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LETTER TO THE EDITOR

COVID-19 disease in New York City pediatric hematology and oncology patients

To the Editor:

It is well established that viral respiratory infections in chronically ill and immunocompromised children are associated with increased morbidity and mortality compared to the general population.[1] Specifically, immunocompromised children have an increased risk of severe lower respiratory tract disease caused by human coronaviruses including strains OC43, NL63, HKU1, and 229E.[2] Little is known about the effect of COVID-19 disease on pediatric hematology, oncology, and hematopoietic stem cell transplant (HCT) patients.[3] A report from Italy describes five pediatric cancer patients with COVID-19 each having a mild, self-limited course.[4] A single case from China details a child with acute lymphoblastic leukemia who required prolonged intensive care treatment.[5,6]

To date, New York City (NYC) is home to nearly one-third of all pediatric cases (<18 years) of COVID-19 in the United States.[7] Together, Memorial Sloan Kettering Cancer Center (MSK) and New York Presbyterian Hospital (NYP, affiliated with both Columbia University Irving Medical Center (CUIMC) and Weill Cornell Medical Center [WCMC]) care for a sizeable portion of the city's pediatric hematology, oncology, and HCT community, providing an opportunity to describe the impact of COVID-19 in this vulnerable population.

This retrospective study was approved by the Institutional Review Boards of MSK, CUIMC, and WCMC. Informed consent was waived. All patients 21 years old or younger with clinical laboratory COVID-19 testing at MSK and NYP were included. For COVID-19 positive (COVID-19+) patients, data on demographics, presence of COVID-19 symptoms, complete blood counts, inflammatory markers, imaging, hospital course, and impact on cancer-directed therapy were extracted from the electronic medical record. All laboratory and radiologic assessments were performed at the discretion of the treating physicians.

Testing strategies varied between institutions during the observational period. MSK tested all symptomatic patients and screened all patients prior to admission, procedures requiring sedation, and planned myelosuppressive chemotherapy. NYP tested only those patients for whom a positive test would alter management, including those who were symptomatic, likely COVID-19 exposed, or with planned disposition to a chronic care facility. A confirmed case of COVID-19 was defined as a positive result by reverse transcriptase polymerase chain reaction (RT-PCR) on a nasopharyngeal swab specimen. Only laboratory-confirmed cases were included in this review. Descriptive statistics were used to summarize the data. No imputation was made for missing data. Associations between patient demographics and the COVID-19 PCR result were examined using chi-square analysis and logistic regression. All statistical tests were two-sided with statistical significance level of .05. Statistical analysis was performed using SPSS v26.

From March 10 through April 6, a total of 174 patients underwent laboratory testing for COVID-19. Demographic characteristics are shown in Table 1. Nineteen patients tested positive (11%): three patients with nonmalignant hematologic diagnoses, 14 with cancer, and two postallogeneic HCT. The mean age of COVID-19+ patients was 10.2 years (range 5 months to 20 years); 79% were male; 58% were non-Hispanic White, 21% Hispanic, 11% African American, and 11% Asian. The two institutions differed in the prevalence of COVID-19+ cases (7% at MSK compared with 20% NYP; $P < .01$), consistent with the different testing criteria; they also differed in insurance payer distribution. A trend toward higher incidence of COVID-19 infection was observed in males. After adjusting for institution, insurance, and ethnicity, males appeared three times more likely to have positive test results compared with females (OR 3.2 95% confidence interval 0.90, 11.1) with borderline significance ($P = .08$).

Table 2 shows the clinical findings of the COVID-19+ pediatric patients. Sixteen (84%) were symptomatic, beginning a median of 1 day prior to testing (range 0-14). The most common symptoms were fever (68%), cough (47%), and dyspnea (37%). Eleven patients were hospitalized, four (21%) required supplemental oxygen, and two (11%) required mechanical ventilation. Only three of 19 (16%) received COVID-19-directed therapy. All five patients requiring pediatric intensive care unit (PICU) level care were male. Four had cancer: three with significant comorbidity including chronic graft versus host disease, trisomy 21, and cerebral mutism, and one with hyperleukocytosis and new onset B-ALL presenting 2 days after losing his father to COVID-19. One 12-year-old boy with previously mild hemoglobin SC disease developed acute chest syndrome and died of COVID-19-related complications on hospital day 4. Full patient details can be found in the Supporting Information (case descriptions and Tables S1 and S2).

Most COVID-19+ patients had relatively mild disease, with almost half treated outpatient. Hospitalized COVID-19+ cancer patients were generally admitted for expected complications of cancer therapy rather than complications of COVID-19 disease. Nine of 14 had their cancer-directed treatments delayed for COVID-19+ infection. Five tested positive for COVID-19 during or immediately postmyelosuppressive chemotherapy; all did well without any significant complications from COVID-19. Even the four cancer patients requiring PICU level care and demonstrating clear evidence of lung involvement

TABLE 1 Clinical characteristics of the patients at baseline

Total patients tested	Total Patients N = 174	COVID-19 status PCR positive N = 19 (%)	PCR negative N = 155 (%)
Institution[a]			
MSK	120	8 (42)	112 (72)
NYP	54	11 (58)	43 (28)
Disease type			
Hematology	13	3 (16)	10 (7)
Oncology	134	14 (74)	120 (77)
Hematopoietic cell transplantation	27	2 (10)	25 (16)
Age groups			
<1 year	12	2 (10)	10 (7)
1-4.9 years	52	3 (16)	49 (32)
5-9.9 years	37	4 (21)	33 (21)
10-14.9 years	34	7 (37)	27 (17)
15-21.9 years	39	3 (16)	36 (23)
Sex			
Female	71	4 (21)	67 (43)
Male	103	15 (79)	88 (57)
Ethnicity			
African American	29	2 (11)[b]	27 (17)
Asian	22	2 (11)[b]	20 (13)
Hispanic	27	4 (21)	23 (15)
Non-Hispanic White	93	11 (58)	82 (53)
Unknown	3	0 (0)	3 (2)
Insurance[c]			
Private	96	6 (35)	90 (66)
Public	57	11 (65)	46 (34)

[a]The difference in the proportion of cases positive for COVID-19 by institution is significant by chi-square; $P < .05$.
[b]Due to rounding off from 10.5 to 11, the column total adds up to 101%.
[c]Payer information was not available for 21 patients.

TABLE 2 Clinical snapshot of COVID-19-positive patients

COVID-19-positive patients	Patients N = 19 (%)
Service	
Hematology	3 (16)
Oncology	14 (74)
Leukemia/lymphoma	6
Solid tumors	8
Hematopoietic cell transplant	2 (11)
Reason for testing	
Symptomatic	16 (84)
Prechemotherapy/admission/procedure	3 (16)
Symptoms	
Fever	13 (68)
Rhinorrhea	6 (32)
Cough	9 (47)
Difficulty breathing	7 (37)
Chest pain	4 (21)
Respiratory support	
None	13 (68)
Nasal canula/face mask	4 (21)
Intubation	2 (11)
Treatment delay due to COVID-19 status (oncology patients only)	
Yes	9 (64)
No	5 (36)

(Figure S1) are recovering well. No COVID-19+ patients who were initially managed as outpatients subsequently required admission.

The total percentage of COVID-19-positive tests (11%) demonstrates a generally low infection rate in our population and is consistent with the rates previously reported in pediatric patients.[8-10] Since social distancing to prevent infections is a well-established behavior in pediatric hematology, oncology, and HCT patients, this may not be reflective of the general pediatric population. Nevertheless, our data reinforce the impression that pediatric patients have a lower burden of COVID-19 disease compared to adults.

Most of our COVID-19+ patients had relatively mild disease and could be treated outpatient or without the need for respiratory support. Interestingly, in our cohort, male patients appeared more likely to have a more severe clinical course. This finding is consistent with previous reports in children and adults,[7,8] but the mechanisms underlying the observed sex discrepancy are still unknown. The only patient death in this cohort was a child with sickle cell disease without a significant history of prior complications. Although this patient demonstrated pulmonary disease, his death may have been preceded by an acute cardiac event. Autopsy was refused and it is impossible to determine from this single case if children with sickle cell disease are at risk for more severe disease. This patient and two others received COVID-19-directed therapy with hydroxychloroquine and azithromycin; it is not known if these experimental therapies influenced their outcomes.

Nearly two-thirds of the patients with cancer in our cohort experienced treatment delays due to COVID-19; the majority of these delays were due to decisions to defer planned treatment rather than directly due to complications of COVID-19 infection. The decision to delay critical, time-sensitive anticancer therapy in these children is one of the biggest challenges being faced by pediatric oncologists. Our data suggest that in patients without underlying comorbidities beyond their cancer diagnosis, COVID-19 may not pose a significantly greater threat than other intercurrent viral infections and that asymptomatic patients whose anticancer therapy cannot be delayed may be able to safely receive myelosuppressive chemotherapy with close monitoring and follow up. Given the small numbers in our series, there remains an urgent need for prospective longitudinal study of the effects of COVID-19 on the pediatric hematology, oncology, and HCT population.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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DATA AVAILABILITY STATEMENT

Data available on request due to privacy/ethical restrictions.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.