. 2% vs. 1%; sleep disorders: 11% vs. 6% vs. 1%; and anxiety disorders: 15% vs. 7% vs. 6% (all P < 0.001). Antibiotics were more often given to inpatients than outpatients (48% vs. 7%, P < 0.001), as were glucocorticoids (43% vs. 5%, P < 0.001).

DISCUSSION

This study utilized a large sample of healthcare organizations throughout the United States to describe differences in pediatric laboratory-confirmed COVID-19 cases between inpatient and outpatient settings. We found that among younger age groups a larger proportion of inpatient encounters were males whereas among older age groups a larger proportion of inpatient encounters were females. We also found that the proportion of Black/African American pediatric patients was significantly higher than the proportion of outpatients and Hispanic/Latinx children made up nearly one-fourth of all pediatric patients with COVID-19. Previous studies have also observed these disparities among COVID-19 pediatric patients,5 highlighting the urgent need for interventions to address this issue.

We observed differences in the proportion of children admitted to the hospital with COVID-19 based on geographic location. Disparate access to testing and different messaging based on geography has occurred during the COVID-19 pandemic.6 The geographic differences observed in this study may reflect disparities in access to healthcare, higher rates of chronic conditions or other factors, and warrants further investigation.

Pediatric patients with multiple types of comorbidities were more likely to be inpatients, which is supported by previous studies.7 Nearly half (48%) of all pediatric inpatients in this study received antibiotics, despite being hospitalized for a viral infection. Similar antibiotic prescribing rates were observed in adults hospitalized with COVID-198 despite low incidence of bacterial coinfections, indicating a strong need for active antibiotic stewardship programs during this pandemic.

Limitations of this study include race not reported for 21% of patients and the inability to include length of stay or adjusted
analyses based on level of access to TriNetX data. Among the non-COVID-19 encounters, only a small subsample (4%) was available for analysis of comorbidities due to computational limitations, therefore this subsample may not represent all non-COVID-19 patients. The relatively low sample size of comorbidities also limited analysis by specific comorbidities. In addition, no previously published information is available on the representativeness of TriNetX among medical encounters in the United States. Advantages to this study include use of a large, national database with real-time updating, inpatient and outpatient encounters, and being able to include patients with both a positive severe acute respiratory syndrome coronavirus 2 test and corresponding ICD-10 code.

The impact of COVID-19 on children is not fully elucidated, and understanding the epidemiology of pediatric patients presenting to inpatient and outpatient settings may guide future prevention efforts and resource distribution. This pandemic exposed existing healthcare inequities among children that require corrective action.

### TABLE.

Demographic and Comorbidity Differences Between Inpatient and Outpatient Encounters Among Pediatric Patients With COVID-19 as of August 31, 2021

|                        | Inpatient Encounters (n = 1586) | Outpatient Encounters (n = 28,700)* | Non-COVID-19 Encounters (n = 10,255,304) |
|------------------------|----------------------------------|-------------------------------------|------------------------------------------|
| **Age, in years**      |                                  |                                     |                                          |
| Mean (SD)              | 10.1 (6.3)                       | 10.7 (5.7)                          | 10.1 (5)                                 |
| 1–5                    | 107 (7)                          | 733 (3)                             | 133,956 (1)                              |
| 6–12                   | 376 (24)                         | 6079 (21)                           | 2,200,242 (22)                           |
| 13–17                  | 357 (22)                         | 8507 (30)                           | 4,098,291 (40)                           |
| 18                     | 552 (35)                         | 10,380 (36)                         | 3,164,680 (31)                           |
| Sex†                   |                                  |                                     |                                          |
| Male                   | 804 (51)                         | 14,359 (50)                         | 5,359,580 (52)                           |
| Female                 | 779 (49)                         | 14,274 (50)                         | 4,864,481 (48)                           |
| **Race‡**              |                                  |                                     |                                          |
| Black/African American | 429 (33)                         | 6437 (29)                           | 1,722,191 (22)                           |
| Other race§            | 43 (3)                           | 468 (2)                             | 349,446 (5)                              |
| White                  | 820 (64)                         | 15,864 (69)                         | 5,679,387 (73)                           |
| **Ethnicity¶**         |                                  |                                     |                                          |
| Hispanic or Latinx     | 221 (18)                         | 4219 (21)                           | 1,674,474 (24)                           |
| Not Hispanic or Latinx | 991 (82)                         | 15,893 (79)                         | 5,287,879 (76)                           |
| **Geographic region‖** |                                  |                                     |                                          |
| Northeast              | 253 (16)                         | 4696 (16)                           | 1,562,163 (16)                           |
| Midwest                | 355 (22)                         | 4264 (15)                           | 1,635,486 (17)                           |
| South                  | 930 (59)                         | 15,137 (53)                         | 5,709,154 (59)                           |
| West                   | 48 (3)                           | 4603 (16)                           | 790,140 (8)                              |
| **Comorbidities****    |                                  |                                     |                                          |
| Acute kidney failure and chronic kidney disease | 89 (6) | 219 (1) | 1474 (0.3) |
| Anemia                 | 195 (12)                         | 677 (2)                             | 5843 (1)                                 |
| Anxiety disorder       | 239 (15)                         | 2130 (7)                            | 26,867 (6)                               |
| Asthma                 | 227 (14)                         | 2844 (10)                           | 34,583 (8)                               |
| Cardiac arrhythmia     | 54 (3)                           | 199 (1)                             | 2410 (0.5)                               |
| Cardiomegaly           | 74 (5)                           | 235 (1)                             | 1714 (0.4)                               |
| Congenital malformations | 44 (3) | 135 (0.5) | 1581 (0.4) |
| Congenital malformations | 49 (3) | 151 (1) | 1515 (0.3) |
| Diabetes mellitus      | 97 (6)                           | 251 (1)                             | 2244 (0.5)                               |
| Epilepsy and recurrent seizures | 94 (6) | 403 (1) | 5,534 (1) |
| Heart failure          | 42 (3)                           | 90 (0.3)                            | 576 (0.1)                                |
| Hypertensive diseases  | 138 (9)                           | 450 (2)                             | 3417 (0.8)                               |
| Ischemic heart diseases | 38 (2)                           | 64 (0.2)                            | 233 (0.1)                                |
| Malnutrition           | 78 (5)                           | 211 (1)                             | 1419 (0.3)                               |
| Metabolic disorders    | 433 (27)                         | 2044 (7)                            | 29,593 (7)                               |
| Mood affective disorders | 179 (11) | 1,152 (4) | 13,649 (3) |
| Neoplasms              | 136 (9)                           | 1050 (4)                            | 15,252 (3)                               |
| Neutropenia            | 80 (5)                           | 201 (1)                             | 1132 (0.3)                               |
| Overweight and obesity | 153 (10)                         | 1743 (6)                            | 17,513 (4)                               |
| Purpura and other hemorrhagic conditions | 109 (7) | 248 (1) | 1189 (0.4) |
| Sickle-cell disorders  | 47 (3)                           | 196 (1)                             | 1491 (0.3)                               |
| Sleep disorders        | 177 (11)                          | 1665 (6)                            | 2387 (0.5)                               |

* Differences between inpatient and outpatient encounter variables were statistically significant (P < 0.05) except for sex.
†Not reported for n = 3 inpatient encounters, n = 67 outpatient encounters and n = 31,243 non-COVID-19 encounters.
‡Not reported for n = 294 inpatient encounters, n = 6041 outpatient encounters and n = 2,504,280 non-COVID-19 encounters.
¶Includes American Indian or Alaskan Native, Asian and Native Hawaiian or other Pacific Islander.
‖Not reported for 558,361 non-COVID-19 encounters.
**Reported for 446,290 non-COVID-19 encounters.

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Abstract: Comparing first and second wave MIS-C cohorts at our quaternary pediatric institution, second wave were older, presented more frequently with shortness of breath, higher maximum troponin and N-terminal BNP, and more frequently required advanced respiratory and inotropic support. Despite increased severity in the second cohort, both cohorts had similar rates of coronary artery abnormalities, systolic dysfunction, and length of stay.

Key Words: pediatric multisystem inflammatory syndrome, PMIS, multisystem inflammatory syndrome in children, MIS-C, 2019 coronavirus disease, immunomodulation, myocarditis, critical care

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A.S.H. and M.P.S. was involved in study design, data gathering, data analysis, drafting, and editing of the article. E.A. was involved in data gathering, data analysis, and editing of the article. J.E.B. was involved in data analysis, drafting, and editing the article. D.W. was involved in study design, data analysis, and editing of the article. R.L.D. was involved in study design, data gathering, data analysis, drafting, and editing the article. All authors approved the final article as submitted and agree to be accountable for all aspects of the work.

The members of Children’s National Hospital MIS-C Task force listed in Appendix.

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M ultisystem inflammatory syndrome in children (MIS-C) is a newly described severe hyperinflammatory multisystem illness specific to the pediatric population, which is thought to be an immune-mediated complication of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.1–3 Our center managed 2 distinct cohorts of MIS-C patients, each following periods of maximal virus circulation and surge (waves) in our community by 4–6 weeks. Multiple centers (including ours) and consortia, as well as the CDC, have published key demographic and clinical features of MIS-C following the first wave of patients with this rare presentation. These reports have included patients with varying degrees of severity, cardiac dysfunction, requirement for critical care, respiratory, inotropic, and immunomodulatory support.1–3 The second wave of MIS-C patients at our institution was larger than the first wave, following the largest surge in SARS-CoV-2 circulation in the United States and our community. Herein, we provide the first comparison of clinical features and outcomes for MIS-C patient cohorts treated at our facility during the first and second large waves of presentation, under a standard institutional evaluation and treatment protocol that prioritizes prompt immunomodulatory therapy.

MATERIALS AND METHODS

This was a prospective cohort study of 106 patients sequentially diagnosed and treated for MIS-C according to the Centers for Disease Control and Prevention MIS-C case definition and admitted to our quaternary pediatric center in Washington, DC.1 Patients’ demographic, clinical, laboratory, radiographic, including echocardiography, therapies, and outcomes were extracted from electronic medical records. Wave 1 MIS-C Cohort patients (N = 43) were hospitalized between March and October 2020; Wave 2 MIS-Cohort patients (N = 63) were hospitalized between November 2020 and April 2021. All patients were managed on the same standardized institutional protocol that utilizes intravenous immunoglobulin (IVIG) and aspirin with or without Anakinra as initial therapy, as well as escalation to additional corticosteroid immunomodulation depending on defined clinical parameters. The institutional algorithm was developed by a multidisciplinary committee (Children’s National Hospital MIS-C Task force).1,6 Cardiac complications were defined as abnormal coronary artery (Z score ≥ 2) or decreased systolic function (ejection fraction < 55% or shortening fraction < 28%).7,8

Statistical Analysis

The analysis compared the 2 MIS-C cohorts with respect to demographics, clinical features, diagnostic biomarkers, radiographic procedures including echocardiogram, immunomodulatory and vasopressor support, and clinical outcomes. All data were summarized using descriptive statistics of the median and interquartile (IQR) range and frequency. Continuous variables were analyzed using the nonparametric Wilcoxon rank sum test as normality was