Early Experience of COVID-19 in a US Children's Hospital

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abstract

OBJECTIVES: We aim to describe the demographics, clinical presentation, hospital course, and severity of pediatric inpatients with coronavirus disease 2019 (COVID-19), with an emphasis on healthy, immunocompromised, and chronically ill children.

METHODS: We conducted a single-center retrospective cohort study of hospitalized children aged younger than 22 years with COVID-19 infection at Steven and Alexandra Cohen Children's Medical Center at Northwell Health. Cases were identified from patients with fever and/or respiratory symptoms who underwent a nucleic acid amplification–based test for severe acute respiratory syndrome coronavirus 2.

RESULTS: Sixty-five patients were identified. The median age was 10.3 years (interquartile range, 1.4 months to 16.3 years), with 48% of patients older than 12 years and 29% of patients younger than 60 days of age. Fever was present in 86% of patients, lower respiratory symptoms or signs in 60%, and gastrointestinal symptoms in 62%. Thirty-five percent of patients required ICU care. The white blood cell count was elevated in severe disease (P = .0027), as was the C-reactive protein level (P = .0192), compared with mild and moderate disease. Respiratory support was required in 34% of patients. Severity was lowest in infants younger than 60 days of age and highest in chronically ill children; 79% of immunocompromised children had mild disease. One death was reported.

CONCLUSIONS: Among children who are hospitalized for COVID-19, most are younger than 60 days or older than 12 years of age. Children may have severe infection requiring intensive care support. The clinical course of immunocompromised patients was not more severe than that of other children. Elevated white blood cell count and C-reactive protein level are associated with greater illness severity.

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Drs Kainth, Goenka, Williamson, and Rubin conceptualized and designed the study, designed the data collection instruments, coordinated and supervised data collection, drafted the initial manuscript, and critically reviewed and revised the manuscript for important intellectual content; Ms Fishbein and Dr Subramony conducted the analysis, validated the integrity of data collection, and reviewed and revised the manuscript; Dr Schleien critically reviewed and revised the manuscript for important intellectual content; Drs Barone, Belfer, Feld, Krief, Palumbo, Rajan, Rocker, Sharma, and Sokoloff collected data and reviewed and revised the manuscript; Ms Scotto designed the data collection instruments; and all authors approved the final manuscript as submitted.

WHAT'S KNOWN ON THIS SUBJECT: Pediatric coronavirus disease 2019 (COVID-19) is less common than adult COVID-19. Reports of COVID-19 in hospitalized children have varied from severe disease in infants and adolescents to disease primarily in children with underlying conditions.

WHAT THIS STUDY ADDS: Among inpatients, COVID-19 was common and mild in infants younger than age 60 days and severe in older, healthy children. Approximately half of all children were chronically ill or immunocompromised. Elevation of white blood cell count and C-reactive protein level correlated with severity.

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Since its emergence in December 2019, the novel coronavirus, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has created a global pandemic, with >9 million cases and >450 000 deaths worldwide.[1] More than 2 million cases are documented in the United States, with the New York metropolitan area as the epicenter of the coronavirus disease 2019 (COVID-19). The impact of COVID-19 on the pediatric population is incompletely understood.[2]

Data from China suggest that children with COVID-19 have less severe disease and a lower rate of hospitalization than adults.[3,4] Dong et al[5] reported that of 2135 children infected with COVID-19, 6% had critical or severe disease, whereas 51% and 39% had mild or moderate illness, respectively. The severity of infection varied with age; critical or severe disease was observed in 10.6% of children <1 year of age and in 7.5% of children <5 years of age, compared with 3% to 4% in older children.[5] In a series of children with COVID-19 in Madrid, Spain, 10% of pediatric patients were admitted to an ICU.[6]

The Centers for Disease Control and Prevention (CDC) reported on the experience of >2500 pediatric patients positive for SARS-CoV-2 in the United States.[7] Consistent with previous reports, the disease course was milder than in adults, and higher rates of hospitalization were seen in children <1 year old and in children with underlying medical conditions. However, there were limited clinical details in this data set. Herein, we describe clinical and age categories, as well the presentation, hospital course, and severity, with laboratory and imaging correlates, of the first 65 sequentially admitted patients at a New York City tertiary care children's hospital.

METHODS

Study Design and Study Population

We conducted a single-center retrospective cohort study of hospitalized children aged younger than 22 years with COVID-19, as documented by a positive result on a nucleic acid amplification–based test for SARS-CoV-2, who were admitted to the Steven and Alexandra Cohen Children's Medical Center at Northwell Health (New Hyde Park, NY) between January 23, 2020 (date of the first patient tested for SARS-CoV-2) and April 18, 2020; patient data were included through April 23, 2020. During the study period, universal testing of inpatients was not performed; indications for testing were fever without an established alternative diagnosis (eg, cellulitis) and/or respiratory tract symptoms, with a small number of patients screened for SARS-CoV-2. Clinical, laboratory, and radiographic data were abstracted by study investigators from the electronic medical record and subsequently reviewed and validated. Study data were collected and managed by using Research Electronic Data Capture tools hosted at Northwell Health.[8] This study was approved by the Northwell Health Institutional Review Board. A waiver of informed consent was granted. A report of 3 patients included in this study has recently been published.[9]

SARS-CoV-2 Testing

Testing was performed on a single nasopharyngeal swab or a combined nasopharyngeal and oropharyngeal swab by using one of several nucleic acid amplification assays for SARS-CoV-2 in Northwell Health Laboratories. During the study period, availability and indications for testing were expanded from an initial practice of testing only those patients with a household contact with confirmed COVID-19 or travel from designated countries to, as of March 24, 2020, testing hospitalized patients (other than those with an alternative identifiable source of infection) who presented with an acute respiratory and/or infectious illness.

Study Variables

Sociodemographic characteristics and the presence of an underlying medical condition were recorded. Anthropomorphic data were used to classify patients >2 years old by using standard CDC BMI percentile criteria. Data about patients' clinical presentation, including duration and type of symptoms as well as the presence of COVID-19 symptoms in contacts, were abstracted. Upper respiratory infection (URI) was defined by symptoms of sore throat and rhinorrhea or nasal congestion. Symptoms of lower respiratory tract infection (LRTI) included dyspnea and cough, and diagnosis of LRTI required decreased breath sounds or crackles on examination and/or abnormal findings on the chest radiograph or computed tomography scan. Hospital course was reviewed for diagnostic studies, respiratory support, and pharmacologic management. For patients readmitted within 48 hours of discharge from the index admission, clinical data for the subsequent admission were also included in the data set.

Patients were categorized into 4 mutually exclusive clinical groups on the basis of their age and medical history: (1) healthy infants (HIs) (previously healthy patients younger than 60 days old), (2) healthy children (HC) (previously healthy patients 60 days of age and older), (3) immunocompromised children (IC) (patients with cancer or primary immunodeficiency or those on immunosuppressive medication), or (4) chronically ill children (CI) (patients with an underlying medical condition [other than an immunocompromised state] that has lasted >1 year and limits activities of daily living). Patients' COVID-19 illness severity was classified as mild,

moderate, or severe on the basis of the maximum clinical severity during hospitalization: (1) mild, no requirement for supplemental oxygen; (2) moderate, supplemental oxygen with or without noninvasive respiratory support or need for frequent bronchodilator therapy; or (3) severe, mechanical ventilation with or without use of vasopressors and/or inotropes, extracorporeal membrane oxygenation (ECMO), and renal replacement therapy (RRT).

Statistical Analysis

Continuous variables were summarized with means and SDs or medians and interquartile ranges (IQRs), as appropriate, whereas categorical variables were summarized with frequencies and percentages. Fisher's exact tests and Monte Carlo estimation for the exact Wilcoxon rank tests were used to compare demographic and clinical variables by categories of patients and disease severity. No correction for multiple pairwise comparisons was performed because of the exploratory nature of the study. All analyses were performed by using SAS version 9.4 (SAS Institute, Inc, Cary, NC).

RESULTS

Between January 23, 2020, and April 18, 2020, 65 hospitalized children with a positive SARS-CoV-2 test result were identified; the initial case was identified on March 15, 2020, and the epidemic curve is shown in Fig 1. Of the 65 patients, 7 remained hospitalized as of April 23, 2020.

Patient Characteristics

In Table 1, demographic and clinical characteristics of the entire cohort, as well as within 4 patient clinical categories, are summarized. The median age of patients with COVID-19 was 10.3 years (IQR, 1.4 months to 16.3 years). Patient age was not evenly distributed; the largest number of cases was among children 12 years of age or older (48%), followed by infants <60 days old (29%) (Fig 2). In contrast, during the study period, of the 351 children hospitalized, 52 (15%) were <60 days of age, 125 (36%) were 60 days to <5 years of age, 62 (18%) were 5 to <12 years of age, and 112 (32%) were 12 years of age and older, indicating that infants younger than 60 days and children 12 years and older were overrepresented in the COVID-19 cohort. During the study period, 30 infants younger than 57 days of age were admitted at our hospital with fever, 19 of whom had COVID-19, indicating that COVID-19 was the most common etiology of fever resulting in hospitalization in children younger than 60 days of age. Age, sex, and weight status were not significantly different among the illness severity groups. Overall, 36 patients (55%) had an underlying medical condition.

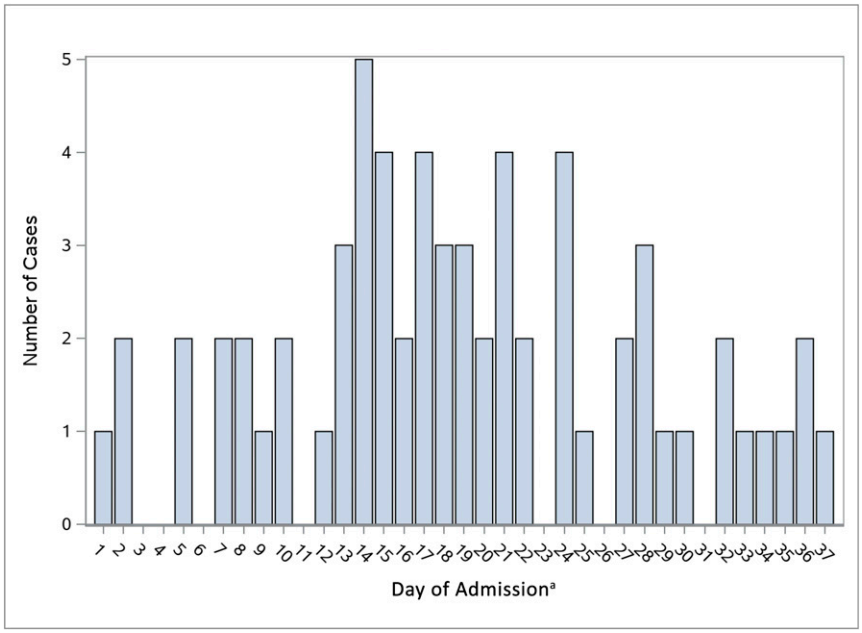

FIGURE 1

Epidemic curve of pediatric hospital admissions during peak of COVID-19 pandemic in a New York City children's hospital. Dates have not been specified to protect patient-protected health information. Data include 1 patient who had been hospitalized for 7 weeks at the time of symptoms and SARS-CoV-2 testing. [a] The admission date for 1 patient admitted in February was amended to the date of the COVD-19 test.

Clinical Presentation

The most common reported symptoms were fever (69%), cough (49%), poor feeding and/or anorexia (40%), shortness of breath (35%), and nausea and/or vomiting (28%) (Table 1). Fever was present in 74% of patients either by history or on presentation.

Patients in the HC, IC, and CI groups presented with lower respiratory symptoms or signs more frequently than patients in the HI group (P = .03). A significantly higher proportion of abnormal lung findings were present in those with a history of asthma or chronic lung disease compared with all others (50% vs 13%; P = .0143). Of 10 patients with a history of asthma, wheezing was present in 4. Signs of respiratory distress at presentation, such as tachypnea or shortness of breath, decreased breath sounds, or wheezing on lung auscultation and hypoxia, were each associated with

TABLE 1 Demographic and Clinical Characteristics of Inpatient Children With COVID-19

	No. (%)					*P*
	Total Cohort (*N* = 65)	HIs, <60 d of Age (*n* = 19)	HC, ≥60 d of Age (*n* = 16)	IC (*n* = 14)	CI (*n* = 16)	
Demographic characteristics						
Age[a]						<.001
<60 d	19 (29)	19 (100)	0 (0)	0 (0)	0 (0)	
60 d to <5 y	8 (12)	0 (0)	3 (19)	1 (7)	4 (25)	
5–<12 y	7 (11)	0 (0)	2 (13)	4 (29)	1 (6)	
≥12 y	31 (48)	0 (0)	11 (69)	9 (64)	11 (69)	
Male sex	33 (51)	10 (53)	8 (50)	7 (50)	8 (50)	>.99
Race						.14
White	14 (22)	7 (37)	2 (13)	2 (14)	3 (19)	
Black	17 (26)	2 (11)	3 (19)	4 (29)	8 (50)	
Asian American	8 (12)	1 (5)	3 (19)	3 (21)	1 (6)	
Other or multiracial	24 (37)	8 (42)	7 (44)	5 (36)	4 (25)	
Unknown or declined	2 (3)	1 (5)	1 (6)	0 (0)	0 (0)	
Ethnicity						.95
Hispanic	15 (23)	4 (21)	3 (19)	4 (29)	4 (25)	
Non-Hispanic	49 (75)	15 (79)	12 (75)	10 (71)	12 (75)	
Unknown or declined	1 (2)	0 (0)	1 (6)	0 (0)	0 (0)	
Insurance status						.01
Private	24 (37)	5 (26)	10 (63)	7 (50)	2 (13)	
Public	41 (63)	14 (74)	6 (38)	7 (50)	14 (88)	
Wt status categories[b]						.07
Normal wt	22 (58)	NA	5 (42)	8 (62)	9 (69)	
Overweight	5 (13)	NA	0 (0)	3 (23)	2 (15)	
Obesity	11 (29)	NA	7 (58)	2 (15)	2 (15)	
Clinical characteristics						
Known sick contact[c]	33 (57)	11 (58)	10 (63)	6 (50)	6 (55)	.93
Underlying medical condition						
Asthma or reactive airway disease	10 (15)	0 (0)	4 (25)	4 (29)	2 (13)	
Chronic lung disease	3 (5)	0 (0)	0 (0)	0 (0)	3 (19)	
Immunosuppression	8 (12)	0 (0)	0 (0)	8 (57)	0 (0)	
Immunodeficiency	4 (6)	0 (0)	0 (0)	4 (29)	0 (0)	
Neuromuscular disease or disorder	6 (9)	0 (0)	0 (0)	1 (7)	5 (31)	
Congenital heart disease	3 (5)	0 (0)	0 (0)	1 (7)	2 (13)	
Cancer	5 (8)	0 (0)	0 (0)	5 (36)	0 (0)	
Hemoglobinopathies	4 (6)	0 (0)	0 (0)	1 (7)	3 (19)	
Diabetes	4 (6)	0 (0)	1[d] (6)	1 (7)	2 (13)	
Other[e]	21 (32)	0 (0)	1[f] (6)	9 (64)	11 (69)	
Clinical features, symptoms and signs						
Fever						
Fever by history or on presentation	48 (74)	16 (84)	13 (81)	11 (79)	8 (50)	.12[g]
Fever by history or on presentation or during hospitalization	57 (88)	18 (95)	14 (88)	12 (86)	13 (81)	.96[g]
Hypothermia, <35.6°C	5 (8)	1 (5)	1 (6)	1 (7)	2 (13)	.93
Rash	5 (8)	1 (5)	3 (19)	1 (7)	0 (0)	.27
URI symptoms or signs	22 (34)	7 (37)	5 (31)	5 (36)	5 (31)	>.99
Sore throat	5 (8)	0 (0)	1 (6)	2 (14)	2 (13)	
Nasal congestion or rhinorrhea	17 (26)	7 (37)	4 (25)	3 (21)	3 (19)	
LRTI symptoms or signs	39 (60)	6 (32)	12 (75)	10 (71)	11 (69)	.03
Dyspnea, tachypnea, or respiratory distress	34 (52)	3 (16)	11 (69)	7 (50)	13 (81)	.0004
Cough	32 (49)	2 (11)	12 (75)	10 (71)	8 (50)	
Crackles on examination	2 (3)	0 (0)	1 (6)	0 (0)	1 (6)	
Rhonchi on examination	5 (8)	1 (5)	2 (13)	0 (0)	2 (13)	
Decrease breath sounds on examination	7 (11)	0 (0)	3 (19)	0 (0)	4 (25)	
Wheezing on examination	4 (6)	0 (0)	1 (6)	1 (7)	2 (13)	
Hypoxia on presentation, ≤92%	6 (9)	2 (11)	2 (13)	0 (0)	2 (13)	.67
GI symptoms	40 (62)	13 (68)	10 (63)	5 (36)	12 (75)	.16
Abdominal pain	11 (17)	NA	5 (31)	3 (21)	3 (19)	
Poor feeding or anorexia	26 (40)	10 (53)	3 (19)	2 (14)	11 (69)	

TABLE 1 Continued

	No. (%)					*P*
	Total Cohort (*N* = 65)	HIs, <60 d of Age (*n* = 19)	HC, ≥60 d of Age (*n* = 16)	IC (*n* = 14)	CI (*n* = 16)	
Nausea	5 (8)	1 (5)	2 (13)	0 (0)	2 (13)	
Vomiting	17 (26)	3 (16)	5 (31)	2 (14)	7 (44)	
Diarrhea	7 (11)	1 (5)	2 (13)	1 (7)	3 (19)	
Neurologic symptoms	21 (32)	4 (21)	6 (38)	4 (29)	7 (44)	.5
Headache	11 (17)	NA	4 (25)	3 (21)	4 (25)	
Seizures	2 (3)	0 (0)	1 (6)	0 (0)	1 (6)	
Anosmia	1 (2)	NA	0 (0)	1 (7)	0 (0)	
Dysgeusia	2 (3)	NA	0 (0)	0 (0)	2 (13)	
Altered mental status or irritability	7 (11)	4 (21)	1 (6)	0 (0)	2 (13)	
Chest pain	1 (2)	NA	1 (6)	0 (0)	0 (0)	
Myalgia or fatigue	22 (34)	4 (21)	7 (38)	7 (50)	5 (31)	.38

NA, not applicable for age.

[a] Statistical comparison of age compared by combining HI and HC groups.

[b] BMI was compared across groups, excluding HIs. Twenty-five subjects were excluded because of age <2 y, and 2 subjects were excluded because of missing or unreliable anthropomorphic data. Patients aged ≥20 y were categorized by using the CDC criteria for adult wt categories (BMI: 18.5–24.9, normal wt; 25.0–29.9, overweight; >30, obesity).

[c] Known sick contacts included household and nonhousehold contacts. Data were unknown for 7 subjects (2 IC and 5 CI); reported percentages are among patients with known status.

[d] Patient with diabetes mellitus type 2 on metformin.

increased illness severity ($P < .05$ for all).

Sixty-two percent of patients had gastrointestinal (GI) symptoms (primarily poor feeding and/or anorexia [40%]), but only 11% experienced diarrhea. Twenty-one children (32%) presented with neurologic symptoms (Table 1): generalized tonic-clonic seizures (2), headache (11), infants with irritability (4), children with altered mental status (4), and children reported anosmia or dysgeusia (3). Three children without symptoms suggestive of COVID-19 were identified as infected with SARS-CoV-2 by screening; 2 children were tested before an appendectomy procedure, and a neonate was born to a woman with COVID-19.

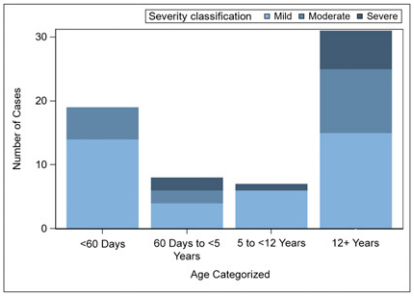

FIGURE 2
Age distribution of hospitalized pediatric patients with COVID-19 by severity. Illness severity was classified as follows: (1) mild (no requirement for supplemental oxygen), (2) moderate (supplemental oxygen with or without noninvasive respiratory support or need for frequent bronchodilator therapy), and (3) severe (mechanical ventilation with or without use of vasopressors and/or inotropes, ECMO, and RRT).

Laboratory Findings

The results of selected initial laboratory tests are reported by patient category in Table 2 and by patient severity in Table 3. There was a significant difference in the white blood cell count (WBC) among the severity groups, with a tendency for a higher WBC among higher severity groups ($P = .0027$). For C-reactive protein (CRP), there was also a significant tendency for higher values in more severe diseases ($P = .0192$; Table 3). Presence of neutropenia and lymphopenia were not significantly different across the disease severity groups ($P = .14$ and $P = .58$, respectively; Table 3).

Seven patients (11%) had an initial negative result for SARS-CoV-2 but tested positive for SARS-CoV-2 after repeat testing. Eight patients who tested positive for SARS-CoV-2 underwent repeat testing after hospitalization for a median (IQR) of 10 (3–15) days, and 5 patients (33%) remained positive. Coinfection based on a multiplex nucleic acid–based detection of respiratory pathogens was uncommon (Table 2).

Radiologic Findings

Forty-three of 65 patients (68%) had chest radiographs; 21 (49%) had abnormal findings on the initial radiograph. Chest radiographic findings were bilateral on 33% of initial radiographs and 42% of the most significant radiographs.

Hospital Course

Respiratory support was required in 34% of patients and in a higher proportion of the HC and CI groups (44% for each) than the HI and IC groups (26 and 21%, respectively). Among the patients in the CI group, 3 required mechanical ventilation, whereas only 1 in the HC group and 1 in the IC group required mechanical ventilation. The median duration of respiratory support was relatively low: 3 days (IQR, 1.0–4.0) for patients on noninvasive support, 5 days (IQR, 2.0–29.0) for patients on bilevel positive airway pressure (BiPAP) or continuous positive airway pressure (CPAP), and 5 days for patients on

TABLE 2 Hospital Course of Inpatient Children With COVID-19

	Total cohort (N = 65)	HIs, < 60 d of Age (n = 19)	HC, ≥60 d of Age (n = 16)	IC (n = 14)	CI (n = 16)	P
Initial laboratory test results[a]						
Complete blood cell count, n (%)	62 (95)	19 (100)	13 (81)	13 (93)	16 (100)	—
WBC, $\times 10^9$/L, median (IQR)	7.8 (5.0–14.5)	7.7 (4.8–9.3)	7.8 (5.2–10.0)	5.4 (2.1–11.0)	14 (6.2–19.1)	.12
Neutropenia,[a] n (%)	10 (16)	5 (26)	0 (0)	5 (38)	0 (0)	.009
Lymphopenia,[a] n (%)	27 (44)	8 (42)	3 (23)	10 (77)	6 (38)	.6
Platelet count, K/μL, median (IQR)	263.5 (199–384)	381 (254–455)	236 (201–298)	194 (130–240)	285.5 (203–395)	.004
CRP (reference: <5.0 mg/L), n (%)	30 (46)	1 (5)	11 (69)	8 (57)	10 (63)	—
CRP, mg/L, median (IQR)	20.1 (4.5–87.9)	NA	12.7 (4.1–106)	32.9 (6.1–71.7)	29.7 (8.9–54.1)	—
D-dimer value abnormal,[b] n (%)	21 (81)	1 (100)	5 (63)	6 (86)	9 (90)	—
Ferritin value abnormal,[b] n (%)	24 (89)	1 (100)	7 (88)	6 (75)	10 (100)	—
Lactate dehydrogenase value abnormal,[b] n (%)	25 (93)	1 (100)	7 (88)	7 (88)	10 (100)	—
Microbiology testing, n (%)						
SARS-CoV-2 PCR test result positive on first test	58 (89)	18 (95)	13 (81)	13 (93)	14 (88)	.67
Bacterial culture result positive[c]	3 (5)	0 (0)	0 (0)	0 (0)	3 (19)	—
Respiratory virus panel result positive[d]	3 (5)	0 (0)	2 (13)	0 (0)	1 (6)	—
Radiology, n (%)						
Chest radiography performed	43 (66)	8 (42)	12 (75)	10 (71)	13 (81)	—
Initial chest radiograph abnormal[e]	21 (49)	4 (50)	8 (67)	4 (40)	5 (38)	.53
Infiltrates	21 (32)	4 (21)	8 (50)	4 (29)	5 (31)	.32
Pleural effusion	2 (10)	0 (0)	1 (8)	1 (50)	0 (0)	.68
Unilateral	7 (33)	0 (0)	4 (33)	1 (14)	2 (15)	.48
Bilateral	14 (67)	4 (50)	4 (33)	3 (21)	3 (23)	
Most significant chest radiograph findings, n (%)						
Infiltrates	24 (37)	3 (16)	8 (50)	6 (43)	7 (44)	.15
Pleural effusion	5 (12)	0 (0)	1 (8)	3 (30)	1 (8)	.28
Unilateral	6 (14)	0 (0)	4 (33)	0 (0)	2 (15)	.17
Bilateral	18 (42)	3 (38)	4 (33)	6 (60)	5 (38)	—
Respiratory support						
Patients requiring any respiratory support, n (%)	22 (34)	5 (26)	7 (44)	3 (21)	7 (44)	.42
Supplemental oxygen (NC, FM, HFNC), n (%)	17 (26)	4 (21)	7 (44)	3 (21)	3 (19)	—
Days on supplemental oxygen (NC, FM, HFNC), median (IQR)	3 (1.0–4.0)	1 (0.8–1.8)	4 (0.5–4.0)	5 (1.0–5.0)	4 (0.5–6.0)	—
Noninvasive ventilation (BiPAP, CPAP), n (%)	5 (8)	1 (5)	0 (0)	2 (14)	2 (13)	—
Days on noninvasive ventilation (BiPAP, CPAP), median (IQR)	5 (2.0–29.0)	2 (2.0–2.0)	—	3.5 (2.0–5.0)	19.5 (10.0–29.0)	—
Mechanical ventilation, n (%)	5 (8)	0 (0)	1 (6)	1 (7)	3 (19)	—
Days on mechanical ventilation, median (IQR)	5 (5.0–27.0)	0 (0–0)	14 (14.0–14.0)	27 (27.0–27.0)	5 (0.0–5.0)	—
Critical care, n (%)						
Use of vasopressors	8 (12)	0 (0)	2 (13)	2 (14)	4 (25)	—
Use of ECMO	1 (2)	0 (0)	1 (6)	0 (0)	0 (0)	—
Use of RRT	2 (3)	0 (0)	0 (0)	2 (14)	0 (0)	—
Duration of symptoms, median (IQR)						
Maximum temperature in hospital, °C	38.3 (37.8–39.1)	38.1 (37.7–38.3)	38.8 (38.1–39.4)	38.2 (37.5–39)	39.2 (37.9–39.5)	—
Days of fever in hospital	1 (0.0–2.0)	0 (0.0–1.0)	1 (0.0–1.5)	1 (0.0–5.0)	3 (0.0–7.0)	—
COVID-19 therapies, n (%)						
Received COVID-19 treatment	26 (40)	0 (0)	8 (50)	10 (71)	8 (50)	—
Hydroxychloroquine	11 (17)	0 (0)	2 (13)	5 (36)	4 (25)	—
Hydroxychloroquine and azithromycin	13 (20)	0 (0)	5 (31)	5 (36)	3 (19)	—
Remdesivir	4 (6)	0 (0)	1 (6)	1 (7)	2 (13)	—
Tocilizumab	3 (5)	0 (0)	2 (13)	1 (7)	0 (0)	—
Anakinra	7 (11)	0 (0)	1 (6)	3 (21)	3 (19)	—
Corticosteroids	7 (11)	0 (0)	2 (13)	2 (14)	3 (19)	—
Anticoagulation	18 (28)	0 (0)	5 (31)	7 (50)	6 (38)	—
LOS						
Total LOS, d, median (IQR)	3.2 (2.0–6.8)	2 (1.8–2.9)	3.2 (2.0–5.0)	5.3 (2.8–6.8)	6 (3.3–9.9)	.02
Medical unit LOS, d, median (IQR)	2.5 (1.3–6.0)	1.7 (1.2–2.5)	3.1 (1.6–6.6)	3.4 (1.3–6.4)	3.7 (0.0–8.8)	.34
Patients admitted to PICU, n (%)	23 (35)	4 (6)	5 (31)	5 (36)	9 (56)	.2
PICU LOS, d, median (IQR)	5.4 (2.9–11.3)	3.1 (2.7–6.5)	5.4 (2.1–15.0)	10 (9.5–14.9)	5 (3.1–8.7)	.47

TABLE 2 Continued

	Total cohort (N = 65)	HIs, < 60 d of Age (n = 19)	HC, ≥60 d of Age (n = 16)	IC (n = 14)	CI (n = 16)	P
Disposition, n (%)						
Total discharged	57 (88)	19 (29)	14 (88)	10 (71)	14 (88)	—
Discharged well	54 (83)	19 (29)	13 (81)	8 (57)	14 (88)	—
Discharged with sequelae	3 (5)	0 (0)	1 (6)	2 (14)	0 (0)	—
Still hospitalized	7 (11)	0 (0)	2 (13)	4 (29)	1 (6)	—
Died	1 (2)	0 (0)	0 (0)	0 (0)	1 (6)	—

ANC, absolute neutrophil count; ALC, absolute lymphocyte count; FM, face mask; HFNC, high-flow nasal cannula; NA, not applicable; NC, nasal cannula;—, inferential statistics not performed.

[a] Neutropenia was defined as an ANC $<1 \times 10^9$/L, and lymphopenia was defined as a low ALC per age-based normal values. ANC and ALC were compared across all groups except for IC.

[b] D-dimer (reference: < 230 ng/mL) values were obtained in 26 (40%) patients out of the total cohort: 1 (5%) HI, 8 (50%) HC, 7 (50%) IC, and 10 (63%) CI groups; ferritin (reference: 15–150 ng/mL) and lactate dehydrogenase (reference: 135–225 U/L) values were obtained in 27 (42%) patients out of the total cohort: 1 (5%) HI, 8 (50%) HC, 8 (57%) IC, and 10 (63%) CI.

[c] Two patients had a positive urine culture result; 1 patient had positive urine and tracheal culture results.

[d] Positive results included *Mycoplasma* pneumonia (1 patient), parainfluenza type 3 (1 patient), and rhinovirus or enterovirus (1 patient).

[e] Chest radiograph findings were measured as a proportion of the total number of patients who received chest radiographs.

mechanical ventilation (IQR, 5.0–27.0).

Specific antiviral therapy was initiated in 26 patients (40%), and sequential antiviral therapies were commonly prescribed (Table 2). A higher proportion of patients in the CI group required vasopressors (4 [25%]) compared with the other groups. Additionally, RRT was used in 2 (14%) patients in the IC group, and ECMO was used in 1 patient, who was in the HC group.

The median duration of hospitalization was 3.2 days (IQR, 2.0–6.8) (Table 2). The distribution of hospital length of stay (LOS) was significantly different across patient groups (P = .02). Patients who were in the IC or CI groups had longer LOS compared with the other groups; the HI group had the lowest LOS, with a median LOS of 2.0 days (IQR, 1.8–2.9) (Table 2). Twenty-three patients (35%) required ICU care, with a median ICU stay of 5.4 days (IQR, 2.9–11.3). The proportion of patients with an ICU stay varied among the patient groups, with a higher proportion in the CI group (56%) and a lower proportion in the HI group (6%).

Severity of disease was classified as mild (39 [60%]), moderate (17 [26%]), and severe (7 [14%]) (Table 3, Fig 3). A greater proportion of those with a chronic medical condition developed severe disease (25%) compared with the other 3 groups (HI, 0%; HC, 19%; IC, 14%), but this difference was not significant (P = .07). Most patients in the IC group had mild disease (11 [79%]), but 2 patients had severe disease: 1 patient who had newly diagnosed leukemia, with a WBC of 91×10^9/L, who required RRT and in whom COVID-19 may have been subclinical and another patient who, 2 weeks post allogeneic stem cell transplant, required prolonged mechanical ventilation because of COVID-19. Similarly, most of the patients in the HI group had a mild severity; in contrast, only 38% of the children in the CI group had mild disease.

Fifty-seven patients were discharged, including 54 patients with no significant sequelae. At the close of the study period, 7 patients were still hospitalized. One death was reported from this cohort, a toddler with advanced progressive neuromuscular disease with gastrostomy tube and oxygen dependence who was admitted with respiratory failure and acute decompensation. One patient admitted with primary COVID-19 disease was later treated for multisystem inflammatory syndrome in children (MIS-C).

DISCUSSION

This study of consecutively admitted patients with COVID-19 is the largest US-based inpatient series, to our knowledge, describing pediatric SARS-CoV-2 infection. Our pediatric patients with COVID-19 were classified into 4 clinical categories with a specific focus on differences in demographic and clinical features. This novel approach of categorizing affected patients may be helpful in recognition and management of these patients.

We found that 35% of patients had severe infection requiring ICU care. Our rate of ICU care is higher than what was reported in an initial series from China, where 0.6% of pediatric patients required ICU care. This difference is possibly due to broader, nonclinical, and laboratory-based admission criteria in their study. Our ICU rate is also higher than that reported by other US pediatric studies. A CDC report described that ∼10% of hospitalized pediatric patients with COVID-19 were admitted to the ICU, although this number may reflect a bias in reporting due to incomplete data.[7] More recent US studies reported that 21% to 28% of inpatients required ICU care, which is somewhat lower than our experience.[10–12] There was a single fatal case of infection in our cohort, which is consistent with the infrequent reporting of fatalities among pediatric patients with COVID-19.[5–7,13,14]

There was a trend toward a higher proportion of children with obesity in

TABLE 3 Demographic and Clinical Characteristics of Inpatient Children With COVID-19 by Disease Severity

	Severity				*P*
	Total Cohort (*N* = 65)	Mild	Moderate	Severe	
Disease category, *n* (%)					.07
HIs, younger than 60 d	19 (29)	14 (36)	5 (29)	0 (0)	—
HC, 60 d of age and older	16 (25)	8 (21)	5 (29)	3 (33)	—
IC	14 (22)	11 (28)	1 (6)	2 (22)	—
CI	16 (25)	6 (15)	6 (35)	4 (44)	—
Demographic characteristics, *n* (%)					
Age					.12
<60 d	19 (29)	14 (36)	5 (29)	0 (0)	—
60 d to <5 y	8 (12)	4 (10)	2 (12)	2 (22)	—
5–<12 y	7 (11)	6 (15)	0 (0)	1 (11)	—
≥12 y	31 (48)	15 (38)	10 (59)	6 (67)	—
Male sex	33 (51)	20 (51)	9 (53)	4 (44)	.99
Race					.71
White	14 (22)	9 (23)	5 (29)	0 (0)	—
Black	17 (26)	9 (23)	5 (29)	3 (33)	—
Asian American	8 (12)	4 (10)	2 (12)	2 (22)	—
Other or multiracial	24 (37)	15 (38)	5 (29)	4 (44)	—
Unknown or declined	2 (3)	2 (5)	0 (0)	0 (0)	—
Ethnicity					
Hispanic	15 (23)	9 (23)	2 (12)	4 (44)	.35
Non-Hispanic	49 (75)	29 (74)	15 (88)	5 (56)	—
Unknown or declined	1 (2)	1 (3)	0 (0)	0 (0)	—
Insurance status					.69
Private	24 (37)	16 (41)	5 (29)	3 (33)	—
Public	41 (63)	23 (59)	12 (71)	6 (67)	—
Weight status categories[a]					.98
Normal wt	22 (58)	12 (60)	6 (55)	4 (57)	—
Overweight	5 (13)	3 (15)	1 (9)	1 (14)	—
Obesity	11 (29)	5 (25)	4 (36)	2 (29)	—
Clinical characteristics, *n* (%)					
Known sick contact[b]	33 (57)	20 (51)	11 (65)	2 (22)	.56
Underlying medical condition					
Asthma or reactive airway disease	10 (15)	6 (15)	4 (24)	0 (0)	—
Chronic lung disease	3 (5)	0 (0)	1 (6)	2 (22)	—
Immunosuppression	8 (12)	6 (15)	1 (6)	1 (11)	—
Immunodeficiency	4 (6)	4 (10)	0 (0)	0 (0)	—
Neuromuscular disease or disorder	6 (9)	3 (8)	1 (6)	2 (22)	—
Congenital heart disease	3 (5)	2 (5)	0 (0)	1 (11)	—
Cancer	5 (8)	4 (10)	0 (0)	1 (11)	—
Hemoglobinopathies	4 (6)	2 (5)	2 (12)	0 (0)	—
Diabetes	4 (6)	3 (8)	1 (6)	0 (0)	—
Other[c]	21 (32)	12 (31)	5 (29)	4 (44)	—
Clinical features, symptoms and signs, *n* (%)					
Fever[d]					
Fever by history or on presentation	48 (74)	29 (74)	12 (71)	7 (78)	.92
Fever by history or on presentation or during hospitalization	57 (88)	33 (85)	16 (94)	8 (89)	.76
Hypothermia, <35.6°C	5 (8)	0 (0)	1 (6)	4 (44)	.0003
Rash	5 (8)	4 (10)	0 (0)	1 (11)	
URI symptoms or signs	22 (34)	14 (36)	7 (41)	1 (11)	.27
Sore throat	5 (8)	3 (8)	2 (12)	0 (0)	—
Nasal congestion or rhinorrhea	17 (26)	11 (28)	5 (29)	1 (11)	—
Cough	32 (49)	17 (44)	10 (59)	5 (56)	—
GI symptoms	40 (62)	23 (59)	12 (71)	5 (56)	.66
Abdominal pain	11 (17)	6 (15)	3 (18)	2 (22)	—
Poor feeding or anorexia	26 (40)	14 (36)	9 (53)	3 (33)	—
Nausea	5 (8)	4 (10)	0 (0)	1 (11)	—
Vomiting	17 (26)	11 (28)	5 (29)	1 (11)	—
Diarrhea	7 (11)	5 (13)	1 (6)	2 (22)	—

TABLE 3 Continued

	Severity				*P*
	Total Cohort (*N* = 65)	Mild	Moderate	Severe	
Neurologic symptoms	21 (32)	13 (33)	4 (24)	4 (44)	.54
Headache	11 (17)	7 (18)	3 (18)	1 (11)	—
Seizures	2 (3)	0 (0)	0 (0)	2 (22)	—
Anosmia	1 (2)	1 (3)	0 (0)	0 (0)	—
Dysgeusia	2 (3)	0 (0)	2 (12)	0 (0)	—
Altered mental status or irritability	7 (11)	5 (13)	1 (6)	1 (11)	—
Chest pain	1 (2)	(0)	(0)	(0)	—
Myalgia or fatigue	22 (34)	13 (33)	6 (35)	3 (33)	.99
Initial laboratory test results					
WBC, $\times 10^9$/L, median (IQR)	7.8 (5.0–14.5)	7.8 (5.0–11.4)	5.3 (4.4–8.6)	18.3 (13.0–21.6)	.0027
Neutropenia,[e] *n* (%)	10 (16)	9 (24)	1 (6)	0 (0)	.14
Lymphopenia,[e] *n* (%)	27 (44)	18 (50)	6 (38)	3 (33)	.58
CRP,[f] mg/L, median (IQR)	20.1 (4.5–87.9)	6.9 (4.0–13.9)	26.2 (8.9–49.4)	106 (54.1176.0)	.0192
LOS					
Total LOS, d, median (IQR)	3.2 (2.0–6.8)	2.2 (1.8–4.0)	6.1 (4.1–9.4)	13.5 (5.5–25.9)	—
Medical unit LOS, d, median (IQR)	2.4 (1.2–4.5)	2.2 (1.5–4.0)	3.8 (0.0–7.7)	0 (0.0–3.6)	—
Patients admitted to PICU, *n* (%)	23 (35)	4 (10)	10 (59)	9 (100)	—
PICU LOS, d, median (IQR)	5.4 (2.9–11.3)	3.1 (2.0–6.3)	4.5 (2.5–8.7)	13.9 (5.4–18.2)	—

ANC, absolute neutrophil count; ALC, absolute lymphocyte count; —, inferential statistics not performed.

[a] BMI was compared across groups, excluding HIs. Twenty-five subjects were excluded because of age <2 y, and 2 subjects were excluded because of missing or unreliable anthropomorphic data. Patients aged ≥20 y were categorized by using the CDC criteria for adult wt categories (BMI: 18.5–24.9, normal wt; 25.0–29.9, overweight; >30, obesity).

[b] Known sick contacts included household and nonhousehold contacts. Data were unknown for 7 subjects (2 IC and 5 CI); reported percentages are among patients with known status.

[c] Other conditions include, but are not limited to, genetic syndromes, endocrinopathies, epilepsy, multiple sclerosis, and feeding-tube dependence.

[d] HIs <60 d of age were excluded from analyses involving fever status.

[e] Neutropenia was defined as an ANC $<1 \times 10^9$/L, and lymphopenia was defined as a low ALC per age-based normal values.

[f] Statistical significance based on limited CRP values obtained and exclusion of HI group.

our cohort, as compared with national and regional estimates of childhood obesity (18%–18.5% with obesity),[15] and in the HC group, 60% had obesity. Obesity is an established risk factor for severity of illness in adults,[16] whereas the pediatric data have been limited and variable. Consistent with findings of Chao et al,[10] our data suggested that obesity was not associated with greater illness severity, although the authors of another study found an increased need for mechanical ventilation among children with obesity.[12]

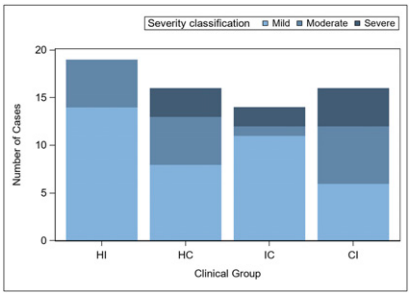

FIGURE 3
Clinical group of hospitalized patients according to severity. Illness severity was classified as follows: (1) mild (no requirement for supplemental oxygen), (2) moderate (supplemental oxygen with or without noninvasive respiratory support or need for frequent bronchodilator therapy), and (3) severe (mechanical ventilation with or without use of vasopressors and/or inotropes, ECMO, and RRT). HIs were aged <60 days. HC were aged ≥60 days. IC had cancer or primary immunodeficiency or received immunosuppression. CI had a condition (other than immunocompromise) for >1 year that interfered with activities of daily life.

Among HC, LRTI was common, with lower respiratory tract signs and symptoms present in 60% of patients. These results differ from previous reports of shortness of breath and cough in 11% to 13% and 44% to 54% of patients, respectively.[2,7] Most patients had fever either before or during hospitalization (86%), and 5 patients (8%) presented with hypothermia, which, to our knowledge, has not been reported to date.

Authors of previous reports have found higher rates of hospitalization among children <1 year of age,[1] but they were not more likely to be admitted to the ICU.[7] Our data suggest that an important subgroup in this cohort are infants younger than 60 days of age, most of whom were hospitalized as per institutional guidelines for evaluation of serious bacterial infection, and this group accounted for the majority of children younger than 1 year of age with COVID-19 who were hospitalized. Most HIs had an unremarkable hospital course, which is consistent with findings in other smaller case series.[9,17,18]

Overall, IC had a relatively low severity of illness compared with HC and CI, but the relatively small numbers of patients in each group does not allow for a firm conclusion, and further research is required. The mild severity of disease in our immunocompromised patients is consistent with the experience in Italy, in which none of the 3 children with COVID-19 post liver transplant

had pulmonary findings.[19] The CI patients tended to have a more severe hospital course.

In addition to the 3 patients identified by screening, the symptoms of several patients in our cohort with a positive test result for SARS-CoV-2 may have been caused by another illness, and the positive test result may have reflected subclinical or recent past infection rather than acute disease. Two patients who were admitted for diabetic ketoacidosis were found to be SARS-CoV-2–positive without related findings, such as fever, cough, or hypoxemia. It is possible that the viral infection could have contributed to the development of the episode of diabetic ketoacidosis, which has been seen with influenza.[20] Additionally, a 21-year-old patient with newly diagnosed lymphoma was admitted to the PICU for concern for airway compromise and had a positive SARS-CoV-2 test result. This patient's lungs were normal on the basis of a computed tomography chest scan, and he did not develop fever, tachypnea, or hypoxia over the following 2 weeks. These cases are consistent with reports of asymptomatic cases of COVID-19 in children,[3,5] pregnant women,[21] and adults.[22]

Limitations of this study include that it was conducted at a single institution, limited to hospitalized patients, and may not be representative of children with SARS-CoV-2 in the ambulatory setting. Although our sample size is relatively small, the number of hospitalized patients is larger than that in most studies of pediatric patients, and our catchment area encompasses a diverse population regarding demographic parameters and underlying medical conditions. In addition, this is an early study of pediatric COVID-19, and as such, the extent of its clinical impact in various patient populations is not fully understood. The closing date of this study predated the onset of hospitalization of multiple children at our center with MIS-C associated with COVID-19[23,24]; 1 patient in this cohort who was hospitalized toward the end of the study period met the case definition for MIS-C.

In this cohort study, we describe specific clinical categories of children hospitalized with COVID-19 using information about their clinical presentation, diagnostic evaluation, treatment course, and severity. This classification may be helpful for clinicians as COVID-19 continues to emerge in other areas. Clinicians should be aware that infants younger than 60 days of age who present with fever may have COVID-19 and require testing and appropriate isolation precautions. Also, HI and IC generally have a mild course of infection, whereas hospitalized adolescent-aged and chronically ill patients tend to have a more severe hospital course. Elevated WBC and CRP levels are associated with a more severe course of infection.

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ABBREVIATIONS

BiPAP: bilevel positive airway pressure
CDC: Centers for Disease Control and Prevention
CI: chronically ill children
COVID-19: coronavirus disease 2019
CPAP: continuous positive airway pressure
CRP: C-reactive protein
ECMO: extracorporeal membrane oxygenation
GI: gastrointestinal
HC: healthy children
HI: healthy infant
IC: immunocompromised children
IQR: interquartile range
LOS: length of stay
LRTI: lower respiratory tract infection
MIS-C: multisystem inflammatory syndrome in children
RRT: renal replacement therapy
SARS-CoV-2: severe acute respiratory syndrome coronavirus 2
URI: upper respiratory infection
WBC: white blood cell count

The data that support the findings of this study are available on request from COVID19@northwell.edu. The data are not publicly available, owing to restrictions, because it could compromise the privacy of research participants.

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Early Experience of COVID-19 in a US Children's Hospital

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