Received: 1 January 2021 | Revised: 29 January 2021 | Accepted: 19 February 2021

DOI: 10.1002/pbc.29005

Pediatric Blood & Cancer

REVIEW

Clinical presentations and outcomes of children with cancer and COVID-19: A systematic review

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Abstract

Information regarding the novel coronavirus disease (COVID-19) in pediatric oncology is limited. We conducted a systematic review of the available published literature on children with cancer affected by COVID-19. The last date of the study search was October 20, 2020, and 33 studies comprising 226 children were included for the final analysis. Data were extracted in a predefined data collection form, and the variables were extracted and analyzed. Patients with hematological malignancies were more in number. Males and children on intensive treatment were more frequently affected. Fever was the commonest symptom. The disease was asymptomatic/mild in 48% and severe in 9.6%. Consolidation, peribronchial cuffing, and consolidation with ground glass opacities were the common imaging findings. Hydroxychloroquine was the most frequently used drug for COVID-19. About 10% of children required intensive care, and about 32% had oxygen requirements. The percentage of children who died due to COVID-19 was 4.9%. The severity, morbidity, and mortality of COVID-19 in pediatric oncology were more compared to the general pediatric population. This information can help in risk stratification for the management of COVID-19.

KEYWORDS
cancer, children, COVID-19, SARS-CoV-2

1 | INTRODUCTION

The coronavirus disease (COVID)-19 characterization in pediatric cancer patients is limited in the available literature to case reports and descriptive case series. The pandemic of COVID-19, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has been evolving rapidly. To date, more than 40 million people have been affected, and over a million deaths have occurred.[1] Previous reports have suggested that the severity of the disease is mild, and it is a self-limiting upper respiratory tract infection in most children. The proportion of children who are affected by COVID-19 is less in comparison to adults.[2]

Children with cancer and on treatment for it are a vulnerable population. Cancer and its treatment cause immune suppression and increase the likelihood of acquiring an infection and the severity of any infection is more. Frequent visits to the hospital for treatment make it difficult to adhere to social distancing and compromise the use of facemasks: the two most imperative measures advocated for the prevention of the novel coronavirus infection. In adults, COVID-19 in cancer patients has higher fatality compared to the normal population.[3] This has also been supported by the findings of a recent systematic review and pooled analysis by Saini et al.[4] The incidence of COVID-19 in children with cancer has been reported to be higher than in the general pediatric population.[5]

Abbreviations: ARDS, acute respiratory distress syndrome; CBNAAT, cartridge-based nucleic acid amplification test; COVID-19, coronavirus disease-19; CT, computed tomography; GGO, ground glass opacity; HSCT, hematopoietic stem cell transplant; ICU, intensive care unit; RTPCR, reverse transcriptase polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

Although children with cancer are considered a high-risk population, data specifically in relation to outcomes of COVID-19 in the pediatric oncology population are limited and are still emerging. In the available studies, the sample size is small, and the findings in these studies have diverse reporting. The data in relation to COVID-19 and pediatric cancers are from different countries, which have diverse health infrastructures and policies, making the available data heterogeneous.

We aimed to conduct a systematic review of the available published literature on pediatric cancer patients affected by COVID-19 and analyzed the clinical manifestations and outcomes.

2 | MATERIAL AND METHODS

The title was prospectively registered in PROSPERO.[6]

2.1 | Types of studies

The studies that described the outcomes of pediatric oncology patients who were positive for SARS-CoV-2 were included. Eligibility criteria for inclusion of the studies for review were, the ones in which the subject/subjects had a laboratory-proven diagnosis of COVID-19 in a child under the age of 18 years and who was undergoing/had undergone cancer treatment. Those patients who had either a positive test on a respiratory sample either by reverse transcriptase polymerase chain reaction (RTPCR) for SARS-CoV-2, cartridge-based nucleic acid amplification test (CBNAAT) for SARS-CoV-2, or a rapid antigen test were included along with those who were positive for SARS-CoV-2 antibody test from the blood. We included only those studies in which the description of the clinical characteristics and outcomes were available. The last date of the literature search was October 20, 2020. Only case reports and case series were available, so the authors decided to include as many studies as possible, that fulfilled the eligibility criteria.

Exclusion criteria were as follows: unpublished reports, unspecified date and location of the study or duplicate reporting, cases with suspected COVID-19 that were not confirmed by a laboratory test, unreported outcomes of subjects, studies not in English, and systematic reviews.

2.2 | Search methodology

A comprehensive literature search using MEDLINE, Embase, and Google Scholar was conducted. We used combinations of the following search terms: COVID-19, pediatrics, children, child, outcomes, complications, clinical manifestations, morbidity, mortality, cancer, neoplasm, oncology, and SARS-CoV-2. The details of MEDLINE and Embase search strategies are given in Appendices SA1 and SA2, respectively (Supporting File).

2.3 | Selection of studies

Titles and abstracts were reviewed by two authors (Jagdish Prasad Meena, Aditya Kumar Gupta) to evaluate for inclusion and screening of full text. Any discrepancy was resolved by a third author (Kana Ram Jat). Full-text articles were retrieved for further consideration for inclusion.

2.4 | Data extraction

The review authors (Jagdish Prasad Meena, Aditya Kumar Gupta) extracted data on a predesigned proforma independently. Variables that were extracted and analyzed included geographic location, age, sex, type of malignancy, phase of treatment, clinical symptoms and signs recorded at admission, complications, impact on cancer treatment, therapy given, and outcomes.

The primary objective was to describe the clinical and radiological characteristics of children with cancer diagnosed with COVID-19.

The secondary objectives were to find out the proportion of children with the need for hospitalization, the need for oxygen therapy, need for intensive care unit (ICU) admission, COVID-19-specific treatment, delay in chemotherapy administration, complications, and mortality. The severity of the disease was classified as asymptomatic, mild, moderate, and severe/critical based on the criteria by Dong et al.[7]

2.5 | Statistical analyses

Statistical analysis was done using the STATA 14.0 software. We used descriptive statistics. Continuous variables were expressed as mean (SD) or median (range/interquartile range [IQR]) depending on the distribution. Categorical variables were expressed as the number of cases and percentages (%).

The PRISMA checklist for systematic reviews for this review is given in Table S6.

3 | RESULTS

A search of the above databases yielded 753 results, out of which 27 were removed due to duplication. The abstracts and titles of 726 articles were screened and 56 studies were considered for eligibility. After screening the full text of each of the studies, 23 studies were excluded, and 33 studies were included in the final analysis (Figure 1).[5,8–39]

3.1 | Demographics

A total of 226 children (33 studies) with pediatric malignancies were diagnosed to be positive for the SARS-CoV-2, of which 30.5% were

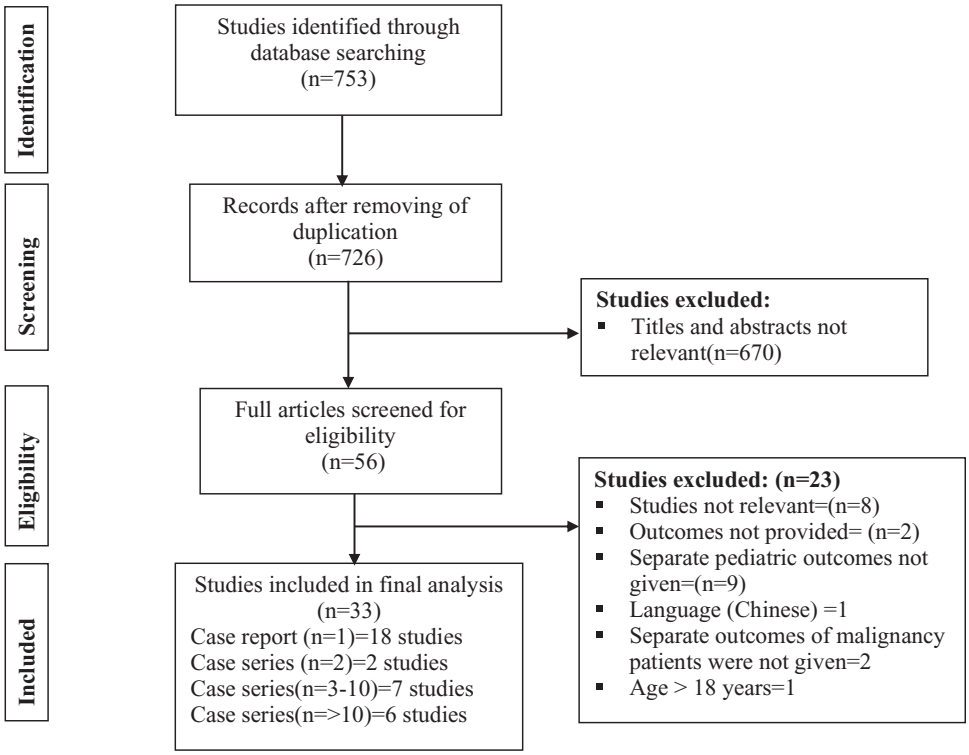

FIGURE 1 Flow diagram showing inclusion and exclusion of studies

from Peru, 27.9% from Italy, 12.8% from the United States, 11.1% were Spanish, 7.5% were Mexican, and the remaining were from other nations. There were 133 males out of the 210 subjects (31 studies) for which data on gender were available (M:F = 1.7:1) and the median age was 7 years (IQR 4, 9) (Table 1).

For our first analysis to find out the rate of positivity on screening, out of the 33 studies we selected studies in which COVID-19 in pediatric cancer patients was diagnosed after screening a larger number of patients regardless of symptoms. Seven studies mentioned data in relation to positivity after the screening (Table 2).[8–14] In these seven studies (n = 1219), a total of 77 children were detected to be positive for the SARS-CoV-2 out of 1219 screened (6.3%).

In 29 studies (n = 177 patients),[8,11–14,16–39] there was a mention of the type of test used to detect SARS-CoV-2. Among the 177 patients in these studies, PCR-based tests were used to establish the diagnosis in 142 (one was also positive on CBNAAT) and antibody-based tests in 23 (the type of test used was not mentioned for 12 patients in the study by Montoya et al.[18]; we have considered these patients in the analysis as the remaining patients in that study were diagnosed either by RTPCR or antibody-based tests) (Table 3).

In 196 patients (31 studies),[5,10–39] there was a mention about the type of malignancy, and 120 (53%) had hematological malignancies, and 76 (47%) had solid tumors. In studies that reported remission status (18 studies), 23 patients out of 47 were in remission from the underlying malignancy[10,11,14,20–26,29–37] (Table 1).

Among 24 studies including 102 patients[5,10,13–17,20–25,27–35,37] for whom information was available on the phase of chemotherapy/hematopoietic stem cell transplant (HSCT) status, 34 were on the intensive phase of chemotherapy, 13 were on low-dose chemotherapy, six had completed treatment, and 17 post HSCT (Table 1).

3.2 | Clinical features

Twenty-six studies (n = 184 patients) reported about clinical symptoms.[5,10–14,16–18,20–28,30–36,38] Amongst the 184 patients included in these studies, fever was the commonest symptom in 77 (41.4%), followed by cough (12.3%). Other symptoms related to the respiratory tract were present in 50 subjects, and 20 had hypoxia. Gastrointestinal symptoms were present in 17, and skin involvement was mentioned for three patients. In 30 studies (n = 209 patients),[5,8,10–18,20–38] the severity of the symptoms was reported. Sixty-three patients had no symptoms, 38 had mild symptoms, nine had moderate symptoms, and 20 (9.6%) had severe symptoms. In the remaining studies, the symptom severity was not mentioned (Table 3).

3.3 | Radiological findings

The X-ray findings were mentioned in 11 studies (n = 59 patients).[5,13,16,17,25,28,30,31,33,34,38] The X-ray was mentioned as normal for six patients and abnormal for 20 patients. In six patients, it showed consolidation, peribronchial cuffing in four, and interstitial infiltrates in three. Other findings seen on the X-ray were fluffy

TABLE 1 Demographics and baseline characteristics for pediatric oncology children with COVID-19

Characteristics	Total number of patients *n* (%)
Nationality (studies = 33, *n* = 226)	
Peru	69 (30.5)
Italy	63 (27.9)
USA	29 (12.8)
Spain	25 (11.1)
Mexico	17 (7.5)
Egypt	7 (3.1)
Switzerland, Austria, Poland, UK, Brazil	5 (2.2) (one case from each country)
India, Georgia	4 (1.8) (two cases from each country)
China	4 (1.8)
France	3 (1.3)
Median age (IQR) (years)	7 (4, 9)
Gender (studies = 31, *n* = 210)	
Males	133 (63.4)
Females	77 (36.6)
Type of malignancy (studies = 31, *n* = 196)	
HematologicalSolid	120 (53)76 (47)
Remission status (studies = 18, *n* = 47)	
Patients in remission	23 (48.9)
Phase of chemotherapy (studies = 24, *n* = 102)	
Intensive chemotherapy	34 (33.3)
Post-HSCT	17 (16.7)
Low-dose chemotherapy/maintenance	13 (12.7)
Post completion of chemotherapy	6 (5.9)
Not mentioned	32 (31.4)

Abbreviations: HSCT, hematopoietic stem cell transplant; IQR, interquartile range.

TABLE 2 Details of studies providing data on COVID-19 positivity after screening of pediatric oncology patients

irst author (Country)	Total screened	Total positive	Age (years)	Male/female	Type of malignancy (hematological/solid)	RTPCR positive
Boulad (USA)[8]	178	20	15.9 ± 6.6[a]	17/3	–	20
Cesaro (Italy)[9]	282	10	–	–	–	–
Ferrari (Italy)[10]	286	21	6 (1–17)[b]	10/11	10/11	–
Hamdy (Egypt)[11]	24	7		4/3	5/2	7
Lopez-Aguillar (Mexico)[12]	24	14	10 (3–15)[b]	8/6	9/5	14
Sieni (Italy)[13]	170	4	1.3	1/0	1/0	4
Wang (China)[14]	255	1	8	1/0	1/0	1

Abbreviation: RTPCR, reverse transcriptase polymerase chain reaction.
[a]Mean + SD.
[b]Median (range).

TABLE 3 Clinical and radiological details for pediatric oncology children with COVID-19

Parameters Symptoms (studies = 26, *n* = 184)	Number (%)
Fever	77 (41.8)
Cough	23 (12.5)
Hypoxia	20 (10.8)
Flu-like symptoms	13 (7)
Dyspnea	10 (5.4)
LRTI	11 (6)
URTI	5 (2.7)
Coryza	3 (1.6)
Sore throat	2 (1)
Chest pain	2 (1)
Pharyngeal congestion, wheezing, expectoration, and stridor	1 each
GIT symptoms	7 (3.8)
▪ Diarrhea	5
▪ Vomiting	2
▪ Abdominal pain	3
Dermatological symptoms	3 (1.6)
Other symptoms	
▪ Dysuria, fatigue, and shock	1 each
Severity of illness (studies = 30, *n* = 209)	
Asymptomatic patients	63 (30.1)
Mild symptoms	38 (18.1)
Moderate symptoms	9 (4.3)
Severe symptoms	20 (9.6)
Not mentioned	79 (37.8)
X-ray findings (studies = 11, *n* = 59)	
Normal	6 (10)
Abnormal X-ray	20 (33.9)
Not mentioned	33 (55.9)
Abnormal X-ray findings	
▪ Consolidation	6
▪ Peribronchial cuffing	4
▪ Interstitial infiltrate	3
▪ Fluffy opacities	2
▪ Bibasilar infiltrates, basilar opacities, alveolar hemorrhage, whiteout lungs, ARDS-like picture	1 each
CT findings (studies = 7, *n* = 42)	
Abnormal CT chest scan	12 (28.6)
Not mentioned	30 (71.4)
Abnormal CT chest findings	
▪ GGO	6
▪ Consolidation	6
▪ Reticular opacities	3
SARS-CoV-2 test used (studies = 29, *n* = 177)	
RTPCR	142 (80.2)
(RTPCR and CBNAAT positive)	1
Antibody-based testsNot mentioned	23 (13)12 (6.8)

Abbreviations: ARDS, acute respiratory distress syndrome; CBNAAT, cartridge-based nucleic acid amplification test; CT, computed tomography; GGO, ground glass opacity; GIT, gastrointestinal tract; LRTI, lower respiratory tract infection; RTPCR, reverse transcriptase polymerase chain reaction; URTI, upper respiratory tract infection.

opacities, acute respiratory distress syndromes (ARDS) like the picture, alveolar hemorrhage, and whiteout lung (Table 3).

Computed tomography (CT) chest findings were mentioned in seven studies with 42 patients.[11,14,16,21,33,37,38] It was abnormal in 12 patients, and the presence of ground glass opacity (GGO) and consolidation were the commonest findings (six each), followed by reticular opacities in three (Table 3).

3.4 | Treatment and outcomes

Thirty-one studies (*n* = 204 patients) reported data about patients who were admitted.[5,8,9,11–18,20–39] Among the 204 patients who were mentioned in these studies, 96 were admitted with a median duration of hospital stay of 12.5 days (IQR 10, 27.5 days). Forty-seven patients were kept under home isolation. Twenty-one (10.3%) patients required admission to the ICU (Table 4; Figure 2) .

In 15 studies (169 patients),[5,9,10,12,16,18,20,21,24,26,27,29–31,33] there was a mention about change/modification in chemotherapy. The chemotherapy was delayed in 123, and in 10, there was a modification of the chemotherapy regimen (Table 4).

In 20 studies (*n* = 87 patients), there was a mention of oxygen requirement,[5,11–16,21,22,24,25,28–33,35,37,38] and oxygen requirement was present in 28 (32.3%) patients. The other complications encountered were pneumothorax, pleural effusion, pleural thickening, pulmonary arterial hypertension (PAH), bronchiolitis, bronchiolitis obliterans, diffuse alveolar hemorrhage, septic shock, and ARDS (Table 4). Seven patients had evidence of multisystemic inflammatory syndrome (MIS-C) (Table 5).

Forty-one patients received treatment specific for the COVID-19 disease. Hydroxychloroquine (HCQ) was used in 41 patients, steroids in nine, ivermectin in nine, lopinavir/ritonavir combination in five, azithromycin in four, remdesivir in four, and tocilizumab in three.

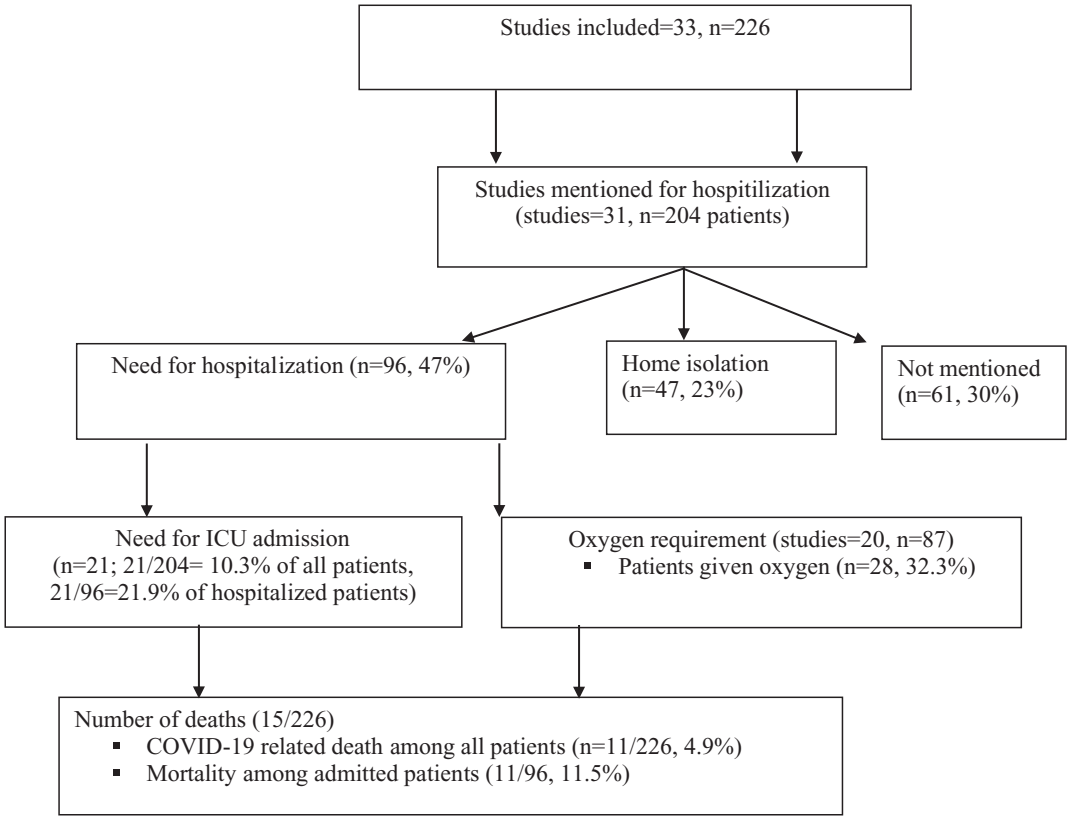

FIGURE 2 Flowchart of patients with hospitalization and outcome

Oseltamivir was also used in seven patients and convalescent plasma in two (Table 4).

Of the 226 patients, the outcomes were reported for all. Two hundred eleven patients recovered, and 15 died. Of the deaths, four deaths were not related to COVID-19.[18] The mortality in the cohort was 11/226, that is, 4.9% (Table 4) (Figure 2) .

The details of all studies are provided in Table 5.

4 | DISCUSSION

SARS-CoV-2 has spread throughout the world at an alarming rate. Little is known about the effects of COVID-19 on children with cancer. In this systematic review on COVID-19 in pediatric cancer patients, we found that males were affected more, the infection was more common in hematological malignancies and during the intensive phase of treatment. RTPCR was the commonest modality for the detection of SARS-CoV-2 infection. Fever was the commonest symptom, followed by cough. Hypoxia was present in 10.8% of patients, and overall, 48% were either asymptomatic or mild in symptomatology. Forty-seven percent of patients were admitted, and chemotherapy was changed or modified in majority of the cases.

Ten percent of patients required ICU admission. About one third of patients in those studies where the oxygen requirement was mentioned needed oxygen therapy. CT chest scans and chest X-ray reports were mentioned in only a few studies, and consolidation, peribronchial cuffing, and GGO were reported as common findings. HCQ was the most common drug used for COVID-19-specific treatment. The mortality attributed to COVID-19 was 4.9%.

Previous reports suggest that children infected with SARS-CoV-2 are highly resilient to the disease and generally progress with a mild course.[2] Ludvigsson similarly had shown in a systematic review published in the initial months of the pandemic that COVID-19 in children seemed to have a milder disease course and a better prognosis than adults. Deaths were reported rarely.[40]

The COVID-19 pandemic poses numerous challenges to pediatric oncology patients, as they are immunocompromised and treatment disruptions are frequent due to the lockdowns. Once in hospital, the risk of exposure to the COVID-19 infection is high. Pediatric cancer patients are provided with general recommendations for infection control like use of face masks, hand hygiene, and avoidance of crowding. The adherence to these recommendations however may be dependent on many factors; for example, in a toddler, mask adherence for long may be difficult and the education and facilities available to the caregivers may influence the hygiene and infection control measures. Compared to the study by Ludvigsson, the present review had a higher percentage of children who had severe disease and deaths. The majority of affected patients also had a delay/change in chemotherapy.[40]

In adult cancer patients, COVID-19 poses a potential risk of morbidity and mortality. In a systematic review, El Gohary et al. in 22 studies (n = 1018 patients) found that cancer frequency among patients with confirmed COVID-19 was 2.1%. They found a higher risk of

TABLE 4 Outcomes of pediatric oncology children with COVID-19

Patient characteristics	Number (%)
Hospitalization (studies = 31, *n* = 204 patients)	
Need of hospitalization	96 (47)
Home isolation	47 (23)
Not mentioned	61 (30)
Median duration of hospital stays in days (IQR)	12.5 (10, 27.5)
Need for ICU admission	21 (10.3)
Oxygen requirement (studies = 20, *n* = 87)	
Patients given oxygen	28 (32.2)
Complications	
Pleural effusion (one required chest tube)	2
Septic shock	1
ARDS	11
PAH	
Pneumothorax	1
Pleural thickening	1
Bronchiolitis	1
Bronchiolitis obliterans	1
Change in chemotherapy (studies = 15, *n* = 169 patients)	
Delay in chemotherapy	123 (72.8)
Modified chemotherapy	10 (5.9)
Not mentioned	36 (21.3)
COVID-19-specific treatment given (*n* = 41)	
HCQ	41
Azithromycin	4
Steroids	9
Remedesivir	4
Tocilizumab	3
Lopinavir/ritonavir	5
Enoxaparin	3
Convalescent plasma	2
Oseltamivir	7
Chloroquine	1
IVIG	1
Outcome (studies = 33, *n* = 226 patients)	
Recovered	211 (93.4)
Died	15 (6.6)
Mortality attributable to COVID-19	11 (4.9)

Abbreviations: ARDS, acute respiratory distress syndrome; HCQ, hydroxychloroquine; ICU, intensive care unit; IQR, interquartile range; IVIG, intravenous immunoglobulin; PAH, pulmonary arterial hypertension.

mortality, severe/critical disease, ICU admission, and mechanical ventilation in cancer patients with COVID-19 than noncancer patients. These patients had significantly lower platelet levels and higher D-dimer levels, C-reactive protein levels, and prothrombin times. The authors concluded that cancer patients are at a higher risk of COVID-19 infection-related complications.[41]

Patients with hematological malignancies were more in number than those with solid tumors in this review. Patients with hematological malignancies are usually on chemotherapy regimens that are more intensive or require more frequent hospital visits.

The severity of symptoms in children with cancer affected by COVID-19 is more than the general pediatric population, with more chance of developing severe symptoms and need for oxygen therapy. In a recent systematic review of COVID-19 by Hoang et al. collating 131 studies (n = 7780 patients) in the pediatric population, fever and cough were the commonest symptoms and the rate of complications was low.[42] They reported echanical ventilation in 0.54% and death in 0.09% of patients. Bellino et al. reported mild disease in 32.4% of cases and severe in 4.3% (n = 3836), particularly in children less than 6 years of age (10.8%) and reported only four deaths in a retrospective data analysis from the Italian case-based surveillance system of confirmed COVID-19 infections until May 8, 2020. Lower risk of disease severity was associated with increasing age, and the overall disease severity was lower in pediatrics.[43] Children are known to have milder symptoms and are less likely to be hospitalized when compared to adults.[44]

Meena et al. reported clinical features of COVID-19 and outcome in children and found that about half of the patients had each fever and cough, 11% (6–17%) had fast breathing, and 6–13% had gastrointestinal manifestations. Most of the patients had mild to moderate disease, and only 4% had a severe or critical illness.[45] We too found fever to be the commonest symptom in the cancer patients, but the percentage of children having severe disease was more.

The systematic scoping review published by Dorantes-Acosta et al. (June 2020) focused on survival in pediatric oncology patients during the COVID-19 pandemic and included five studies also collated in our review, a 100% survival was reported.[46] Most cases in this review were reported in patients with leukemia, and fever was the commonest symptom in children requiring admission.

Contrary to the findings reported in the above studies on COVID-19 in pediatric patients, in this review, pediatric oncology patients were more likely to have severe disease due to COVID-19. Most of the patients also had a delay or modification in chemotherapy. Fifty-seven percent were admitted, and a higher death rate (4.9%) was observed than what has been reported in the pediatric population overall.[42,43]

A limitation of our study was that the majority of studies in our review were case reports and case series. A few studies did not mention the clinical characteristics, and some did not describe secondary outcomes. We could not do risk-of-bias assessment and meta-analysis of the data as most of the data were extracted from case reports and descriptive case series. Another limitation of our study is the heterogeneous nature of the collected data due to the studies from many

TABLE 5 Details of all included studies

	Clinical variables										
			Type of malignancy								
First author	*n*	Age (years)	Hematologic	Solid	Clinical presentation	Hospitalization	ICU admission	Invasive ventilation	MIS-C	COVID-19-specific treatment	Died
de Rojas[5]	15	10.6	11	4	Fever: 10 Cough: 6 Sore throat: 1 Chest pain: 1	11				HCQ: 11 Azithromycin: 2 Steroid: 1 Remdesivir: 1 Tocilizumab: 1	0
Boulad[8]	20	15.9	–	–	–	1				–	0
Cesaro[9]	10	–	–	–	–	2				–	0
Ferrari[10]	21	6	10	11	Flu-like symptoms: 9	–				–	0
Hamdy[11]	7		5	2	Fever: 7 Respiratory symptoms: 4 GIT symptoms: 4	7	3			HCQ: 7 Steroid: 3 Oseltamivir: 7	3
Lopez-Aguillar[12]	14	10	9	5	Fever: 14 Cough: 7 Dyspnea: 1 Abdominal pain: 3 Diarrhea: 2	14				–	1
Sieni[13]	1	1.3	1	0	Fever, diarrhea	1				HCQ: 1 lopinavir/ritonavir: 1	0
Wang[14]	1	8	1	0	Fever, cough, dyspnea, pharyngeal congestion	1	1			–	0
Andre[15]	3	7	2	1	–	3	3			–	0
Bisogno[16]	29	7	16	13	Fever: 8 Vomiting: 1 Chest pain: 1	15				HCQ: 9 lopinavir/ritonavir: 2	0
Perez-Martinez[17]	3	9	2	1	Fever: 2 Cough: 2	1			1	HCQ: 1 HCQ + steroid + remdesevir + tocillizumab: 1	0

(Continues)

TABLE 5 (Continued)

	Clinical variables										
			Type of malignancy								
First author	*n*	Age (years)	Hematologic	Solid	Clinical presentation	Hospitalization	ICU admission	Invasive ventilation	MIS-C	COVID-19-specific treatment	Died
Montoya[18]	69	6	39	30	Fever: 12 URTI: 11 LRTI: 5 GIT symptoms: 3 Skin rash: 1	13	3			Azithromycin + steroid + ivermectin: 9	7
Almassi[19]	1	17	0	1	–	–				–	0
Bernar[20]	1	7	1	0	Fever, coryza, skin blisters	1				–	0
Dantonello[21]	1	4	1	0	Fever, cough, dyspnea, coryza	1	1		1	–	0
Flores[22]	3	8	3	0	Fever: 3	3			1	Enoxaparin: 2	1
Jarmolinski[23]	1	7	1	0	Fever, cough, fatigue, chills, disuria	1				Azithromycin + chloroquine	0
Marcia[24]	1	3	1	0	Fever, skin rash: 1	1				HCQ + lopinavir/ritonavir	0
Offenbacher[25]	1	11	0	1	Dyspnea	1		1		–	1
Orf[26]	1	5	1	0	Fever, Stridor	1	1			Remdesivir	0
Perez Heras[27]	2	7.5	0	2	Fever: 2 Sore throat: 1 Diarrhea: 1	2				HCQ: 2 lopinavir/ritonavir: 1	0
Puyo[28]	1	1.8	1	0	Fever, dyspnea	1			1	HCQ + azithromycin + tocillizumab	0
Radhakrishnan[29]	1	4	1	0		1				–	0
Schied[30]	1	6	1	0	Cough	1				–	0
Shankar[31]	1	4	1	0	Fever, dyspnea	1			1	Steroid + convalescent plasma	0
Smith[32]	1	1.11	0	1	Fever, shock	1	1	1	1	HCQ + remdesivir + enoxaparin + convalescent plasma	1

(Continues)

TABLE 5 (Continued)

	Clinical variables										
			Type of malignancy								
First author	*n*	Age (years)	Hematologic	Solid	Clinical presentation	Hospitalization	ICU admission	Invasive ventilation	MIS-C	COVID-19-specific treatment	Died
Stokes[33]	2	16	1	1	Fever: 2 Dyspnea: 2 Vomiting: 1 Diarrhea: 1	–	2	2		HCQ: 2 Remdesivir: 2 Tocillizumab: 1	0
Vicent[34]	4		4	0	Fever: 4 Cough: 1 Coryza: 1 Diarrhea: 1	–	2	1 + 1 (ECMO)		–	1
Zamperlini-Netto[35]	1	2	1	0	Fever, cough, dyspnea, wheezing	1	1			HCQ: 1 Azithromycin: 1 Steroid: 1	0
Zhao[36]	1	1.11	1	0	Fever, cough	1				–	0
Zhou[37]	1	17	1	0		1				lopinavir/ritonavir: 1 Steroid: 1	0
Sun[38]	1	8	1	0	Fever, cough, dyspnea, expectoration	1	1	1	1	Steroid: 1 IVIG: 1	0
Rosoff[39]	6	8.5	3	3		3	1			–	0

Abbreviations: ECMO, extracorporeal membrane oxygenation; GIT, gastrointestinal tract; HCQ, hydroxychloroquine; IVIG, intravenous immunoglobulin; LRTI, lower respiratory tract infection; MIS-C, multisystem inflammatory syndrome; URTI, upper respiratory tract infection.

countries. The impact of differences in socioeconomic factors and resource availability for health care in different countries cannot be ignored. Most of the deaths in this review were reported from a single study from a middle-income country.[18] In the same study, there is mention of intensive care beds not being available for two patients.

5 | CONCLUSIONS

In this review, we described the clinical characteristics and outcome of pediatric cancer patients having COVID-19. The disease was more common in children with hematological malignancies and ones getting intensive treatment. Fever followed by cough were the commonest symptoms. This review found more mortality and complications in pediatric oncology patients with COVID-19 in contrast to other published studies describing pediatric outcomes. This information can be helpful in risk stratification for management of COVID-19. There is a need for more prospective studies with a large sample size to formulate policies and guidelines in this specific population for this relatively novel disease.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

DATA AVAILABILITY STATEMENT

All datasets generated for this study are included in the article and will be provided upon reasonable request.

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SUPPORTING INFORMATION

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

How to cite this article: Meena JP, Gupta AK, Tanwar P, Jat KR, Pandey RM, Seth R. Clinical presentations and outcomes of children with cancer and COVID-19: A systematic review. *Pediatr Blood Cancer*. 2021;68:e29005. https://doi.org/10.1002/pbc.29005