Article published online: 2023-05-17

SARS-CoV-2 Infection in Children with Cancer: Experience from a Tertiary Care Center in North India

Pritam Singha Roy[1] Manjinder Singh Randhawa[2] Karthi Nallasamy[2] Mini P. Singh[3] Srinivasan Peyam[1] Prashant Chhabra[1] Gnanamani Senguttuvan[1] Safal Muhammed[1] Mukesh Dhankar[1] Richa Jain[1] Deepak Bansal[1] Amita Trehan[1]

[1] Pediatric Hematology-Oncology Unit, Department of Pediatrics, Postgraduate Institute of Medical Education and Research, Chandigarh, India
[2] Pediatric Critical Care Unit, Department of Pediatrics, Postgraduate Institute of Medical Education and Research, Chandigarh, India
[3] Department of Virology, Postgraduate Institute of Medical Education and Research, Chandigarh, India

Address for correspondence Amita Trehan, MD, Hematology-Oncology Unit, Department of Pediatrics, Advanced Pediatrics Center, Postgraduate Institute of Medical Education and Research, Chandigarh 160012, India (e-mail: trehanamita@hotmail.com; trehan.amita@pgimer.edu.in).

Ind J Med Paediatr Oncol 2023;44:428–435.

Abstract

Introduction Children with cancer are immunocompromised due to the disease per se or anticancer therapy. Children are believed to be at a lower risk of severe coronavirus disease 2019 (COVID-19) disease.

Objective This study analyzed the outcome of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children with cancer.

Materials and Methods A retrospective analysis was performed on patients (≤ 14 years) with cancer attending the pediatric oncology services of our institute who tested positive for the SARS-CoV-2 infection and those who had COVID-19 disease between August 2020 and May 2021. Real-time reverse transcriptase-polymerase chain reaction performed on the nasopharyngeal swab identified the SARS-CoV-2 infection. The primary endpoints were clinical recovery, interruption of cancer treatment, and associated morbidity and mortality.

Results Sixty-six (5.7%) of 1,146 tests were positive for the SARS-CoV-2 infection. Fifty-two (79%) and 14 (21%) patients had hematolymphoid and solid malignancies. Thirty-two (48.5%) patients were asymptomatic. A mild-moderate, severe, or critical disease was observed in 75% (18/24), 12.5% (3/24), and 12.5% (3/24) of the symptomatic patients. The "all-cause" mortality was 7.6% (5/66), with only one (1.5%) death attributable to COVID-19. Two (3%) patients required ventilation. Two (3%) patients had a delay in cancer diagnosis secondary to COVID-19 infection. Thirty-eight (57.6%) had a disruption in anticancer treatment.

Conclusion Children with cancer do not appear to be at an increased risk of severe illness due to SARS-CoV-2 infection. Our findings substantiate continuing the delivery of nonintensive anticancer treatment unless sick. However, SARS-CoV-2 infection interrupted anticancer therapy in a considerable proportion of children.

Keywords
- cancer
- coronavirus
- leukemia
- oncology
- pediatric
- SARS-CoV-2

article published online
May 17, 2023

DOI https://doi.org/10.1055/s-0043-1764366.
ISSN 0971-5851.

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has posed the greatest challenge to the health care delivery system. As has been experienced across the globe, the incidence and severity of coronavirus disease 2019 (COVID-19) infection are noticeably lesser in children than adults. Children with SARS-CoV-2 infection are commonly asymptomatic or have mild illness.[1–3] However, children on treatment with cancer are a vulnerable population. Cancer and its treatment cause immunosuppression, increase the likelihood of acquiring infection, and augment its severity. The clinical course of COVID-19 in children on treatment for cancer remains unclear, though a trend toward a benign clinical course is observed.[4–8] A systematic review of the clinical presentation and outcome of SARS-CoV-2 infection in children with cancer demonstrated an asymptomatic infection or mild disease in about half of the study subjects, comparable to the general pediatric population.[9]

In pediatric oncology, wide-ranging impacts have been identified worldwide, including reductions in available clinical staff, pediatric cancer beds, and personal protective equipment.[10] In addition, the effects in low- and middle-income countries (LMIC) are more pronounced. Inability to access timely care owing to lockdowns, changes to chemotherapy due to treatment agent shortages, treatment abandonment, and disruptions to radiotherapy and surgery are the issues most frequently reported.[7,11] SARS-CoV-2 has placed enormous pressure on hospitals and health care systems worldwide. India has witnessed two "waves" of the pandemic since March 2020, with a devastating second wave from March to May 2021.

This study analyzed the morbidity and mortality in children with an underlying malignancy who contracted SARS-CoV-2 infection.

Materials and Methods

Patients

This retrospective study was performed on children and young adolescents (age $\leq$ 14 years) with malignancy treated at the Pediatric Hematology-Oncology Unit of the Postgraduate Institute of Medical Education and Research, Chandigarh, India, who tested positive for SARS-CoV-2 between August 1, 2020 and May 31, 2021. SARS-CoV-2 infection was diagnosed from the nasopharyngeal swab specimen with the real-time reverse transcriptase-polymerase chain reaction (RT-PCR) according to the testing guidelines endorsed by the Government of India. The test results were interpreted by the cycle threshold (Ct) value; the threshold varied depending on the test kit. All patients requiring hospitalization for any reason, including planned procedures and chemotherapy, were tested for SARS-CoV-2 as per the prevailing testing policy of the institute. Children attending the oncology outpatient clinic were not tested for SARS-CoV-2 unless symptomatic. Symptomatic children were admitted to the dedicated COVID-19 ward and managed as per COVID-19 protocol. Admitted patients underwent laboratory evaluations as clinically indicated. Serum levels of COVID-19 biomarkers, such as C-reactive protein, ferritin, D-dimer, interleukin 6, etc., were not performed routinely as per the institutional pediatric COVID-19 management policy. Children who tested positive were not retested for clearance of the virus as per the testing strategy endorsed by the National Task Force on COVID-19 (Version VI, dated September 4, 2020). Cancer therapy was resumed after a minimum of 14 days or longer in case of persistently symptomatic disease. Status of vaccination of contacts was not recorded as vaccination for the general population commenced only on May 1, 2022.

Inclusion and Exclusion Criteria for SARS-CoV-2 Testing

Inclusion Criteria

Children with cancer were tested for SARS-CoV-2 either due to illness suggestive of COVID-19 or as a component of universal screening prior to diagnostic procedures, surgery, radiotherapy, or hospitalization for administration of chemotherapy or febrile neutropenia or evaluation of suspected malignancy.

Exclusion Criteria

Asymptomatic children with cancer visiting pediatric oncology clinic or daycare services were not routinely tested.

Data Collection

Data concerning epidemiology, underlying malignancy, phase of anticancer therapy, clinical features attributable to COVID-19 illness, clinical severity, respiratory support requirement, need and duration of hospitalization, outcome, and the effect on the delivery of anticancer therapy were collected from the case record files on a predesigned, structured proforma.

The Severity of COVID-19 Disease

The severity of COVID-19 was categorized as mild, moderate, severe, and critical based on clinical and/or radiological features.[12]

- *Mild*: asymptomatic or only upper respiratory tract symptoms.
- *Moderate*: clinical and/or radiological evidence of pneumonia, without hypoxia.
- *Severe*: presence of one of the following: tachypnea/hypoxia/encephalopathy/convulsions/dehydration/myocardial injury/elevated liver enzymes/coagulopathy.
- *Critical*: respiratory failure requiring mechanical ventilation/shock/vital organ dysfunction requiring intensive monitoring.

Outcome Measures

The clinical outcome of SARS-CoV-2 infection in children with cancer was the primary outcome measure of the study. The secondary outcome measures included: the severity of illness, frequency of hospitalization, and detrimental effects of SARS-CoV-2 infection on the timely delivery of anticancer treatment.

Statistical Analysis

Baseline clinical variables were summarized using descriptive statistics. Proportions were compared using the chi-square test. The Mann–Whitney test was used to compare the duration of hospitalization between two or more groups. The statistical tests were performed at a significance level of 0.05. Analysis was performed using the statistical software SPSS Statistics (Version 23, Armonk, New York, United States).

Ethics

The institutional ethics committee approved the study (NK/7558/Study/625). Informed consent from parents was waivered due to the retrospective nature of the study. The study was conducted in accordance with the Declaration of Helsinki.

Results

A total of 1,146 tests were performed. Sixty-six (6.07%) patients tested positive. The rate of RT-PCR positivity in all pediatric patients during the study period at our center was 3% (262/8,780) ($p < 0.0001$).

Demographic Details

The study population included infants ($n = 2$, 3%), young children (1–5 years) ($n = 19$, 28.8%), and older children/adolescents (6–14 years) ($n = 45$, 68.2%). The rate of test-positivity was comparable between the two waves of the SARS-CoV-2 pandemic in India (6.4% [31/479] in the first wave and 5.2% [35/667] in the second wave) ($p = 0.42$). Demographic parameters, the underlying malignancy, and the phase of therapy of the patients with SARS-CoV-2 infection are presented in ►**Table 1**. A history of contact with a proven case of SARS-CoV-2 was obtained from 4 (6.1%) patients.

Clinical Features of SARS-CoV-2 Infection

(1) Asymptomatic infection ($n = 32$): About half ($n = 32$, 48.4%) of the SARS-CoV-2-positive children were asymptomatic. The indications for testing included: (1) before an invasive procedure or imaging ($n = 12$; 38%), (2) admission for the administration of chemotherapy ($n = 11$; 34%), (3) newly diagnosed malignancy ($n = 6$; 19%), (4) surgery ($n = 2$; 6%), and (5) initiation of radiotherapy ($n = 1$; 3%).

(2) Symptomatic COVID-19 disease ($n = 24$): The spectrum of symptoms included (1) fever ($n = 24$), (2) cough ($n = 12$), (3) rhinorrhea ($n = 5$), (4) respiratory distress ($n = 11$), (5) watery diarrhea ($n = 5$), and (6) vomiting ($n = 3$). The severity profile of these 24 patients was as follows:

- *Mild-to-moderate illness*: The majority ($n = 18$; 75%) had "mild-to-moderate" illness.
- *Severe/critical illness*: Six patients had a "severe" ($n = 3$) or "critical" ($n = 3$) illness. The clinical profile of the patients with "severe" or "critical" COVID-19 disease is summarized in ►**Table 2**. On the chest radiograph, one of these six patients, a case of newly diagnosed acute myeloid leukemia (AML), had bilateral bronchopneumonia. However, in the absence of any microbiologic or serologic evidence of invasive fungal infection, the precise etiology of pneumonia remained elusive. No patient had the multisystemic inflammatory syndrome of childhood.

Table 1 Demographic profile of the patients with SARS-CoV-2 infection

Patient characteristics	($N = 66$), *n* (%)
Age	6.8 y (IQR: 3.4, 9.8)
Sex	Male: 43 (65) Female: 23 (35)
Underlying malignancy	
ALL	36 (54.5)
Relapsed ALL	3 (4.5)
AML	4 (6.1)
Burkitt lymphoma	6 (9.2)
Lymphoblastic lymphoma (one each of B-and T-lineage)	2 (3)
Hodgkin lymphoma	1 (1.5)
Ewing sarcoma	6 (9.2)
Relapsed Ewing sarcoma	1 (1.5)
Neuroblastoma	1 (1.5)
Germ cell tumor	2 (3)
Hepatoblastoma	2 (3)
Synovial sarcoma	1 (1.5)
Malignant rhabdoid tumor of kidney	1 (1.5)
Phase of therapy	
Leukemia/lymphoma	($N = 52$), *n* (%)
At diagnosis	10 (19.2)
Induction	19 (36.5)
Consolidation	7 (13.5)
Interim maintenance	4 (7.7)
Intensification	2 (3.8)
Maintenance	10 (19.2)
Solid malignancies	($N = 14$), *n* (%)
Phase of neoadjuvant chemotherapy	8 (57.2)
Phase of adjuvant chemotherapy	4 (28.6)
During radiotherapy	1 (7.1)
At diagnosis of disease relapse (Ewing sarcoma)	1 (7.1)

Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; IQR, interquartile range; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Table 2 Clinical profile, chest radiograph, and outcome of children with "severe" or "critical" illness due to COVID-19

S. No.	Age/Sex/Underlying cancer/ Phase of therapy	Severity of illness	Maximum respiratory support	Nonrespiratory complications	Chest X-ray	Days of hospitalization	Outcome
1.	5½ y/F/ALL/ maintenance	Severe	Low-flow oxygen	–	Bronchiectasis (preexisting)	12	Recovery
2.	8 y/M/AML/ treatment naive	Severe	Low-flow oxygen	–	Bronchopneumonia	20	Recovery
3.	6½ y/F/Relapsed ALL/maintenance	Severe	Low-flow oxygen	–	Consolidation of the right lower lobe	12	Recovery
4.	2 y/F/Burkitt lymphoma/ consolidation	Critical	Low-flow oxygen	Septic shock, GI symptoms	Normal	9	Recovery
5.	1½ y/M/Burkitt lymphoma/ treatment naive	Critical	Invasive ventilation (conventional)	–	Bronchopneumonia	13	Recovery
6.	10 ½ y/F/ALL/ treatment naive	Critical	Invasive ventilation (conventional)	–	Consolidation of the left middle lobe	11	Death

Abbreviations: ALL, acute lymphoblastic leukemia; AML, acute myeloid leukemia; COVID-19, coronavirus disease 2019; F, female; GI, gastrointestinal; M, male.

(3) Non-COVID-related illnesses: Ten children had an unrelated illness at admission, and SARS-CoV-2 was detected incidentally. This included status epilepticus ($n=3$), appendicitis ($n=1$), neutropenic colitis with gut perforation ($n=1$), pneumococcal sepsis and lobar pneumonia ($n=1$), disseminated staphylococcal sepsis and empyema ($n=1$), refractory malignant rhabdoid tumor of the kidney with overt pulmonary metastases ($n=1$), refractory hepatoblastoma with massive abdominal distension ($n=1$), and abdominal Burkitt lymphoma with tense ascites ($n=1$). None of these children had symptomatology attributable to SARS-CoV-2 infection.

Laboratory Parameters

- Chest X-ray: The chest X-ray in the six children who had severe/critical illness had the following findings: (1) normal X-ray ($n=1$), (2) lobar consolidation ($n=2$), (3) bronchopneumonia ($n=2$), and (4) bilateral bronchiectasis ($n=1$, the patient had preexisting bronchiectasis for nearly a year). No patient underwent computed tomography of the chest.
- Hematological findings: Neutropenia (absolute neutrophil count $< 1.5 \times 10^9$/L) and thrombocytopenia (platelet count $< 100 \times 10^9$ /L) were documented in 18 (75%) and 19 (79%) of the 24 hospitalized patients, respectively. The median neutrophil-to-lymphocyte ratio (NLR) of the hospitalized patients was 0.114 ($n=23$). A high NLR (>3) was documented in only two children (NLR: 3.3 and 6.3, respectively).

Treatment

Hospitalization

Twenty-nine patients required hospitalization. The clinical profile of the hospitalized patients is summarized in ►**Table 3**. A comparison of the patients hospitalized vis-à-vis not hospitalized is presented in ►**Table 4**. The median duration of hospital stay was 7 days (range: 1–26). Younger

Table 3 Indication of admission and clinical profile of the hospitalized patients ($n=29$)

Indication of admission	*n* (%)	Presence of fever	Lower respiratory sign/symptom	Associated problems
Evaluation of fresh undiagnosed cases of childhood cancer	9 (31)	3	2	Massive ascites ($n=1$), large oropharyngeal mass ($n=1$)
Uncomplicated FN	9 (31)	In all	Nil	Gastroenteritis-like illness ($n=2$)
Complicated FN	7 (24)	In all	4	Disseminated staphylococcal sepsis ($n=1$), pneumococcal blood-stream infection ($n=1$), bronchiectasis ($n=1$)
Others	4 (14)	None	None	Seizures due to hypertensive PRES ($n=2$) or CNS relapse of ALL ($n=1$); appendicitis ($n=1$)

Abbreviations: ALL, acute lymphoblastic leukemia; CNS, central nervous system; FN, febrile neutropenia; PRES, posterior reversible encephalopathy syndrome.

Table 4 Comparison of the patients requiring vis-à-vis not requiring hospitalization

Parameter	Hospitalized patients ($n = 29$)	Nonhospitalized patients ($n = 37$)	p-Value
Age (median/IQR)	6.6 (3.2, 9.2)	7.35 (3.5, 10.5)	0.32
Sex	Male: 20, female: 9	Male: 23, female: 14	0.75
Type of underlying malignancy	Hematolymphoid: 28, solid: 1	Hematolymphoid: 24, solid: 13	0.002
Phase of therapy	Intensive: 23, nonintensive: 5	Intensive:16, nonintensive: 8	0.22

Abbreviation: IQR, interquartile range.

age (< 7 years) ($p = 0.44$), sex ($p = 0.65$), type of malignancy (hematolymphoid vis-à-vis solid) ($p = 0.39$), or the phase of therapy ($p = 0.67$) did not influence the duration of hospitalization.

Treatment of Patients with Severe/Critical COVID-19 Illness

Of the 6 patients with severe/critical COVID-19 disease, 2 required mechanical ventilation for 1 and 10 days, respectively, and 4 needed low-flow oxygen. The patient requiring ventilatory support for 10 days received remdesivir (4 doses) and dexamethasone (for 7 days). The mean duration of hospitalization and respiratory support requirement for the 6 patients was 13.3 days (range: 9–20) and 8.7 days (range: 5–12), respectively. No patient received interleukin-directed therapy or prophylactic anticoagulant.

Treatment of Hospitalized Patients with Mild-Moderate Illness

In addition to the symptom-directed therapy, all patients with febrile neutropenia were treated with antimicrobials and supportive care per the unit's protocol. Patients with culture-proven bacterial sepsis ($n = 3$) received antimicrobial treatment guided by the antibiogram.

Treatment of Asymptomatic Patients

Asymptomatic patients were quarantined for 14 days (home or hospital as per the state policy). The hematology-oncology registrar telephoned them regularly for well-being. Children with acute lymphoblastic leukemia (ALL) in the maintenance phase of therapy with asymptomatic SARS-CoV-2 infection were advised to hold antimetabolite drugs for 2 weeks.

Deleterious Impact of the SARS-CoV-2 Infection on the Delivery of Anticancer Therapy

There was a delay in establishing the diagnosis in two patients. A delay, interruption, or modification in administering at least one modality of anticancer treatment secondary to the SARS-CoV-2 infection was noted in 38 (57.6%) patients. There was a postponement of chemotherapy for patients who tested COVID-19 positive at diagnosis. The gap was bridged with oral prednisolone at 50% of the per-protocol dose for the children with newly diagnosed ALL. Thirty-five (53%) patients experienced a delay in receiving chemotherapy, with a median delay of 14 days (range: 7–27). Definitive surgery was deferred in two patients (one with hepatoblastoma and the other with malignant germ cell tumor) for 21 and 35 days from the scheduled date, respectively. One child with synovial sarcoma had an interruption of radiotherapy due to asymptomatic SARS-CoV-2 infection.

Outcome

Fifty-nine of 66 (89.4%) patients recovered. Five (7.6%) patients died, and 2 (3%) abandoned therapy.

Deaths: Five (7.6%) patients died; 1 (1.5%) death was attributable to severe COVID-19 pneumonia during induction therapy for ALL. The other deaths included: (1) hepatoblastoma with refractory disease, (2) fulminant polymicrobial sepsis in a patient with AML, (3) intracranial hypertension due to central nervous system relapse of ALL, and (4) hypertensive encephalopathy in a child with Burkitt lymphoma. None of these four children had clinical symptoms of COVID-19 disease.

Discussion

The SARS-CoV-2 pandemic is the most cataclysmic event in the past 100 years, threatening all facets of the global health care delivery system. The available data on SARS-CoV-2 illness in children has projected a milder disease than in adults. However, children with cancer are profoundly immunocompromised, and a general apprehension of severe disease in this specific population exists. The current study analyzed the clinical profile and outcome of SARS-CoV-2 infection in children with cancer. We also evaluated the deleterious effect of SARS-CoV-2 infection on the timely administration of anticancer therapy.

The rate of test positivity for SARS-CoV-2 was 6.07%, comparable between the first and second waves of the SARS-CoV-2 pandemic ($p = 0.42$). The rate of test-positivity among the children with cancer in our cohort was double that observed in all pediatric admissions in our hospital ($p < 0.0001$). We attribute this to frequent hospital visits of oncology patients for chemotherapy, transfusions, and check-ups. Also, a breach of COVID-19 protective measures among the patients in the hostel/Sarai and dining hall is a plausible explanation. A relatively higher frequency (12.1% in the first wave and 17.4% in the second wave) of test positivity among pediatric oncology patients is reported from another center in North India.[13] A report of a single-center experience from South India documented a remarkably high rate (54%) of SARS-CoV-2 -positivity among children and young adolescents with cancer.[14] However, this study had a questionnaire-based

Table 5 Selected studies from low- and middle-income countries on clinical profile and outcome of COVID-19 in children with cancer

S No.	Author, year of publication, country	*n*	Underlying malignancy	Severity profile	Hospitalization	ICU admission	Mechanical ventilation	Mortality rate
1	Raj et al[15], 2022, India	659	Hematolymphoid: 73%, solid: 27%	Asymptomatic: 72%	Not included	Not included	Not included	1%
2	Verma et al[16], 2022, India	50	Not included	Asymptomatic: 74%, mild-moderate: 22%, and severe: 4%	8%	Not included	4%	Not included
3	Mohapatra et al[17], 2022, India	68	Hematolymphoid: 81%, solid: 19%	Asymptomatic: 76.5%, mild-moderate: 19%, severe-critical: 4.4%	34%	4.4%	Not included	4.4%
4	Corso et al[18], 2021, Brazil	179	Hematolymphoid: 56%, solid: 34%	Asymptomatic to mild: 37%, moderate to severe: 40.2%, and critical: 23%	80%	19%	6%	12%
5	Parambil et al[19], 2022, India	122	Hematolymphoid: 69%, solid: 31%	Asymptomatic: 18%, requirement of respiratory support: 5.7%	All	Not included	2.5%	4.9%
6	Hammad et al[20], 2021, Egypt	76	Hematolymphoid: 86%, solid: 14%	Severe-to-critical illness: 35.4%	93%	Not included	15.7%	13%
7	Radhakrishnan et al[11], 2021, India	15	Hematolymphoid: 80%, solid: 20%	Asymptomatic: 67%, critical illness: 6.6%	All	6.6%	None	Nil
8	Bhayana et al[13], 2021, India	22	Hematolymphoid: 91%, solid: 9%	Asymptomatic: 54.5%, moderate: 22.7%, critical: 13.6%	36%	13.6%	None	Nil
9	Totadri et al[14], 2022, India	37	Hematolymphoid: 57%, solid: 43%	Mild: 27%, moderate: 35%, severe: 32%, and critical: 6%	All	32%	None	Nil
10	Hamdy et al[21], 2021, Egypt	7	Hematolymphoid: 86%, solid: 14%	Not included	Not included	43%	14%	43%
11	Current study	66	Hematolymphoid: 79%, solid: 21%	Asymptomatic: 48.5% Mild-moderate: 27% Severe: 4.5% Critical: 4.5% Illness not attributable to COVID-19: 15.5%	44%	9%	3%	1.5%

Abbreviations: COVID-19, coronavirus disease 2019; ICU, intensive care unit.

testing approach, which probably overestimated the test positivity.

A large fraction of children with SARS-CoV-2 infection were asymptomatic (48.5%) or mild-to-moderately symptomatic (42.5%). Only 6 (9%) children had a severe or critical illness, and 2 (3%) required invasive ventilation. A systematic review of the clinical profile of COVID-19 in children with cancer reported the following statistics: severe illness 9.6%, intensive care unit admission 10.3%, and mortality 4.9%, comparable to our experience.[9] In sharp contrast to our finding, Totadri et al[14] experienced a higher frequency of severe or critical illness (37%), hemodynamic compromise (21%), or requirement of supplemental oxygen (14%). However, none required invasive ventilation, and there were no deaths. The co-occurrence of oncologic emergencies and systemic infections in 50% of the children with a severe or critical illness is a potential confounder in the study. Selected studies on the clinical profile and outcome of SARS-CoV-2 infection in children with cancer are summarized in ►**Table 5**.[11,13–21] In our cohort, a substantial proportion of admitted patients had cytopenias. However, as most had active hematological malignancy or recent exposure to myelosuppressive chemotherapy, the precise contribution of COVID-19 to the causation of cytopenia is elusive.

A sizeable proportion (38/66; 57.6%) of children in our cohort had a delay in receiving scheduled therapy. A systematic review including 33 studies comprising 226 children with cancer and SARS-CoV-2 infection revealed a noticeable rate (78.7%) of treatment delay or modification of therapy.[9] The apprehension of fulminant COVID-19 illness in SARS-CoV-2 infected children following chemotherapy has resulted in a global practice of delaying anticancer therapy. However, the interruption of timely delivery of anticancer therapy raises concerns about the compromised oncologic outcome. A report from western India has demonstrated that the continuation of systemic chemotherapy in stable children with SARS-CoV-2 infection is safe.[19] Experience from the United Kingdom is also reassuring, where 71% of the patients with SARS-CoV-2 infection received standard or very myelosuppressive chemotherapy with no COVID-19-related mortality.[22] Conceivably, the continuation of non-intensive chemotherapy in nonsick SARS-CoV-2 infected children is safe. There is a scarcity of consensus guidelines for managing newly diagnosed malignancy in children with SARS-CoV-2 infection. However, for children with newly diagnosed ALL, the World Health Organization Global Initiative in Childhood Cancer endorses the initiation of steroid prophase, especially in an oncologic emergency.[23]

During the pandemic, a universal testing policy before elective procedures or admissions was adopted globally, the rationale of which is debatable. In our cohort, the rates of test positivity prior to an elective procedure (2%) or admission for chemotherapy (2.9%) were considerably low. Hence, the cost-effectiveness of universal PCR testing, especially in regions where the *R*-value is < 1, is debatable.[24,25] A questionnaire-based screening approach might be a cost-effective alternative to select asymptomatic patients for preadmission or preprocedure testing.[26]

Our study has several strengths:

1. One of the largest studies on the clinical effect of SARS-CoV-2 infection in children with cancers from LMIC.
2. Universal testing strategy picking up most infected children.

The limitations of this analysis include the retrospective nature of the analysis and a lack of family screening/contact tracing.

Conclusion

Our study demonstrates a low frequency of SARS-CoV-2 infection and noticeably low severity of COVID-19 in children with cancer in an LMIC setting. These findings are reassuring that children immunocompromised with an underlying malignancy do not have greater morbidity and mortality with the SARS-CoV-2 infection compared with the general pediatric population. However, the pandemic has significantly impacted the delivery of anticancer treatment, which may have later adverse consequences.

Data Availability Statement
The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Funding
None.

Conflict of Interest
None declared.

Acknowledgment
We acknowledge the Pediatric COVID management team of our institute.

References

1 Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. Acta Paediatr 2020;109(06):1088–1095
2 Castagnoli R, Votto M, Licari A, et al. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in children and adolescents: a systematic review. JAMA Pediatr 2020;174(09): 882–889
3 Patel NA. Pediatric COVID-19: systematic review of the literature. Am J Otolaryngol 2020;41(05):102573
4 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(07):e28397
5 Bisogno G, Provenzi M, Zama D, et al. Clinical characteristics and outcome of severe acute respiratory syndrome coronavirus 2 infection in Italian pediatric oncology patients: a study from the Infectious Diseases Working Group of the Associazione Italiana di Oncologia e Ematologia Pediatrica. J Pediatric Infect Dis Soc 2020;9(05):530–534
6 Pérez-Martinez A, Guerra-García P, Melgosa M, et al. Clinical outcome of SARS-CoV-2 infection in immunosuppressed children in Spain. Eur J Pediatr 2021;180(03):967–971
7 Montoya J, Ugaz C, Alarcon S, et al. COVID-19 in pediatric cancer patients in a resource-limited setting: national data from Peru. Pediatr Blood Cancer 2021;68(02):e28610

8 Rossoff J, Patel AB, Muscat E, Kociolek LK, Muller WJ. Benign course of SARS-CoV-2 infection in a series of pediatric oncology patients. Pediatr Blood Cancer 2020;67(09):e28504
9 Meena JP, Kumar Gupta A, Tanwar P, Ram Jat K, Mohan Pandey R, Seth R. Clinical presentations and outcomes of children with cancer and COVID-19: a systematic review. Pediatr Blood Cancer 2021;68(06):e29005
10 Kuderer NM, Choueiri TK, Shah DP, et al; COVID-19 and Cancer Consortium. Clinical impact of COVID-19 on patients with cancer (CCC19): a cohort study. Lancet 2020;395(10241):1907–1918
11 Radhakrishnan V, Ovett J, Rajendran A, et al. COVID19 in children with cancer in low- and middle-income countries: experience from a cancer center in Chennai, India. Pediatr Hematol Oncol 2021;38(02):161–167
12 Dong Y, Mo X, Hu Y, et al. Epidemiology of COVID-19 among children in China. Pediatrics 2020;145(06):e20200702
13 Bhayana S, Kalra M, Sachdeva P, Sachdeva A. Clinical profile and outcomes of COVID-19 infection during the first wave in children with hematological illnesses and cancer: an observational study from a tertiary care center in North India. Cancer Res Stat Treatment 2021;4(02):262
14 Totadri S, Srinivasan HN, Joseph LL, et al. The unique balancing act of managing children with cancer and COVID-19 infection: a single center experience from South India. J Pediatr Hematol Oncol 2022;44(01):e287–e292
15 Raj R, Uppuluri R, Parambil B, et al. Outcomes of COVID-19 in children with cancer – report from the Indian Pediatric Oncology Group (InPOG) COVID-19 registry in India. Pediat Hematol Oncol J 2022;7(02):34–37
16 Verma C, Taneja K, Mahajan A. COVID-19 in pediatric oncology patients: clinical course and outcomes from a tertiary care center in North India. Indian J Pediatr 2022;89(02):207
17 Mohapatra S, Das PK, Mishra B, Panigrahi A. Clinical review of COVID-19 in children and adolescents with cancer: experience from a tertiary care center in East India. Pediatr Hematol Oncol 2022;39(06):517–528
18 Corso MCM, Soares VJ, Amorim AMP, et al. SARS-CoV-2 in children with cancer in Brazil: results of a multicenter national registry. Pediatr Blood Cancer 2021;68(12):e29223
19 Parambil BC, Moulik NR, Dhamne C, et al. COVID-19 in children with cancer and continuation of cancer-directed therapy during the infection. Indian J Pediatr 2022;89(05):445–451
20 Hammad M, Shalaby L, Sidhom I, et al. Management and outcome of coronavirus disease 2019 (COVID-19) in pediatric cancer patients: a single centre experience from a developing country. Clin Lymphoma Myeloma Leuk 2021;21(11):e853–e864
21 Hamdy R, El-Mahallawy H, Ebeid E. COVID-19 infection in febrile neutropenic pediatric hematology oncology patients. Pediatr Blood Cancer 2021;68(02):e28765
22 Millen GC, Arnold R, Cazier JB, et al. Severity of COVID-19 in children with cancer: report from the United Kingdom Paediatric Coronavirus Cancer Monitoring Project. Br J Cancer 2021;124 (04):754–759
23 Sullivan M, Bouffet E, Rodriguez-Galindo C, et al; Contributing Authors. The COVID-19 pandemic: a rapid global response for children with cancer from SIOP, COG, SIOP-E, SIOP-PODC, IPSO, PROS, CCI, and St Jude Global. Pediatr Blood Cancer 2020;67(07): e28409
24 Nakamura I, Itoi T. Universal PCR screening for coronavirus disease 2019 in asymptomatic patients on admission. Clin Microbiol Infect 2021;27(04):658–659
25 Jung J, Kim J, Lim JS, Kim EO, Kim MN, Kim SH. Pitfall of universal pre-admission screening for SARS-CoV-2 in a low prevalence country. Viruses 2021;13(05):804
26 Mei-Dan E, Satkunaratnam A, Cahan T, Leung M, Katz K, Aviram A. Questionnaire-based vs universal PCR testing for SARS-CoV-2 in women admitted for delivery. Birth 2021;48 (01):96–103