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Clinical Manifestations and Outcomes of Critically Ill Children and Adolescents with Coronavirus Disease 2019 in New York City

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Objectives To describe the clinical manifestations and outcomes of critically ill children with coronavirus disease-19 (COVID-19) in New York City.

Study design Retrospective observational study of children 1 month to 21 years admitted March 14 to May 2, 2020, to 9 New York City pediatric intensive care units (PICUs) with severe acute respiratory syndrome coronavirus 2 infection.

Results Of 70 children admitted to PICUs, median age was 15 (IQR 9, 19) years; 61.4% male; 38.6% Hispanic; 32.9% black; and 74.3% with comorbidities. Fever (72.9%) and cough (71.4%) were the common presenting symptoms. Twelve patients (17%) met severe sepsis criteria; 14 (20%) required vasopressor support; 21 (30%) developed acute respiratory distress syndrome (ARDS); 9 (12.9%) met acute kidney injury criteria; 1 (1.4%) required renal-replacement therapy, and 2 (2.8%) had cardiac arrest. For treatment, 27 (38.6%) patients received hydroxychloroquine; 13 (18.6%) remdesivir; 23 (32.9%) corticosteroids; 3 (4.3%) tocilizumab; and 1 (1.4%) anakinra; no patient was given immunoglobulin or convalescent plasma. Forty-nine (70%) patients required respiratory support: 14 (20.0%) noninvasive mechanical ventilation, 20 (28.6%) invasive mechanical ventilation (IMV), 7 (10%) prone position, 2 (2.8%) inhaled nitric oxide, and 1 (1.4%) extracorporeal membrane oxygenation. Nine (45%) of the 20 patients requiring IMV were extubated by day 14 with median IMV duration of 218 (IQR 79, 310.4) hours. Presence of ARDS was significantly associated with duration of PICU and hospital stay, and lower probability of PICU and hospital discharge at hospital day 14 ($P < .05$ for all).

Conclusions Critically ill children with COVID-19 predominantly are adolescents, have comorbidities, and require some form of respiratory support. The presence of ARDS is significantly associated with prolonged PICU and hospital stay. *(J Pediatr 2020;226:55-63)*.

As the novel coronavirus disease 2019 (COVID-19) pandemic began in December 2019, children were reported to be at lower risk of developing severe symptoms or critical illness compared with adults with a large study from China demonstrating critical illness in <1% of children.[1,2] Preliminary studies from Europe and the US have provided early data on critically ill children.[3-7]

The clinical manifestations, including pulmonary findings, and outcomes of critically ill children with confirmed severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection have been described only in a small number of cases, and the factors associated with development of progressive critical illness and mortality are unclear. The objectives of this study are to describe the clinical

AKI	Acute kidney injury	MIS-C	Multisystem inflammatory syndrome in children
ARDS	Acute respiratory distress syndrome	OI	Oxygenation index
BMI	Body mass index	OSI	Oxygen saturation index
COVID-19	Coronavirus disease 2019	PICU	Pediatric intensive care unit
IMV	Invasive mechanical ventilation	PIM-2	Pediatric Index of Mortality-2
LOS	Length of stay	SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2

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manifestations of critically ill children with COVID-19 admitted to pediatric intensive care units (PICUs) across New York City during the first wave of the US pandemic and to identify factors associated with PICU and hospital length of stay (LOS).

Methods

The Albert Einstein College of Medicine institutional review board reviewed and approved this multicenter retrospective observational study. The institutional review boards at each individual center approved this study, as applicable. Only deidentified data were transmitted and analyzed. Informed consent was waived.

We identified critically ill pediatric patients 1 month to 21 years of age with confirmed SARS-CoV-2 infection from March 14 to May 2, 2020 (7 weeks) admitted to 9 New York City teaching hospitals (Children's Hospital at Montefiore, New York-Presbyterian Morgan Stanley Children's Hospital of New York, Kravis Children's Hospital at Mount Sinai, State University of New York Downstate Medical Center, Jacobi Medical Center, Kings County Medical Center, Lincoln Medical and Mental Health Center, The Brooklyn Hospital Center, and Richmond University Medical Center) located in 4 of 5 boroughs of New York City with a total catchment area encompassing all 5 boroughs (**Figure 1**; available at www.jpeds.com). These 9 of 25 PICUs (approximately 46% of the PICU beds) in New York City were included as collaborators were able to obtain institutional review board approval in time for enrollment.

A COVID-19 case was defined as due to SARS-CoV-2 infection by a positive real-time reverse transcription polymerase chain reaction test of a specimen using nasopharyngeal swab, using one of several different testing platforms due to institutional preference, as well as limited testing kits in the early phase of the pandemic (Abbott Laboratories, Abbot Park, Illinois; Bioreference Laboratories, Elmwood, New Jersey; Cepheid Xpert Xpress, Sunnyvale, California; Hologic Panther Fusion, San Diego, California; LabCorp, Raritan, New Jersey; Luminex Aries; Northwell Health Laboratories, Lake Success, New York; New York City Department of Health and Mental Hygiene Public Health Laboratory; Roche diagnostics, Basel, Switzerland). Patients with the more recently recognized entity of multisystem inflammatory syndrome in children (MIS-C) were not represented in this study because the description was defined, and cases began to occur after the study time period.

Data from each institution's electronic medical record were obtained through a research form in Research Electronic Data Capture software (REDCap, Vanderbilt University, Nashville, Tennessee). Demographic and clinical data and laboratory and radiologic results were obtained. All tests and treatments were performed at the discretion of the treating physicians.

A total of 31 of the 70 patients described in this study were included in other published reports, including 3 patients who met criteria the Centers for Disease Control use definition for MIS-C.[5,6,8-10]

Definitions

Acute respiratory distress syndrome (ARDS) was defined using Pediatric Acute Respiratory Distress criteria[11]: oxygenation index (OI) 4-8 or oxygen saturation index (OSI) 5-7.5 as mild-severity ARDS, OI 8-16 or OSI 7.5-12.3 as moderate-severity ARDS, and OI >16 or OSI >12.5 as severe ARDS. Management of ARDS was at the discretion of the treating physician and generally was based on Pediatric Acute Respiratory Distress recommendations of low tidal volume and limiting plateau pressure to ≤30 cm of water.[11,12] Acute kidney injury (AKI) was defined using the Kidney Disease: Improving Global Outcomes classification based upon a change in serum creatinine level and creatinine clearance.[13] Sepsis, severe sepsis, and septic shock were defined using the Pediatric Surviving Sepsis Guidelines.[14] Virus-associated sepsis was defined as the presence of ≥2 systemic inflammatory syndrome criteria; severe sepsis as sepsis with organ dysfunction or tissue hypoperfusion; and septic shock as severe sepsis with volume-refractory hypotension.[14] Obesity was considered a comorbidity and was defined as body mass index (BMI) >30 kg/m^2. Asthma was considered a respiratory comorbidity. Severity of illness was described using Pediatric Index of Mortality-2 (PIM-2) scores, and standardized mortality ratio was calculated as standardized mortality ratio = observed mortality of our cohort/expected mortality using PIM-2 score.[15]

Outcomes

Outcomes reported included need for invasive mechanical ventilation, PICU LOS, hospital LOS, and mortality within the first 14 days and 28 days of PICU admission.

Statistical Analyses

Demographic and clinical characteristics were summarized as frequencies and percentages for categorical variables, as medians and IQRs for continuous variables, and compared between patients with and without ARDS by using χ^2 test or Fisher exact test, and Wilcoxon rank-sum test for categorical and continuous variables, respectively. Patients were followed up at 14 days and 28 days from PICU admission, and Kaplan–Meier curves of PICU and hospital LOS were compared in patients with and without ARDS using log-rank tests. Cox proportional hazards regression was employed to investigate the association of presence of ARDS with PICU and hospital discharges, adjusting for need for mechanical ventilation during PICU stay and platelet count measured on admission day 1 in multivariable analyses. $P < .05$ was considered statistically significant. Data were analyzed by using SAS software (version 9.4; SAS Institute Inc, Cary, North Carolina).

Results

Seventy children with COVID-19 were hospitalized in the PICUs of the 9 participating hospitals in New York City from March 14 to May 2, 2020. Thirty-three (47%) patients were

from the borough of the Bronx and 16 (22.8%) from the borough of Brooklyn (Figure 1).

Of the 70 patients, 21 (30%) had a diagnosis of ARDS within the first 14 days of hospitalization. Demographics and baseline characteristics of the whole cohort as well as for those with and without ARDS are shown in Table I. Forty-three (61.4%) patients were male; 27 (38.6%) were Hispanic, and 23 (32.9%) were black. Median age was 15 years (IQR 9, 19); median weight was 56.6 kg (IQR 27.7, 96.1) and BMI was 22.7 kg/m^2 (IQR 19.1, 32.7). Fifty-two patients (74.3%) had at least 1 comorbidity. Severity of illness on admission was not significantly different between the ARDS and non-ARDS groups, as reflected by PIM-2 scores on PICU admission with overall risk of mortality of 0.8% (IQR 0.2%, 1.4%).

Fever (72.9%) and cough (71.4%) were the most common presenting symptoms. Ninety percent of patients who developed ARDS came to medical attention with dyspnea, compared with 53.1% who did not develop ARDS ($P = .003$). Median duration of symptoms before hospitalization was 5 days (IQR 2.0, 7.0), and a known sick contact was reported in 50.8% of patients.

Table II summarizes the laboratory and radiographic testing results. The median total white blood cell count for

Table I. Demographics and baseline characteristics of critically ill pediatric patients with COVID-19

Characteristics	Total (n = 70)	No ARDS (n = 49)	ARDS (n = 21)	*P* value*
Age, y, median (IQR)	15.0 (9.0, 19.0)	15.0 (11.0, 18.0)	14.0 (9.0, 19.0)	.7237
Sex				
Female, n (%)	27 (38.6)	19 (38.8)	8 (38.1)	.9573
Male, n (%)	43 (61.4)	30 (61.2)	13 (61.9)	
Race				
Black, n (%)	23 (32.9)	19 (38.8)	4 (19.0)	.1699
White, n (%)	7 (10.0)	6 (12.2)	1 (4.8)	
Latino, n (%)	27 (38.6)	15 (30.6)	12 (57.1)	
Other, n (%)	13 (18.6)	9 (18.4)	4 (19.0)	
Weight, kg, median (IQR)	56.6 (27.7, 96.1)	63.4 (27.7, 96.1)	45.2 (28.0, 83.8)	.8526
BMI, kg/m^2, median (IQR) [n = 66]	22.7 (19.1, 32.7)	23.5 (19.2, 32.7)	21.4 (19.1, 30.6)	.9561
PIM-2 score: % risk of mortality, median (IQR) [n = 69]	0.8 (0.2, 1.4)	0.8 (0.2, 1.8)	0.8 (0.4, 1.3)	.6417
Comorbidities				
Obesity (BMI>30), n (%) [n = 66]	20 (30.3)	13 (28.9)	7 (33.3)	.7144
BMI >35, n (%) [n = 66]	14 (21.2)	9 (20.0)	5 (23.8)	.7534
BMI >40, n (%) [n = 66]	12 (18.2)	8 (17.8)	4 (19.0)	1.0000
BMI >50, n (%) [n = 66]	4 (6.1)	2 (4.4)	2 (9.5)	.5865
Respiratory, n (%)	17 (24.3)	10 (20.4)	7 (33.3)	.2478
Heart disease, n (%)	4 (5.7)	3 (6.1)	1 (4.8)	1.0000
Hematologic/malignancy/immunosuppression, n (%)	12 (17.1)	8 (16.3)	4 (19.0)	.7432
Diabetes/prediabetes, n (%)	9 (12.9)	7 (14.3)	2 (9.5)	.7140
Neurologic, n (%)	10 (14.3)	5 (10.2)	5 (23.8)	.1536
2 or more comorbidities, n (%)	18 (25.7)	12 (24.5)	6 (28.6)	.7203
3 or more comorbidities, n (%)	2 (2.9)	0 (0.0)	2 (9.5)	.0870
Presenting symptoms/history				
Cough, n (%)	50 (71.4)	34 (69.4)	16 (76.2)	.5637
Fever, n (%)	51 (72.9)	34 (69.4)	17 (81.0)	.3187
Shortness of breath, n (%)	45 (64.3)	26 (53.1)	19 (90.5)	.0028
Headache, n (%)	15 (21.4)	9 (18.4)	6 (28.6)	.3564
Rhinorrhea, n (%)	9 (12.9)	4 (8.2)	5 (23.8)	.1155
Nausea/vomiting, n (%)	24 (34.3)	20 (40.8)	4 (19.0)	.0787
Diarrhea, n (%)	18 (25.7)	12 (24.5)	6 (28.6)	.7203
Myalgias, n (%)	13 (18.6)	10 (20.4)	3 (14.3)	.7410
Known sick contacts, n (%) [n = 11 missing]	30 (50.8)	19 (47.5)	11 (57.9)	.4555
Travel history in past month, n (%)	2 (2.9)	1 (2.0)	1 (4.8)	.5130
Duration of symptoms before admission, d, median (IQR) [n = 1 missing]	5.0 (2.0, 7.0)	4.0 (2.0, 8.5)	5.0 (3.0, 7.0)	.7626
Vital signs on admission				
Temp, °C, median (IQR)	37.5 (36.9, 38.3)	37.4 (36.9, 38.3)	37.5 (37.0, 37.9)	.7923
Heart Rate, bpm, median (IQR)	107.0 (99.0, 129.0)	107.0 (101.0, 131.0)	107.0 (99.0, 123.0)	.6628
SBP, mm Hg, median (IQR)	114.0 (101.0, 126.0)	116.0 (102.0, 126.0)	105.0 (95.0, 124.0)	.1421
DBP, mm Hg, median (IQR)	68.5 (58.0, 77.0)	69.0 (58.0, 79.0)	68.0 (58.0, 72.0)	.6909
RR, bpm, median (IQR)	26.0 (22.0, 38.0)	25.0 (22.0, 36.0)	32.0 (26.0, 42.0)	.0724
SpO_2 percentage, median (IQR)	98.0 (96.0, 99.0)	98.0 (96.0, 99.0)	97.0 (94.0, 99.0)	.2375
Admission diagnosis				
Respiratory failure, n (%)	47 (67.1)	26 (53.1)	21 (100.0)	.0090
Shock, n (%)	5 (7.1)	5 (10.2)	0 (0.0)	
Sepsis, n (%)	5 (7.1)	5 (10.2)	0 (0.0)	
DKA, n (%)	7 (10.0)	7 (14.3)	0 (0.0)	
Seizures/neuro, n (%)	5 (7.1)	5 (10.2)	0 (0.0)	
Other, n (%)	1 (1.4)	1 (2.0)	0 (0.0)	

bpm, breaths per minute; *DBP*, diastolic blood pressure; *DKA*, diabetic ketoacidosis; *RR*, respiratory rate; *SBP*, systolic blood pressure; *SpO_2*, arterial oxygen saturation.
*χ^2 test, Fisher exact test, or Wilcoxon rank-sum test.

Table II. Results of laboratory imaging studies on admission to PICU

Variables	Total (n = 70)	No ARDS (n = 49)	ARDS (n = 21)	*P* value*
WBC, k/μL, median (IQR) [n = 69]	8.8 (6.3, 13.0)	8.8 (6.3, 11.7)	8.9 (6.0, 14.3)	.9105
Absolute lymphocyte count, cells/μL, median (IQR) [n = 69]	1117.4 (610.9, 1998.4)	1001.6 (604.5, 2258.7)	1177.0 (766.3, 1914.9)	.3936
Hemoglobin, g/dL, median (IQR) [n = 69]	12.2 (10.8, 14.6)	12.9 (11.1, 14.7)	11.9 (9.6, 13.2)	.1815
Platelets, k/μL, median (IQR) [n = 69]	198.0 (147.0, 264.0)	216.0 (159.0, 309.0)	169.0 (110.0, 242.0)	.0430
AST, U/L, median (IQR) [n = 60]	36.0 (28.0, 60.0)	33.0 (27.0, 57.0)	40.0 (32.0, 61.0)	.3691
ALT, U/L, median (IQR) [n = 60]	26.0 (14.5, 49.5)	30.0 (15.0, 56.0)	20.0 (12.0, 45.0)	.1870
Total bilirubin, mg/dL, median (IQR) [n = 60]	0.4 (0.2, 0.9)	0.4 (0.2, 1.0)	0.3 (0.1, 0.9)	.1987
BUN, mg/dL, median (IQR)	11.0 (8.0, 14.0)	10.0 (8.0, 13.0)	11.0 (7.0, 15.0)	.6528
Creatinine, mg/dL, median (IQR)	0.7 (0.5, 0.9)	0.7 (0.5, 0.9)	0.6 (0.4, 0.9)	.7728
C-reactive protein, mg/dL, median (IQR) [n = 48]	6.8 (2.6, 14.9)	6.0 (2.5, 26.0)	8.1 (3.5, 11.8)	.8716
Procalcitonin, ng/mL, median (IQR) [n = 34]	0.2 (0.1, 0.9)	0.2 (0.1, 0.6)	0.4 (0.2, 1.1)	.1778
Pro-BNP, pg/mL, median (IQR) [n = 14]	940.0 (92.0, 4289.0)	440.8 (60.0, 4289.0)	1734.0 (1112.0, 15 000.0)	.1195
Troponin, ng/mL, median (IQR) [n = 32]	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.1)	.6109
CPK, U/L, median (IQR) [n = 25]	120.0 (74.0, 302.0)	128.5 (74.0, 316.0)	99.0 (60.0, 302.0)	1.0000
Lactate, mmol/L, median (IQR) [n = 43]	1.5 (1.2, 2.5)	1.6 (1.2, 2.6)	1.5 (1.3, 2.3)	.5972
D-dimer, μg/mL FEU, median (IQR) [n = 35]	2.3 (0.8, 161.0)	3.1 (0.8, 161.0)	2.0 (0.7, 20.0)	.8663
LDH, U/L, median (IQR) [n = 39]	370.0 (289.0, 524.0)	318.0 (276.0, 461.0)	421.0 (344.0, 569.0)	.0413
IL-6, pg/mL, median (IQR) (n = 23)	42 (13.7, 112)	16.4 (12.1, 66)	78.7 (34, 201.5)	.0316
+Blood culture, n (%)	8 (11.8)	4 (8.5)	4 (19.0)	.2403
+Respiratory culture, n (%)	3 (5.2)	0 (0.0)	3 (14.3)	.0431
+Urine culture, n (%)	5 (8.2)	1 (2.5)	4 (19.0)	.0437
Chest radiograph				
Clear, n (%)	12 (17.1)	12 (24.5)	0 (0.0)	.0133
B/L infiltrates, n (%)	35 (50.0)	20 (40.8)	15 (71.4)	.0189
Pleural effusions, n (%)	4 (5.7)	1 (2.0)	3 (14.3)	.0776
Pneumothorax, n (%)	1 (1.4)	0 (0.0)	1 (4.8)	.3000
Other, n (%)	16 (22.9)	10 (20.4)	6 (28.6)	.5383
LV dysfunction by echocardiogram, n (%)	6 (40.0)	3 (33.3)	3 (50.0)	.6224
LV EF percentage, median (IQR) [n = 3]	44.1 (25.0, 48.7)	48.7 (48.7, 48.7)	34.6 (25.0, 44.1)	.5403
RV dysfunction by echocardiogram, n (%) [n = 3]	3 (20.0)	2 (22.2)	1 (16.7)	1.0000

ALT, alanine aminotransferase; *AST*, aspartate aminotransferase; *B/L*, Bilatera; *BUN*, blood urea nitrogen; *CPK*, creatine phosphokinase; *EF*, ejection fraction; *FEU*, Fibrinogen equivalent unit; *IL*, interleukin; *LV*, left ventricular; *pro-BNP*, pro-B type natriuretic peptide; *LDH*, lactate dehydrogenase; *RV*, right ventricular; *WBC*, white blood cell count.
*χ^2 test, Fisher exact test, or Wilcoxon rank-sum test.

the entire cohort of patients was 8.8 (IQR 6.3, 13.0) k/μL; median absolute lymphocyte count was 1.1 (IQR 0.6, 2.0) k/μL. Patients with ARDS had significantly lower platelet counts compared with those without ARDS (169 [IQR 110, 242] k/μL vs 216 [IQR 159, 309] k/μL, $P = .04$). Serum levels of C-reactive protein, procalcitonin, lactate, pro-B type natriuretic peptide, and interleukin-6 were elevated among patients with ARDS, but levels were statistically significantly different than patients without ARDS only for interleukin-6 (78.7 [IQR 34, 201.5] vs 16.4 [IQR 12.1, 66] pg/mL, $P = .03$). Eight patients had positive blood cultures; 3 patients had positive respiratory tract cultures, and 5 patients had positive urine cultures; concomitant respiratory infections were reported in 3 patients (4.3%) with rhinovirus in 2 and *Bordetella pertussis* in 1.

On chest radiography, 71% of patients with ARDS had bilateral infiltrates compared with 41% of those without ARDS ($P = .02$). Fifteen patients had documented formal echocardiograms performed, of who 6 had left ventricular dysfunction, and 3 had right ventricular dysfunction.

Medical Therapy and Outcomes

As presented in Table III, 57 patients met criteria for sepsis, of whom 12 patients met criteria for severe sepsis. Ten of these 12 patients meeting severe sepsis criteria also had ARDS compared with 2 in the non-ARDS group ($P < .0001$). Fourteen patients (20%) required vasopressor support: 11 in the ARDS group vs 3 in the non-ARDS group ($P < .0001$), with norepinephrine being the most frequently used vasopressor medication. Nine patients (12.9%) had AKI, and 1 patient required renal-replacement therapy.

Hydroxychloroquine, remdesivir, and antibiotics >48 hours were used more often in the ARDS group ($P < .05$ for all). Corticosteroids were used in 23 patients and 4 patients were treated with immunomodulatory therapies (3 with tocilizumab and 1 with anakinra); none received intravenous immunoglobulin or convalescent plasma.

Prone positioning was used in 7 (10%) of patients, of whom 4 had ARDS. A greater proportion of patients with ARDS received noninvasive mechanical ventilation than patients without ARDS (47.6% vs 8.2%, $P = .0004$). Twenty patients (28.6%) required invasive mechanical ventilation (IMV; 85.6% in the ARDS group vs 4.1% in non-ARDS group, $P < .0001$), 4 of whom were intubated before PICU admission. Of the 16 who required IMV in a PICU, respiratory support before intubation included oxygen by nasal cannula in 4, high-flow nasal cannula oxygen in 4, and bi-level positive airway pressure in 7 patients.

Of the 21 patients with ARDS, 4 had mild, 12 had moderate, and 5 had severe ARDS. Of these, 18 required IMV: 3 with mild ARDS, 10 with moderate ARDS, and 5 with severe ARDS (Figure 2). The 3 patients with mild ARDS who required IMV had significant comorbidities, which included malignancy in 2 patients and severe obesity (BMI 51 kg/m^2) in 1 patient. The median duration of mechanical

Table III. Therapies and clinical outcomes

Characteristics	Total (n = 70)	No ARDS (n = 49)	ARDS (n = 21)	*P* value*
Medical therapy				
Hydroxychloroquine, n (%)	27 (38.6)	14 (28.6)	13 (61.9)	.0087
Azithromycin, n (%)	23 (32.9)	16 (32.7)	7 (33.3)	.9557
Remdesivir, n (%)	13 (18.6)	6 (12.2)	7 (33.3)	.0494
Corticosteroid, n (%)	23 (32.9)	13 (26.5)	10 (47.6)	.0852
IL-6 inhibitor, n (%)	3 (4.3)	3 (6.1)	0 (0.0)	.5488
IL-1 inhibitor, n (%)	1 (1.4)	1 (2.0)	0 (0.0)	1.0000
Antibiotics <48 h, n (%)	20 (28.6)	17 (34.7)	3 (14.3)	.0833
Antibiotics >48 h, n (%)	28 (40.0)	13 (26.5)	15 (71.4)	.0004
Vasopressor use				
Any inotrope use, n (%)	14 (20.0)	3 (6.1)	11 (52.4)	<.0001
Epinephrine, n (%)	3 (4.3)	1 (2.0)	2 (9.5)	.2123
Norepinephrine, n (%)	8 (11.4)	2 (4.1)	6 (28.6)	.0074
Dopamine, n (%)	5 (7.1)	1 (2.0)	4 (19.0)	.0259
Dobutamine, n (%)	1 (1.4)	1 (2.0)	0 (0.0)	1.0000
Milrinone, n (%)	3 (4.3)	2 (4.1)	1 (4.8)	1.0000
Respiratory support				
NC oxygen, n (%)	30 (42.9)	18 (36.7)	12 (57.1)	.1138
Duration of NC oxygen, h, median (IQR)	27.5 (9.0, 36.0)	28.0 (10.0, 48.0)	15.5 (6.5, 25.5)	.3125
HFNC oxygen, n (%)	21 (30.0)	14 (28.6)	7 (33.3)	.6903
Duration of HFNC oxygen, h, median (IQR)	96.0 (59.0, 108.0)	96.0 (87.0, 108.0)	8.0 (8.0, 8.0)	.1349
Non-IMV, CPAP, or BiPAP, n (%)	14 (20.0)	4 (8.2)	10 (47.6)	.0004
Total duration of non-IMV/CPAP/BiPAP, h, median (IQR)	79.5 (41.5, 121.5)	156.0 (156.0, 156.0)	72.0 (11.0, 87.0)	.3711
IMV, n (%)	20 (28.6)	2 (4.1)	18 (85.7)	<.0001
Extubated, n (%)	9 (45.0)	1 (50.0)	8 (44.4)	1.0000
Duration of IMV, h, median (IQR) [among 9 extubated patients]	163.0 (79.0, 308.7)	79.0 (79.0, 79.0)	191.4 (107.5, 309.5)	.5613
Prone positioning while awake, nonintubated, n (%)	4 (5.7)	3 (6.1)	1 (4.8)	1.0000
Prone positioning while intubated, n (%)	3 (15.0)	0 (0.0)	3 (16.7)	1.0000
Neuromuscular blockade, n (%)	15 (75.0)	0 (0.0)	15 (83.3)	.0526
Mechanical support				
ECMO, n (%)	1 (1.4)	1 (2)	0 (0.0)	.1053
RRT, n (%)	1 (1.4)	0 (0.0)	1 (4.8)	.3000
Outcomes				
Sepsis syndrome, n (%)	57 (81.4)	38 (77.6)	19 (90.5)	.3173
Severe sepsis syndrome, n (%) [n = 12]	12 (21.1)	2 (5.3)	10 (52.6)	<.0001
AKI, n (%)	9 (12.9)	5 (10.2)	4 (19.0)	.4366
Cardiac arrest, n (%)	2 (2.9)	0 (0)	2 (2.9)	
Status on hospital day 14, n (%)				<.0001
Discharged	47 (69.1)	42 (89.4)	5 (23.8)	
Hospitalized (floor)	5 (7.4)	4 (8.5)	1 (4.8)	
Hospitalized (PICU)	14 (20.6)	1 (2.1)	13 (61.9)	
Mortality	2 (2.9)	0 (0.0)	2 (9.5)	
Status on hospital day 28, n (%)† [n = 70]				
Discharged	55 (78.5)	46 (93.8)	9 (42.9)	
Hospitalized (floor)	4 (5.7)	2 (4.1)	2 (9.5)	
Hospitalized (PICU)	9 (12.8)	1 (2)	8 (38.1)	
Mortality	2 (2.8)	0	2 (9.5)	

BiPAP, bi-level positive airway pressure; *CPAP*, continuous positive airway pressure; *ECMO*, extracorporeal membrane oxygenation; *HFNC*, high-flow nasal cannula; *IMV*, invasive mechanical ventilation; *NC*, nasal cannula; *RRT*, renal-replacement therapy.
*χ^2 test, Fisher exact test, or Wilcoxon rank-sum test.
†Seven patients did not reach 28 days from PICU admission as they were discharged before this benchmark.

ventilation in the ARDS group was 218.9 (139.8, 310.4) hours with 9 (50%) of these 18 patients still hospitalized and requiring invasive mechanical ventilation on day 14, and 7 (38.9%) on day 28 of hospitalization (Table III). Inhaled nitric oxide was used in 2 patients (2.8%).

One patient (1.4%) was cannulated to venoarterial extracorporeal membrane oxygenation support for acute decompensated heart failure in the setting of the previously diagnosed condition of dilated cardiomyopathy. Two patients (2.9%) required cardiopulmonary resuscitation, 1 of whom survived. Extracorporeal cardiopulmonary resuscitation was not used in any center for this cohort of patients.

By hospital day 14, 49 patients (70%) were discharged home; 14 (20%) remain hospitalized in PICU, and 5 (7.1%) remain hospitalized out of the PICU. Two patients (2.9%) died, one after withdrawal of life-sustaining therapies associated with end-stage osteosarcoma with extensive pulmonary metastases. The second death occurred in a patient with hemoglobinopathy who suffered from a hypoxic bradycardic arrest without return of spontaneous circulation after cardiopulmonary resuscitation.

By hospital day 28, 55 patients (78.6%) were discharged home; 9 (12.9%) remained hospitalized in PICU, and 4 (5.7%) remained hospitalized out of the PICU. Mortality remained at 2 deaths (2.9%) on hospital day 28. The patient on extracorporeal membrane oxygenation remained cannulated on day 28 awaiting cardiac transplant/ventricular assist device placement. The standardized mortality rate at hospital day 14

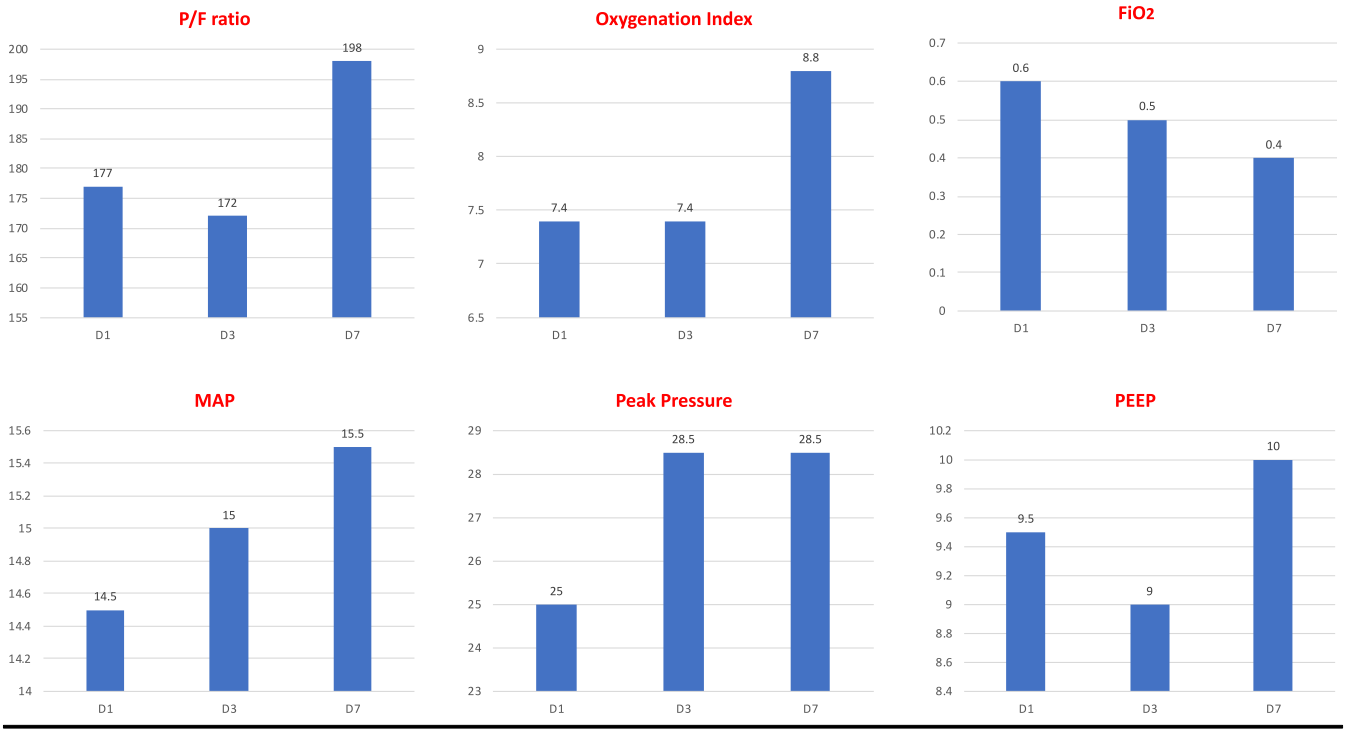

Figure 2. Oxygenation and ventilatory characteristics of intubated patients with COVID-19. *FiO_2*, fraction of inspired oxygen; *MAP*, mean arterial pressure; *PEEP*, positive end-expiratory pressure; *P/F*, arterial pO_2 divided by the FIO_2; *pO_2*, partial pressure of oxygen.

and 28 day for our cohort is 3.4, which represents 3.4 times excess mortality than that predicted by the PIM-2 score.

The presence of ARDS was associated with significantly longer PICU and hospital duration of stay (both $P < .0001$, Figure 3, A and B [available at www.jpeds.com]). In a multivariable analysis of time to discharge, ARDS (but not race or comorbidity) was independently associated with lower probability of PICU and hospital discharge ($P = .001$ for both) and black/Latino race was associated with greater probability of hospital discharge by day 28 ($P = .04$) (Tables IV and V).

Discussion

In this study, we describe clinical manifestations of critically ill children with COVID-19 disease admitted to PICUs in New York City, the epicenter of the COVID-19 pandemic in the US. This study adds to the growing literature on critical illness and outcomes in children with COVID-19, especially that associated with ARDS.

The exact PICU admission rate in children with COVID-19 remains unknown, with previous reports ranging from 1.3% to 28.2%.[1,5,7,13] A systematic review of early studies from China and Singapore identified only 1 critically ill child among 1065 children (0.1%) with confirmed COVID-19.[3] In Spain, only 4 of 41 (16%) confirmed cases were admitted to PICU.[4] In a single-center cohort of 46 hospitalized children positive for SARS-CoV-2 in New York City, 13 (28%) were critically ill, requiring admission to the PICU; 77% of PICU patients developed ARDS; and 61.5% were discharged home.[5] Another study reported with less detail than our study the early experience of critically ill children in a 2-week cross-sectional study of children with COVID-19 admitted to 46 North American PICUs between March 14 and April 3, 2020.[6] Götzinger et al[7] reported an 8% PICU admission rate in their multinational study from Europe. Although some of these studies show a greater rate of critical illness than previously reported, detailed clinical characteristics and multicenter longitudinal outcomes were not reported.

Our study focused on multiple PICUs in the catchment area that includes all of New York City, the epicenter of the

Table IV. Multivariable Cox proportional hazards model of outcome: time to PICU discharge (N = 70)

Variables	AHR (95% CI)	*P* value
ARDS (reference = no)	0.08 (0.03-0.21)	<.0001
Black/Latino (reference = white)	1.78 (0.71-4.48)	.2210
Other race (reference = white)	0.91 (0.33-2.51)	.8539
Any comorbidity (reference = no)	1.29 (0.68-2.45)	.4377

AHR, adjusted hazard ratio.

Table V. Multivariable Cox proportional hazards model of outcome: time to hospital discharge (N = 70)

Variables	AHR (95% CI)	*P* value
ARDS (reference = no)	0.10 (0.04-0.27)	<.0001
Black/Latino (reference = white)	2.76 (0.93-8.24)	.0685
Other race (reference = white)	1.00 (0.29-3.42)	.9951
Any comorbidity (reference = no)	0.98 (0.51-1.91)	.9620

COVID-19 pandemic in the US. A previous report was only from 1 of 25 PICUs in New York City.[6] Although our cohort represents approximately 46% of PICU beds, the proportion of critically ill children represented by our cohort is substantially greater because multiple hospitals' PICU beds were repurposed to accommodate critically ill adults during the pandemic surge. Similarly, a report from China that did not include the epicenter of Wuhan[2] underestimated the presence of critical illness in children compared with studies from Wuhan, the Chinese epicenter.[1] Studies that do not emanate from an epicenter may not represent the experience of a city consumed by pandemic infection. In addition, we report comprehensive details of ventilatory support and oxygenation markers, with concurrent standard scoring of patient criteria for severe sepsis,[14] ARDS,[11,12] and AKI.[13] Compared with previous reports, we provide comprehensive details of patients' multiorgan involvement, longer enrollment duration (7 weeks vs 2 weeks), and longer outcome follow-up (14 and 28 days vs 8 days).

The median age in our cohort was 15 years, different from early reports that suggested infants and preschool-aged children may be at greater risk of critical illness with COVID-19 infection,[1] but similar to a more recent cross-sectional point-prevalence report from North America.[6] Similar to previous findings,[5] approximately 50% of our critically ill patients reported no known sick contact, indicating a high rate of community spread, which may be explained partially by the high population density of New York City.[16]

There was no difference in the median PIM-2 scores in patients with and without ARDS with a median risk of expected mortality of 0.8%. The overall cohort mortality of 2.8% (all in patients with ARDS) is greater than that expected by the PIM-2 scores. In addition, patients with ARDS had significantly greater prevalence of severe sepsis and required greater levels of respiratory and hemodynamic support.

One of the known risk factors for the development of critical illness in adults is the presence of comorbidities.[17-20] A high percentage (74%) of our cohort of critically ill children had at least 1 comorbidity, consistent with data from both pediatric and adult studies.[5,6,16-19] Despite the presence of significant comorbidities, however, these comorbidities were not associated with ARDS in our cohort.

ARDS is reported to occur in 2%-3% of critically ill children[21] and in 17% of critically ill children with viral infections.[22] We found a 30% ARDS prevalence in our COVID-19 cohort, which is substantially greater. When patients with COVID-19 develop ARDS, their intubation rates (86% in our study) are greater than that for other viral infection. One possible reason for a greater intubation rate is the early recommendation to limit use of noninvasive ventilation and to consider early intubation of patients with COVID-19 in an attempt to limit aerosolization of the virus.[23,24]

In patients who required mechanical ventilation, a lung-protective strategy of using a low tidal volume and limiting the plateau pressure as recommended by Pediatric Acute Lung Injury Consensus Conference (PALICC)[11] seem to be effective in COVID-19 ARDS. The moderate median positive end-expiratory pressure of 9.5 cm of water in our cohort is similar to that reported by Grasselli et al[17] in their subcohort of patients <20 years of age and is not unusual in critically ill children.[25] This is in comparison with the median positive end-expiratory pressure of 14 cm water in adults aged 20-80 years with COVID-19 in the same study,[17] which may reflect relatively preserved compliance of pediatric lungs in the early phase of COVID-19–associated ARDS. Preserved compliance is probably also reflected in the low rate of prone positioning used in our study (only 16.7% for intubated patients with ARDS), again similar to Grasselli et al, who reported a 27% use of prone positioning, with no use in patients younger than 20 years of age.[17] This also may reflect a greater adherence to the PROSEVA study[26] recommendations of prone positioning as well as an absence of conclusive data supporting prone positioning in pediatric patients with ARDS.

More than 30% of the patients in our cohort were from a single borough of New York City, the Bronx. This patient distribution is consistent with a report showing a disproportionate involvement of Bronx County in New York City COVID-19 hospitalizations and deaths, despite the Bronx having the greatest number of hospital beds per 100 000 population and the greatest number of tests performed per 100 000 population of all 5 boroughs of New York City.[27] This may reflect the unique sociodemographic factors of Bronx County,[16] particularly the high density of population/transmission and high rate of poverty, which has been associated with prolonged hospital stay and PICU admission.[28]

Reassuringly, our observed discharge rate (70% by 14 days and 78.6% by 28 days) is greater than that reported in adults.[17-20] Those with ARDS, however, had longer PICU and hospital LOS compared with those without ARDS.

Our cohort had mortality rates similar to other pediatric studies[5,6] but lower than that reported in adults.[17-20] However, our 3.5-fold excess standardized mortality of COVID-19 patients is noteworthy. Whether excess mortality ratio is truly related to COVID-19 or is rather an artifact due to low patient numbers or a reflection of sociodemographic factors of New York City is not clear and may be clarified by future large multicenter studies. This early mortality rate of 2.9% in our cohort, however, must be considered in the context of 18.6% of our patients still remaining hospitalized at day 28 and 38.9% of children with ARDS still receiving invasive ventilatory support at day 28.

This study has the limitations of being a retrospective study of a relatively small sample size. Our results may not be applicable to other parts of the country and world, considering the unique demographics of New York City. In addition, this study had not been designed to identify patients with MIS-C, as the first reports to the New York State Department of Health were outside the time frame of our study period.[8] Applying the case definition retroactively following data collection identified some patients who met inflammatory criteria for MIS-C, likely reflecting an overlap in pathophysiology of COVID-19 lung disease, MIS-C, and sepsis. Our cohort primarily represents COVID-19 lower respiratory tract disease, an uncommon feature of MIS-C. Further

studies are needed to better understand underlying pathophysiologies and potential spectrum vs distinctive clinical conditions. Further, larger national and international studies are necessary to determine the true incidence and risk factors for critical illness from SARS-CoV-2 infection and the development of ARDS in the pediatric population. ■

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50 Years Ago in *The Journal of Pediatrics*

Parents Are Crucial to the Development/Prevention of Childhood Obesity

Khan EJ. Obesity in Children: Identification Risk of a Group at Risk in a New York Ghetto. J Pediatr 1970;77:771-4.

In 1970, owing to the poor treatment response of patients with obesity, Dr Khan aimed to identify risk factors for the development of childhood obesity to more adequately prevent it. Comparing 72 patients with obesity with 72 normal weight children presenting to his clinic in New York City, he noted that 65% of cases were obese before 3 years of age. Kahn went on to identify mother-child separation as a significant risk factor for the development of childhood obesity, occurring in 32% of patients with obesity and 8% of normal weight controls. Importantly, socioeconomic status and brief maternal absences from home during the day showed no impact.

Childhood obesity continues to be a significant and growing problem in the US despite attempts at prevention and treatment.[1] Patients with childhood obesity are more likely to be obese in adolescence and adulthood and develop several significant comorbidities.[2] The etiology of childhood obesity is multifactorial—genetic predisposition, early life psychosocial environment, poor diet, and sedentary lifestyle—resulting in excessive caloric intake compared with expenditure.[2] However, prevention and treatment efforts focused on restoring this caloric imbalance are difficult to implement and to sustain.

Since Dr Khan's 1970 study, there has been increased attention on the parent-child relationship and its effect on childhood obesity. Social situations that foster insecurity and stress such as low socioeconomic status and family dysfunction increase the likelihood of childhood obesity.[3] These upstream effects on emotional and behavioral development can lead to an inappropriate, addictive relationship with "junk food" for stress relief and pleasure.[3] Poor quality parent-child interactions negatively impact the child's emotional development and self-regulation increasing their risk of obesity.[4] Therefore, we may attribute the limited success of current prevention and treatment measures to a failure in appropriately addressing the psychosocial risk factors stimulating childhood obesity.

In conclusion, childhood obesity is a growing global health crisis with multifactorial etiology and multiple psychosocial risk factors. Recent efforts to promote positive parent-child interactions have demonstrated improvements in socioemotional outcomes[5] and cognitive stimulation.[6] Research studying the impact of improving parent-child interactions on childhood obesity is ongoing and should be encouraged if we are to see sustained down trends in the prevalence of childhood obesity.[7]

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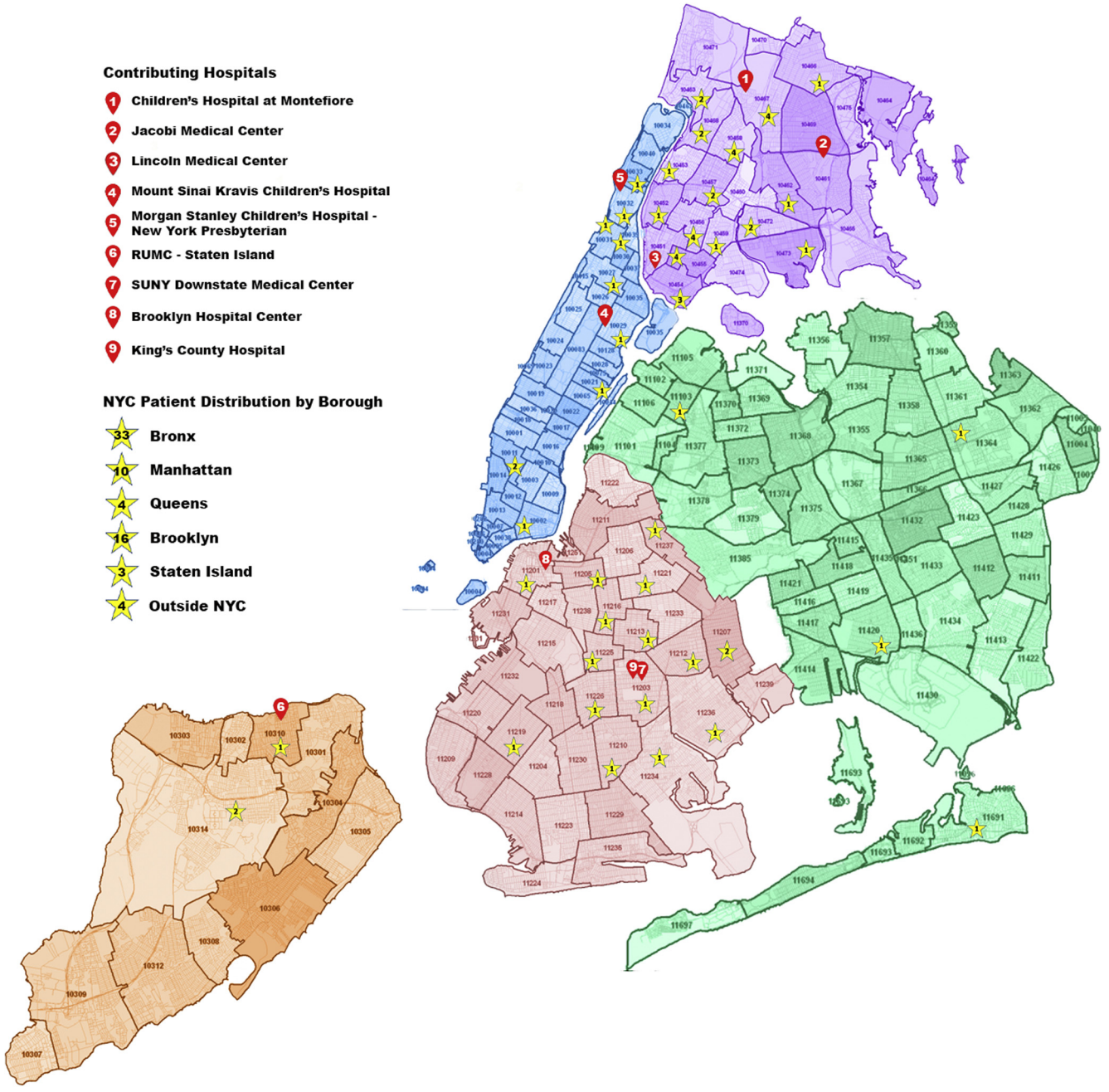

Figure 1. New York City–wide COVID-19 case distribution.

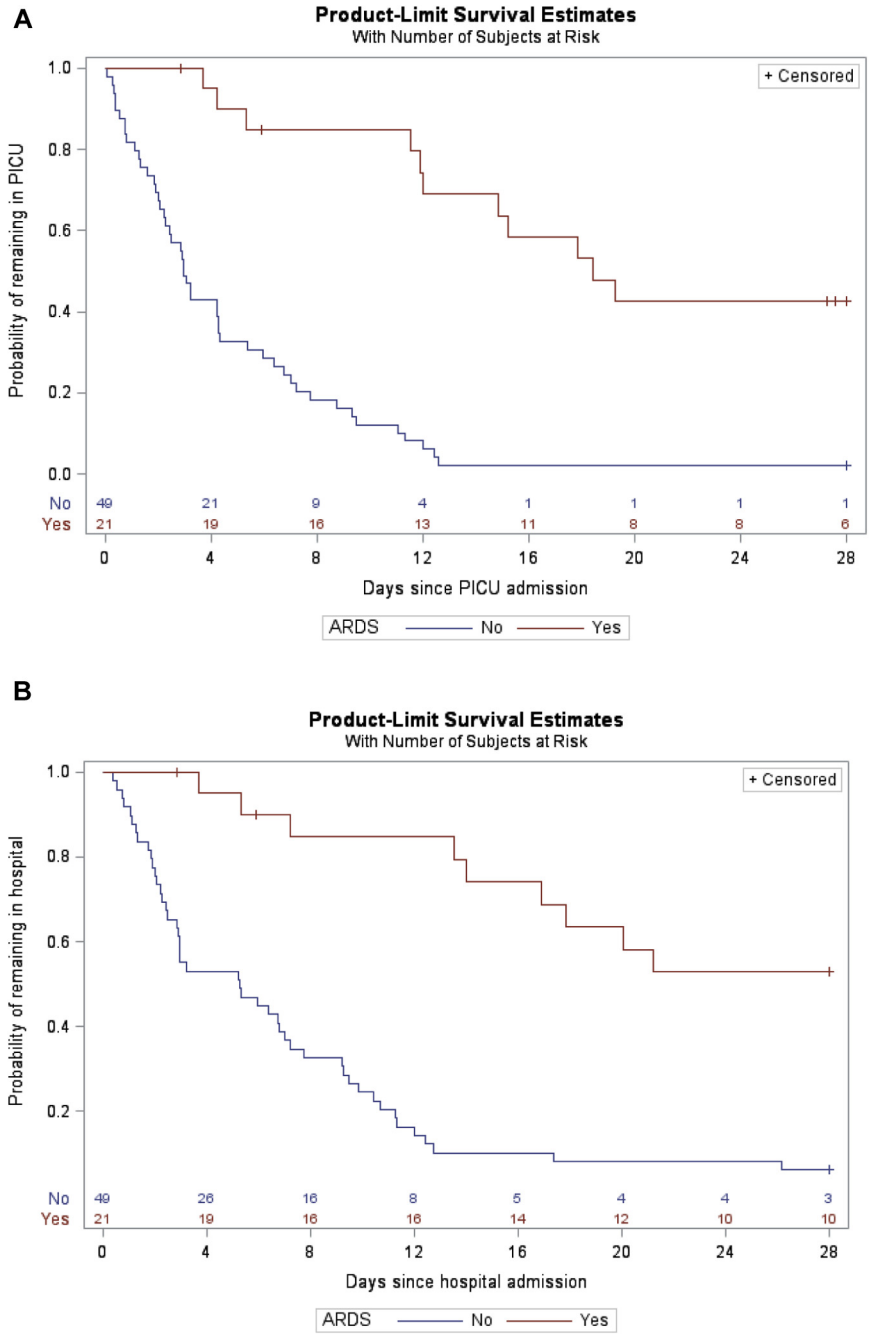

Figure 3. **A,** Kaplan–Meier plot: time to PICU discharge for patients with and without ARDS (N = 70, Log-rank test $P < .0001$). Censored for mortality. Patients still in PICU at study end are censored at last day of follow-up (up to hospital day 28). **B,** Kaplan–Meier plot: time to hospital discharge for patients with and without ARDS (N = 70, log-rank test $P < .0001$). Censored for mortality. Patients still in hospital at study end are censored at last day of follow-up (up to hospital day 28).