Received: 28 October 2020 | Revised: 4 December 2020 | Accepted: 6 December 2020

DOI: 10.1002/pbc.28857

Pediatric Blood & Cancer | SIOP International Society of Paediatric Oncology | aspho The American Society of Pediatric Hematology/Oncology | WILEY

SURVIVORSHIP: BRIEF REPORT

COVID-19 in pediatric survivors of childhood cancer and hematopoietic cell transplantation from a single center in New York City

Lauren Jimenez-Kurlander[1] | **Zoltan Antal**[1,2] | **Amelia DeRosa**[1] | **Deborah Diotallevi**[1] | **Elaine Pottenger**[1] | **Nadia Wilson**[1] | **Stacie Corcoran**[3] | **Farid Boulad**[1,2] | **Danielle Novetsky Friedman**[1,2]

[1] Department of Pediatrics, Memorial Sloan Kettering Cancer Center, New York, New York

[2] Weill Cornell Medical College, New York, New York

[3] Department of Medicine, Memorial Sloan Kettering Cancer Center, New York, New York

Correspondence
Lauren Jimenez-Kurlander, Department of Pediatrics, Memorial Sloan Kettering Cancer Center, 1275 York Avenue, New York, NY 10065.

Funding information
Memorial Sloan Kettering Core, Grant/Award Number: P30 CA008748; Meg Berte Owen Foundation

Abstract

Childhood cancer survivors are at increased risk for treatment-related late effects; data are lacking on how coronavirus disease 2019 (COVID-19) infection impacts this cohort. We assessed COVID-19-related symptoms, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) IgG seroprevalence, and rate of COVID-19-related hospitalization among 321 asymptomatic survivors of childhood cancer or transplantation seen for routine long-term follow-up between May and September 2020 in a New York City tertiary cancer center. While 10.9% (n = 35) reported possible COVID-19-related symptoms, 7.8% (n = 20) of those tested had positive SARS-CoV-2 IgG, and one patient (0.3%) required COVID-19-related hospitalization. This report suggests that childhood cancer survivors appear to be at relatively low risk for COVID-19 complications.

KEYWORDS
childhood cancer, COVID-19, SARS-CoV-2, survivors

1 | INTRODUCTION

The coronavirus disease 2019 (COVID-19) pandemic has unique implications for the growing cohort of survivors of childhood cancer and hematopoietic cell transplantation (HCT) for nonmalignant hematologic/immune disorders,[1,2] referred to herein as "survivors." Investigators have postulated that history of underlying immune dysfunction and/or organ injury due to prior therapeutic exposures increase survivors' risk of contracting severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and/or increased severity of COVID-19.[3–5] Using the Childhood Cancer Survivor Study (CCSS) cohort, Perkins et al previously found an increased incidence of overall infections and a higher risk of infection-related mortality among survivors of childhood cancer as compared to unaffected siblings for at least 35 years after therapy.[6] Whether these infectious risk findings can be applied to the COVID-19 pandemic and inform guidelines for childhood cancer survivors as they return to school or work is unknown.[5,7] In an effort to fill this gap, we assessed reported COVID-19 symptoms, exposures, and/or hospitalization, as well as SARS-CoV-2 IgG status, in a cohort of pediatric survivors presenting for routine long-term follow-up (LTFU) either in-person or virtually in the early months of the COVID-19 pandemic in New York City, one of the original epicenters of the pandemic.

Abbreviations: COVID-19, coronavirus disease 2019; HCT, hematopoietic cell transplantation; LTFU, long-term follow-up; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2

2 | METHODS

This retrospective review included all consecutive survivors seen in Memorial Sloan Kettering (MSK)'s Pediatric LTFU Clinic between May 5 and September 10, 2020, which provides risk-based care to survivors of childhood cancer and HCT diagnosed at age ≤18 who are ≥1-year off-therapy at program entry.

TABLE 1 Demographic and treatment characteristics of all patients seen for routine pediatric long-term follow-up visits between May 5 and Sept 10, 2020

Characteristic	All patients (n = 321)	(%)	Patients with positive SARS-CoV-2 IgG (n = 20)	(%)
Age at diagnosis, years				
Median (range)	3.7 (0-18)		4.1 (0-15.8)	
Sex, No. (%)				
Male	154	(48.0)	9	(45)
Race/Ethnicity, No. (%)				
White, Non-Hispanic	224	(69.8)	11	(55)
White, Hispanic	17	(5.3)	0	(0)
Black, Non-Hispanic	16	(5.0)	3	(15)
Black, Hispanic	8	(2.5)	1	(5)
Asian	39	(12.1)	3	(15)
Other/unknown	17	(5.3)	2	(10)
Diagnosis, No. (%)				
Leukemia/lymphoma	91	(28.4)	5	(25)
Neuroblastoma	61	(19.0)	1	(5)
Nonmalignant hematologic disorders	40	(12.5)	5	(25)
Central nervous system tumor	34	(10.6)	1	(5)
Sarcoma	31	(9.7)	3	(15)
Thyroid cancer	27	(8.4)	1	(5)
Wilms tumor	17	(5.3)	1	(5)
Other solid tumor	9	(2.8)	1	(5)
Retinoblastoma	7	(2.2)	1	(5)
Myelodysplastic syndrome	3	(0.9)	1	(5)
History of hematopoietic cell transplantation				
Total	99	(30.9)	7	(35)
Allogeneic	68	(21.2)	7	(35)
Autologous	31	(9.7)	0	(0)
Blood type, No. (%)				
O positive/O negative	114/8	(38.1)	6 / 0	(30)
A positive/A negative	84/8	(28.8)	7 / 0	(35)
B positive/B negative	40/2	(13.1)	3 / 0	(15)
AB positive/AB negative	17/2	(5.9)	1 / 0	(5)
Records not available	45	(14.1)	3	(15)
Age at study, years				
Median (range)	15.1 (2.7-25.2)		17 (9.1-20.8)	
1-10	57	(17.8)	1	(5)
10-20	229	(71.3)	18	(90)
20-26	35	(10.9)	1	(5)
Years from diagnosis				
Median (range)	8.9 (1.2-20.4)		10.7 (3.3-19.6)	
Years from end of treatment				
Median (range)	6.9 (1.0-18.6)		6.2 (1.7-14.1)	
1-5	113	(35.2)	9	(45)
5-10	127	(39.6)	7	(35)
Over 10	81	(25.2)	4	(20)
Location of primary residence, No (%)				
Bronx	12	(3.7)	4	(20)
Kings County, Brooklyn	47	(14.6)	6	(30)
Manhattan	29	(9.0)	1	(5)
Nassau County	22	(6.9)	0	(0)
New Jersey	70	(21.8)	1	(5)
Other New York county	11	(3.4)	0	(0)
Other state	47	(14.6)	1	(5)
Queens	19	(5.9)	3	(15)
Rockland County	9	(2.8)	2	(10)
Staten Island	12	(3.7)	0	(0)
Suffolk County	25	(7.8)	1	(5)
Westchester	18	(5.6)	1	(5)
Type of visit, No. (%)				
In-person	227	(70.7)	17	(85)
Telehealth	94	(29.3)	3	(15)

All patients were scheduled for routine LTFU (in-person or via telehealth) during this interval; SARS-CoV-2 IgG testing was offered when venipuncture was being performed for clinical indications.[8,9] During all visits, patients were assessed for known COVID-19 exposure(s) after March 1, 2020; COVID-19-related symptoms (fever, cough, respiratory distress, loss of smell/taste); and COVID-19-related hospitalization. A subset of patients had SARS-CoV-2 PCR testing performed locally or on-site if they had traveled from high-prevalence areas, reported active symptoms of infection, or required testing for preprocedural indications.[10]

The protocol was approved by the MSK Institutional Review/Privacy Board.

3 | RESULTS

Table 1 summarizes demographics of 321 unique childhood cancer survivors seen during this interval: 227 (70.7%) in-person and 94 (29.3%) via telehealth. Survivors were 1-18.6 years (median 6.9 years) after completion of all cytotoxic therapies. Most common diagnoses included leukemia/lymphoma (28.4%) and neuroblastoma (19%).

TABLE 2 SARS-CoV-2 IgG results in the context of reported symptoms and exposures among a cohort of childhood and young adult survivors followed in NYC

	SARS-CoV-2 IgG positive		SARS-CoV-2 IgG negative		SARS-CoV-2 IgG not reported[a]		All patients	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
Number of unique patients	20	(6.2)	237	(73.8)	64	(19.9)	321	(100)
History of symptoms	6	(30.0)	24	(10.1)	5	(7.8)	35	(10.9)
Asymptomatic	13	(65.0)	184	(77.6)	28	(43.8)	225	(70.1)
Symptoms not recorded	1	(5.0)	29	(12.2)	30	(48.4)	61	(19.0)
Known exposure	7	(35.0)	12	(5.1)	1	(1.6)	20	(6.2)
No known exposure	12	(60.0)	141	(59.5)	18	(28.1)	171	(53.3)
Exposure not recorded	1	(5.0)	84	(35.4)	44	(70.3)	130	(40.5)
Extended family member death due to COVID-19[b]	1	(5.0)	5	(2.1)	0	(0.0)	6	(1.9)

[a]Sixty-four patients did not have COVID-19 antibodies drawn due to unordered by provider (n = 35), lab cancellation (n = 15), no indicated screening labs (n = 12), local labs not performed by patient (n = 1), or labs hemolyzed (n = 1).
[b]Family member deaths included grandparent (n = 5) and aunt (n = 1).

Ninety-nine patients (30.9%) had history of prior HCT. Thirty-five patients (10.9%) reported prior symptoms consistent with COVID-19 infection. SARS-CoV-2 serology results in the context of reported symptoms and known COVID-19 exposures are summarized in Table 2. History of pulmonary dysfunction, defined as abnormal pulmonary function test, restrictive lung disease, pulmonary fibrosis, sleep apnea, or asthma, was present in 15.6% (n = 50) of all patients, 15% (n = 3) of patients with positive SARS-CoV-2 IgG, and 20% (n = 1) of patients with positive SARS-CoV-2 PCR.

Among 257 (80.1%) patients who had SARS-CoV-2 IgG testing, 20 (7.8%) patients had positive antibodies (Table 1). Most common diagnoses among patients with positive serology included leukemia/lymphoma (25%, n = 5), nonmalignant hematologic disorders (25%, n = 5), and sarcoma (15%, n = 3). One-half of patients with positive SARS-CoV-2 IgG resided in two zip codes located in Kings County, Brooklyn (30%, n = 6), and the Bronx (20%, n = 4). Of all patients seen, these residencies were reported by 14.6% (n = 47) and 3.7% (n = 12), respectively. Among patients with positive SARS-CoV-2 serology, 35% (n = 7) were HCT survivors.

Five (1.6%) patients reported history of PCR-confirmed SARS-CoV-2 infection. At the time of their visits, these five patients were 3.1-14.1 years (median 8.7 years) from completion of therapy. Four of five patients had COVID-19 antibodies drawn at their visits, and all had positive seroconversion between 2 and 5 months after reported infection (100%). Among these patients, two had never developed symptoms; two had mild symptoms including fever (n = 1), headache (n = 1), and loss of sense of smell (n = 2); and one (0.3%) required a 10-day hospitalization for respiratory insufficiency and myocarditis with subsequent full recovery. None of our patients developed multisystem inflammatory syndrome in children (MIS-C).

The patient who required COVID-19-related hospitalization is a survivor of myelodysplastic syndrome/acute myeloid leukemia and completed treatment 3.75 years prior to COVID-19 hospitalization. This patient's treatment included multiagent chemotherapy (including doxorubicin 40 mg/m^2) and a T-cell depleted, allogeneic stem cell transplant from a matched, unrelated donor preceded by cytoreduction with clofarabine, thiotepa, and melphalan. Comorbidities included obesity, diabetes mellitus type 2, mild concentric left ventricular hypertrophy, and obstructive sleep apnea.

4 | DISCUSSION

In this large pediatric survivor cohort followed in New York City (NYC), one of the earliest epicenters of the pandemic, we found a relatively low prevalence of reported COVID-19-related symptoms or hospitalization. Patients residing in just two zip codes, which were known COVID-19 "hot spots,"[11] made up 50% of patients with positive SARS-CoV-2 serology. This suggests that living in high prevalence areas of SARS-CoV-2 may put survivors at increased risk of contracting the virus. While 7.8% of those tested had positive SARS-CoV-2 IgG and probable prior infection, one patient (0.3%) required medical evaluation and subsequent hospitalization. This patient had underlying mild concentric left ventricular hypertrophy, as well as obesity, diabetes mellitus type 2, and obstructive sleep apnea.

Interestingly, 7.8% of our tested cohort had positive SARS-CoV-2 antibodies, compared to 29.9% of individuals aged 0-17 in New York City.[11] This cohort's relatively low seroprevalence is consistent with other reports from oncology settings in which patients on active treatment appear to be at similar risk as nononcology populations for COVID-19.[10,12–14] We hypothesize that survivors and their families were already adept at mask wearing and social distancing and thus less likely to contract disease. Alternatively, a subset of survivors may have been unable to mount a serologic response to COVID-19 due to impaired immunity related to prior underlying diagnosis or cytotoxic treatment(s). Our patient population is also less racially and ethnically diverse than the larger New York City pediatric

population and may partially account for the relatively low disease burden in this cohort. Future investigation is necessary to clarify these findings.

Various limitations must be considered. While the clinical significance of SARS-CoV-2 serology remains unclear, positive antibodies appear to be a reasonable indicator of prior disease in asymptomatic individuals.[9,15] Additionally, since only one patient reported severe disease requiring hospitalization, we were unable to assess associations between prior cancer therapies and COVID-19 severity. The retrospective, single-center design and reliance on patient/family recall also likely introduced bias. However, since nearly one-third of visits were conducted via telehealth, the cohort includes patients who were unable/unwilling to travel to NYC and individuals who were too ill to attend in-person visits.

Our preliminary data suggest that pediatric survivors experience a relatively low burden of COVID-19-related complications. Based on currently available data, childhood cancer survivors should follow national precautions for mask wearing, social distancing, and hand hygiene as the country prepares for a potential upcoming COVID-19 resurgence. Longitudinal follow-up of large survivor cohorts will be required to analyze the impact of treatment exposures and existing comorbidities on COVID-19 severity and inform guideline development for this high-risk population.

ACKNOWLEDGMENTS

This study was supported by the Memorial Sloan Kettering Core Grant (P30 CA008748) and the Meg Berte Owen Foundation. The NIH and the Meg Berte Owen Foundation had no role in the design and conduct of the study.

CONFLICT OF INTEREST

Danielle Novetsky Friedman held an advisory role for Fennec Pharmaceuticals in the past 36 months.

AUTHOR CONTRIBUTIONS

Lauren S. Kurlander designed the study, collected the data, drafted the initial manuscript, and reviewed and revised the manuscript. Danielle Novetsky Friedman conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. Farid Boulad, Zoltan Antal, Amelia DeRosa, Deborah Diotallevi, Elaine Pottenger, Nadia Wilson, and Stacie Corcoran reviewed and revised the manuscript.

ORCID

Lauren Jimenez-Kurlander https://orcid.org/0000-0002-9449-8588
Danielle Novetsky Friedman https://orcid.org/0000-0003-4668-9176

REFERENCES

1. Phillips SM, Padgett LS, Leisenring WM, et al. Survivors of childhood cancer in the United States: prevalence and burden of morbidity. *Cancer Epidemiol Biomarkers Prev*. 2016;24(4):653-663.
2. Cheung AT, Li WHC, Ho LLK, et al. Health support to pediatric cancer survivors and their families during the COVID-19 pandemic [published online ahead of print, 2020 Aug 9]. *Pediatr Blood Cancer*. 2020:e28441.
3. Nekhlyudov L, Duijts S, Hudson SV, et al. Addressing the needs of cancer survivors during the COVID-19 pandemic. *J Cancer Surviv*. 2020;14(5):601-606.
4. Fung M, Babik JM. COVID-19 in Immunocompromised Hosts: what We Know So Far [published online ahead of print, 2020 Jun 27]. *Clin Infect Dis*. 2020:ciaa863.
5. Verbruggen LC, Wang Y, Armenian SH, et al. Guidance regarding COVID-19 for survivors of childhood, adolescent, and young adult cancer: a statement from the International Late Effects of Childhood Cancer Guideline Harmonization Group. *Pediatr Blood Cancer*. 2020;67(12):e28702.
6. Perkins JL, Chen Y, Harris A, et al. Infections among long-term survivors of childhood and adolescent cancer: a report from the Childhood Cancer Survivor Study. *Cancer*. 2014;120(16):2514-2521.
7. Schultz L, Link MP, Rheingold S, et al. Summary of COVID-19 clinical practice adjustments across select institutions [published online ahead of print, 2020 Jul 19]. *Pediatr Blood Cancer*. 2020:e28411.
8. Bryan A, Pepper G, Wener MH, et al. Performance characteristics of the Abbott Architect SARS-CoV-2 IgG Assay and Seroprevalence in Boise, Idaho. *J Clin Microbiol*. 2020;58(8).https://doi.org/10.1128/JCM.00941-20
9. Deeks JJ, Dinnes J, Takwoingi Y, et al. Antibody tests for identification of current and past infection with SARS-CoV-2. *Cochrane Database Syst Rev*. 2020;6(6):CD013652.
10. Boulad F, Kamboj M, Bouvier N, et al. COVID-19 in children with cancer in New York City. *JAMA Oncol*. 2020;6:1459-1460.
11. NYC Department of Health. Coronavirus disease 2019 (COVID-19) data. 2020. https://www1.nyc.gov/site/doh/covid/covid-19-data.page. Accessed September 18, 2020.
12. de Rojas T, Pérez-Martínez A, Cela E, et al. COVID-19 infection in children and adolescents with cancer in Madrid. *Pediatr Blood Cancer*. 2020;67(7):e28397.
13. Fuereder T, Berghoff AS, Heller G, et al. SARS-CoV-2 seroprevalence in oncology healthcare professionals and patients with cancer at a tertiary care centre during the COVID-19 pandemic. *ESMO Open*. 2020;5(5):e000889.
14. André N, Rouger-Gaudichon J, Brethon B, et al. COVID-19 in pediatric oncology from French pediatric oncology and hematology centers: high risk of severe forms. *Pediatr Blood Cancer*. 2020;67(7):e28392.
15. Sethuraman N, Jeremiah SS, Ryo A. Interpreting diagnostic tests for SARS-CoV-2. *JAMA*. 2020;323(22):2249-2251.

How to cite this article: Jimenez-Kurlander L, Antal Z, DeRosa A, et al. COVID-19 in pediatric survivors of childhood cancer and hematopoietic cell transplantation from a single-center in New York City. *Pediatr Blood Cancer*. 2021;68:e28857. https://doi.org/10.1002/pbc.28857