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Profile and Outcomes of COVID-19 Infection in Pediatric Patients with and without Cancer: A Case–Control Study

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Abstract

Objectives Pediatric patients with cancer are considered a vulnerable population to the ill effects of coronavirus disease 2019 (COVID-19). We hereby studied the difference between clinical characteristics, lab parameters, and outcomes of COVID-19 among children suffering from cancer and those without cancer. We also analyzed risk factors for the occurrence of moderate-to-severe COVID-19 disease in pediatric cancer patients.

Materials and Methods This retrospective case–control study was carried out using the medical record review method over 6 months in a tertiary-care center in India. All patients below 18 years of age, with reverse-transcriptase polymerase chain reaction (RTPCR) confirmed COVID-19, were screened for enrolment. Patients were split into two groups: Group A comprised of patients with cancer, while group B consisted of patients without any underlying comorbidity. Patients with other comorbidity except cancer and inadequately recorded case sheets were excluded. Details regarding demography, clinical features, investigations, treatment, and outcomes were recorded.

Statistical Analysis Microsoft Excel and Statistical Package for the Social Sciences (SPSS) software, version 25 was used for data analysis. A *p*-value less than 0.05 was considered significant.

Results Two-hundred-five pediatric inpatients with RTPCR-established COVID-19 infection were screened and final analyses were performed on 97 patients, of which 31 children were classified into group A and 66 into group B. Median age of enrolled children was 5 years with 58.8% males. The prevalence of cancer as a comorbidity in pediatric inpatients with COVID-19 was 15%. Fifty-five percent of cancer patients had hematological malignancies, while 45% had solid tumors. Fever ($p = 0.001$) and gastrointestinal manifestations ($p = 0.0001$) were significantly less common among pediatric cancer patients. Children with cancer had significantly more leukopenia ($p = 0.003$), neutropenia ($p = 0.003$), and lymphopenia ($p = 0.005$). The case fatality rate was higher in children with cancer (3.2%) as compared to noncancer patients (1.5%, $p = 1.0$). Few risk factors for moderate-to-severe COVID-19 among children with

Keywords
- SARS-CoV-2
- pediatric cancer
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- risk factors
- severe disease
- solid tumors

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cancer included age less than 2 years ($p = 0.06$), undernutrition ($p = 0.33$), advanced stage of cancer ($p = 0.49$), and presence of coinfection ($p = 0.35$)

Conclusion Cancer is a significant comorbidity among pediatric COVID-19 patients. While children with cancer have less severe COVID-19, their case fatality rate is higher than those without cancer. Younger age, undernutrition, advanced stage of cancer, and presence of coinfections may predispose to the development of moderate-to-severe COVID-19 among pediatric cancer patients.

Introduction

Ever since the declaration of the coronavirus disease 2019 (COVID-19) pandemic, there have been many publications about COVID-19 infection in children. Most of the studies indicate that COVID-19 infection in the pediatric age group is generally mild and many remain asymptomatic. However, pediatric patients with cancer have been considered a vulnerable population to the harmful effects of COVID-19 due to their immunosuppressed state and also due to reprioritization of healthcare services.[1] To date, studies on COVID-19 in pediatric patients suffering from cancer show an asymptomatic, mild or moderate disease. However, attributable mortality in children with malignant disease is reported to be at least 10 times higher as compared to those children without comorbidities.[2] Indian data on COVID-19 in children with cancer shows low mortality due to COVID-19 infection per se.[3] However, there is limited data on the clinicoepidemiological and laboratory profile of COVID-19 in Indian children especially in the form of a case–control study.

The following research was conducted to understand the difference between clinical characteristics, lab parameters, and outcome of COVID-19 infection among pediatric patients with and without cancer. We also analyzed risk factors for the occurrence of severe COVID-19 disease in pediatric patients with cancer.

Materials and Methods

Study Design and Participants

This is a retrospective observational case–control study conducted using the medical record review method. The research was conducted after acquiring approval from the Institute's Ethics committee, over 6 months from April 2021 to September 2021, in the Department of Pediatrics of a tertiary care center in India.

Inclusion Criteria

All patients below 18 years of age with a definite diagnosis of COVID-19 through a positive nasopharyngeal and/or oropharyngeal reverse-transcriptase polymerase chain reaction (RTPCR) test were screened for enrolment.

Exclusion Criteria

Patients with any comorbidity except cancer and those with inadequately recorded case sheets were excluded.

The study cohort was split into two groups for comparison. Group A comprised pediatric patients with any form of cancer as comorbidity (newly diagnosed or already on treatment), while group B consisted of pediatric patients without any underlying comorbidity.

Primary Outcome

To analyze the Difference between clinical characteristics, lab parameters, and outcome (discharge/death) of COVID-19 infection among pediatric inpatients with and without cancer.

Secondary Outcome

To identify the Risk factors for the occurrence of severe COVID-19 disease in pediatric patients with cancer.

Data Collection

The following recorded data was reviewed for all enrolled patients

1. Demographic details: age, gender, place of current residence
2. Malignancy-related details: Baseline disease, disease stage, date of diagnosis, disease status (active or in remission), date of last chemotherapy/radiotherapy/surgery
3. COVID-19-related details: clinical manifestations, complications, disease severity at presentation, treatment received, duration of hospital stay, and outcome.
4. Details of coinfection: disease status, treatment received, and outcome.
5. The blood investigations including complete blood count, kidney function test, liver function test, coagulation profile, and radiological investigations including chest X-ray and/or computed tomography chest scan were recorded.
6. Outcome details: Discharge/transfer out to another facility as per existing hospital policy at that time or death.

Ethical Consideration

The research was reviewed and approved by the Institute's Ethical board, Maulana Azad Medical College & Associated Lok Nayak Hospital, GB Pant Hospital, Guru Nanak Eye Center, New Delhi-110002, registered (Registration number ECR/329/Inst/DL/2013/RR-2019) with Drug controller general of India, Directorate General of Health Services, New Delhi. All actions executed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments. Complete data anonymity was maintained.

Study Definitions

Confirmed COVID-19 Case[4]

A patient with RTPCR established severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, identified in the nasopharyngeal or oropharyngeal swab.

Disease Severity Classification[5]

Mild: Simple upper respiratory tract infection (fever, cough, sore throat, nasal congestion,) devoid of any respiratory distress and maintaining saturation of more than or equal to 95% without oxygen support. All RTPCR positive patients with isolated symptoms of fever, lassitude, or anorexia were classified into mild disease.[5]

Moderate: Pneumonia with features of fast breathing and maintaining saturation of 90-94% on room air.

Severe: Severe pneumonia with signs of fast breathing and breathlessness and maintaining saturation less than 90% on room air. In patients with severe pneumonia, the presence of the following signs was considered a severe disease: central cyanosis, feed refusal, apathy, and seizures. Acute respiratory distress syndrome, sepsis, or septic shock were considered severe diseases.

Additionally, patients with isolated gastrointestinal (GI) manifestations were classified into mild (no dehydration) or severe (severe dehydration).[6] Those with isolated central nervous system symptoms such as seizures, altered sensorium, or meningitis were classified into severe categories.[6]

Abnormal laboratory parameters were classified as follows[7]: anemia: hemoglobin less than 11 gm/dL, leukopenia: total leucocyte count (TLC) less than 4,000/ µL; leucocytosis: TLC more than 11,000 cells/ µL; neutrophilia: absolute neutrophil count (ANC) more than7,700/µL; neutropenia: ANC less than 1,500/ µL; lymphopenia: for age less than 12months, absolute lymphocyte count (ALC) less than 3000/ µL, for age more than or equal to 12 months, ALC less than 1000/ µL; lymphocytosis: for age less than 10 years, ALC more than 8,000/µL, for age more than or equal to 10 years, ALC more than 4,000/ µL; hypoalbuminemia less than 3.5 g/dL; hyperbilirubinemia more than 1.0 mg/dL elevated urea more than 40 mg/dL; elevated creatinine more than 0.9 mg/dL; elevated ferritin more than 60 ng/mL (till 9 years) and more than 300 ng/mL (10–12 years); elevated procalcitonin 0.5 ng/mL, increased IL-6 more than7 pg/mL; increased D-dimer more than 1 mg/mL.

Statistical Analysis

The data obtained from the medical records were coded into MS Excel spread sheet and evaluated using MS Excel and Statistical Package for the Social Sciences 25 (SPSS). The categorical variables were denoted as percentages and analyzed using chi-squared test or Fisher's exact test as deemed fit. Continuous variables were denoted as mean with standard deviation (normal distribution) or median with interquartile ranges (non-normal distribution). The significant difference amongst non-normally distributed variables was analyzed using Mann–Whitney U tests or Kruskal–Wallis test as necessary. A *p*-value less than 0.05 was taken as statistically significant.

Results

A total of 205 admitted pediatric patients with RTPCR confirmed COVID-19 infection were screened for enrolment in this study. Patients with comorbidities other than cancer ($n = 59$) and those with inadequately recorded case sheets ($n = 49$) were excluded. Final analyses were performed on 97 patients out of which 31 children were classified into group A (children with cancer) and 66 into group B (children without any comorbidity). The study flow is shown in ►**Fig. 1**.

Cancer Type and Prevalence

The prevalence of cancer as a comorbidity in admitted pediatric patients with COVID-19 in this study was 15%. Overall, the median age of enrolled children was 5 years with an interquartile range of 2 to 11 years and 58.8% of them were males. The baseline characteristics, COVID-19 disease severity, and outcomes of the enrolled patients are detailed in ►**Table 1**.

The disease severity by type of cancer in the COVID-19 children is depicted in ►**Fig. 2**. Seventeen patients (54.8%) had hematological malignancies (HM; acute myeloid leukemia = 1, B-cell acute lymphoblastic leukemia = 11, T-cell acute lymphoblastic leukemia = 1, Hodgkin Lymphoma = 3, non-Hodgkin Lymphoma = 1), whereas 14 patients (45.1%) were diagnosed to have solid tumors (retinoblastoma = 3, Ewing sarcoma = 4, choroid plexus tumor = 1, hepatoblastoma = 1, juvenile ossifying fibroma = 1, Wilms tumor = 1, teratoma = 1, posterior fossa mass = 1, neuroblastoma = 1).

Chemotherapy Details

Out of 31 cancer patients, 14 children (45.1%) were receiving intensive chemotherapy, and 15 children (48.3%) were on nonintensive chemotherapy regimens. Two patients (6.45%) were not receiving any chemotherapy. Among the two patients, one was undergoing palliative care, while the other was yet to begin chemotherapy.

Disease Severity

Amongst the enrolled patients, 33% were asymptomatic, 46.4% had mild, 10.3% had moderate, and 10.3% had severe disease overall. Group-wise details are mentioned in ►**Table 1**.

Coinfections

Three patients (9.7%) with cancer had another coinfection (febrile neutropenia = 1, sepsis = 1, tubercular meningitis = 1), whereas 12 children without cancer (18.2%) were diagnosed to have another coinfection (disseminated tuberculosis = 2, pulmonary tuberculosis= 2, abdominal tuberculosis= 1, tubercular lymphadenitis= 1, tubercular meningitis= 1, liver abscess= 2, septic arthritis= 1, enteric fever= 1, scalp abscess = 1; $p = 0.37$).

Clinical Manifestations

Overall, the most common symptoms were fever (47.4%), cough (23.7%), and vomiting (16.5%). There was a significantly higher number of patients in group B who manifested with fever ($p = 0.001$) and vomiting ($p = 0.034$). Among group A,

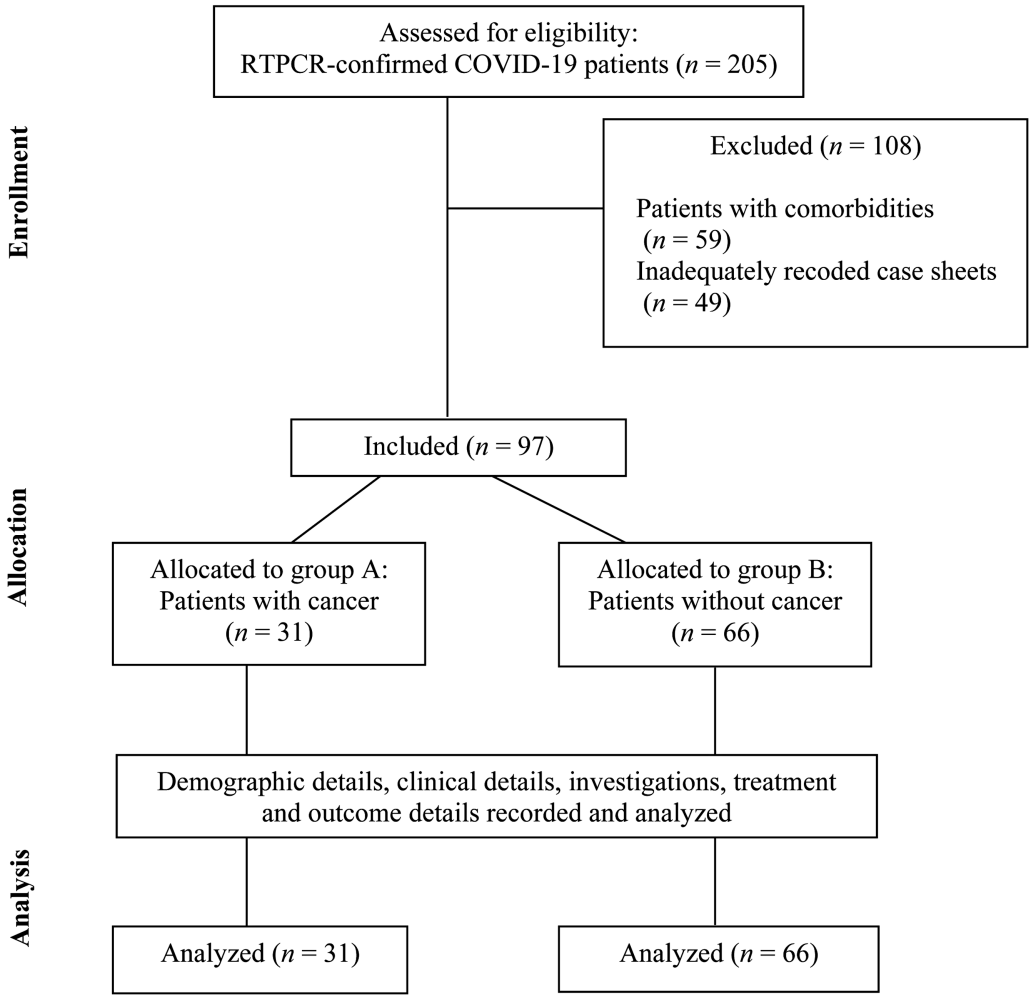

Fig. 1 Study flow. COVID-19, coronavirus disease 2019; RTPCR, reverse-transcriptase polymerase chain reaction.

most common symptom complex at presentation was respiratory (25.8%) followed by neurological (12.9%) as compared to group B patients which showed GI (48.5%) followed by respiratory manifestations (37.9%). Group B patients had significantly higher GI manifestations ($p = 0.0001$). There was no statistically significant difference concerning respiratory, neurological, bleeding, and skin manifestations. A comparison of symptoms and symptom complex is detailed in ►**Table 2**.

Laboratory Investigations

Group A had significantly a greater number of patients who had leukopenia ($p = 0.003$), neutropenia ($p = 0.003$), and lymphopenia ($p = 0.005$). There was no significant difference between the rest of the checked laboratory parameters between the two groups (►**Table 3**).

Radiological Investigations

Among group A, chest X-ray was done for 21 patients out of which 5 showed infiltrates and 1 showed hilar lymphadenopathy. Among group B, a chest X-ray was done for 23 patients, in which 8 showed infiltrates, 3 exhibited hilar lymphadenopathy, and 1 showed pleural effusion.

Oxygen Requirement

Only two patients (6.45%) in group A required oxygen (nasal prongs = 2), while eight patients (12.1%) required oxygen in group B (ventilator support = 1, high-flow nasal cannula = 1, nasal prongs = 2, simple mask = 3, oxygen hood =1; $p = 0.49$).

Mean Duration of Hospital Stay

The mean duration of hospital stay among group A was 11.6 ± 6.8 days as compared to 9.6 ± 5.4 days among group B ($p = 0.33$).

Outcome

The case fatality rate among cancer patients was 3.2% as compared to 1.5% in noncancer patients. However, there was no difference in mortality rate as both the groups had one death each. In both groups, the death was attributed to severe COVID-19 infection. There was no death due to progression of cancer or complications of chemotherapy, during the period of study. Among group A, the expired patient was a 12-month-old female child who was diagnosed to have sacrococcygeal teratoma with hepatic metastasis with severe COVID-19 pneumonia. While in group B, the

Table 1 Baseline characteristics, disease severity, and outcomes of enrolled patients ($N = 97$)

Parameter	Total patients ($N = 97$)	Patients with cancer (group A) ($n = 31$)	Patients without comorbidity (group B) ($n = 66$)	*p*-Value
Median age in years	5	6	5	
(IQR)	2–11	4–11	1.1–10.7	
Sex (%)				0.31
Male	57 (58.8)	21 (67.7)	36 (54.5)	
Female	40 (41.2)	10 (32.3)	30 (45.5)	
Underweight (%)	30 (30.9)	15 (48.4)	15 (22.7)	0.01
Severity of COVID-19 (%)				0.18
Asymptomatic	32 (33.0)	15 (48.4)	17 (25.7)	
Mild	45 (46.4)	12 (38.7)	33 (50.0)	
Moderate	10 (10.3)	2 (6.4)	8 (12.1)	
Severe	10 (10.3)	2 (6.4)	8 (12.1)	
Number of patients with coinfection (%)	15 (15.5)	3 (9.7)	12 (18.2)	0.37
Duration of hospital stay in days (mean ± SD)	10.2 ± 5.9	11.6 ± 6.8	9.6 ± 5.4	0.33
Outcome (%)				1.0
Death	2 (2.0)	1 (3.2)	1 (1.5)	
Discharge	95 (97.9)	30 (96.8)	65 (98.5)	

Abbreviations: COVID-19, coronavirus 2019; IQR, interquartile range; SD, standard deviation.

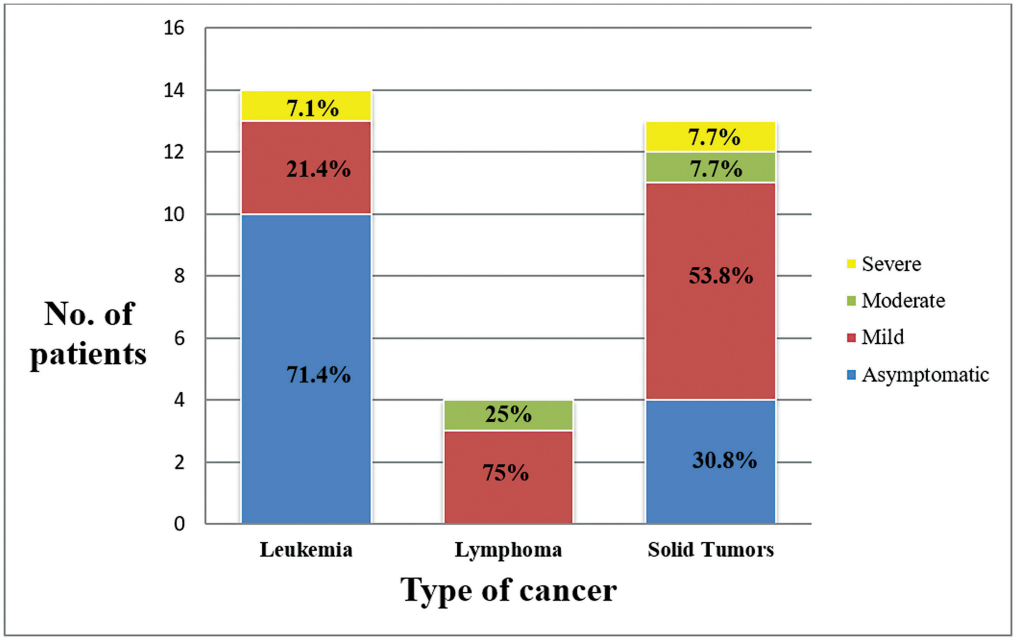

Fig. 2 Disease severity by type of cancer.

expired patient was a 9-year-old male child with tubercular meningitis stage-3 and multiorgan dysfunction.

Risk Factors

Risk factors for moderate-to-severe COVID-19 disease among cancer patients are detailed in ►**Table 4**. Poor nutritional status, higher cancer stage, and presence of coinfections seemed to be associated with moderate-to-severe COVID-19. However, these results were statistically not significant.

Discussion

To our knowledge, this is one of the few studies to directly compare the clinical, biochemical, radiological, and outcome profiles of COVID-19 infection in children with and without cancer.

In our study, we found that 15% of the hospitalized pediatric patients with COVID-19 had cancer as a comorbidity. A previously published meta-analysis showed the

Table 2 Pediatric COVID-19 symptoms and symptom complex at presentation

Parameter	Total ($N = 97$) *N* (%)	Patients with cancer (group A) ($n = 31$) *N* (%)	Patients without comorbidity (group B) ($n = 66$) *N* (%)	*p*-Value
Symptoms				
Fever	46 (47.4)	7 (22.6)	39 (59.1)	0.001
Cough	23 (23.7)	5 (16.1)	18 (27.3)	0.34
Coryza	10 (10.3)	3 (9.7)	7 (10.6)	1.0
Vomiting	16 (16.5)	1 (3.2)	15 (22.7)	0.034
Diarrhea	10 (10.3)	1 (3.2)	9 (13.6)	0.16
Pain abdomen	6 (6.2)	0 (0)	6 (9.1)	0.17
Anorexia	2 (2.0)	0 (0)	2 (3.0)	0.56
Lethargy	4 (4.1)	0 (0)	4 (6.1)	0.30
Excess irritability	6 (6.2)	2 (6.4)	4 (6.1)	1.0
Seizures	2 (2.0)	0 (0)	2 (3.0)	0.56
Headache	7 (7.2)	2 (6.4)	5 (7.6)	1.0
Fatigue	13 (13.4)	5 (16.1)	8 (12.1)	0.75
Bleeding manifestations	2 (2.0)	2 (6.4)	0 (0)	0.10
Rash	7 (7.2)	2 (6.4)	5 (7.6)	1.0
Symptom complex				
Respiratory manifestations	33 (34.0)	8 (25.8)	25 (37.9)	0.34
GI tract manifestations	34 (35.0)	2 (6.4)	32 (48.5)	0.0001
Neurological manifestations	19 (19.6)	4 (12.9)	15 (22.7)	0.38
Bleeding manifestations	2 (2.0)	2 (6.4)	0 (0)	0.10
Skin manifestations	7 (7.2)	2 (6.4)	5 (7.6)	1.0

Abbreviations: COVID-19, coronavirus disease 2019; GI, gastrointestinal.

worldwide prevalence of COVID-19 in adult patients with cancer to be around 4.6%.[8] Other studies have variably reported the prevalence of COVID-19 in patients with cancer to be between 2.6 and 11%.[8,9] Studies done in children hospitalized with COVID-19 in India have reported cancer as a comorbidity in as many as 7-15%.[1,10] The reasons for a high proportion of cancer as comorbidity in children with COVID-19 may be manifold. Due to the nature of their disease and related therapy, children with cancer are at high risk of developing viral infections.[11] Likewise, it is logical to expect higher infectivity of COVID-19 in children with cancer. At our center, we found an even higher proportion of children having cancer as comorbidity. Additional factors that may have contributed to this include a referral bias as our hospital is one of the few public sector hospitals in the area dealing with pediatric cancer patients. Moreover, our hospital was designated as an exclusive COVID-19 treating center during the pandemic; thus, all children with COVID-19 with any comorbidity were referred to us. Another reason for the difference in this prevalence may be the difference in admission criteria for COVID-19 children in various centers.

Overall, the median age, gender, and distribution of disease severity of the enrolled cohort were similar to the previously published literature.[3] However, children with cancer were significantly underweight as compared to children without cancer that may be due to their underlying disease or therapy-related anorexia leading to malnutrition.

In this study, a greater proportion of admitted pediatric cancer patients with COVID-19 had HM (54.8%) as comorbidity as compared to solid tumors (45.1%). This result corroborates with the data reported in the global registry which showed that among pediatric patients with COVID-19, 67.1% had HM, while only 32.9% had solid tumors.[12] It has been reported that patients with HM have a more severe course of COVID-19 as compared to solid tumors and consequently a higher hospitalization rate.[13] Patients with HM have been shown to have delayed seroconversion, prolonged viral shedding, higher viral load, and immune disturbance following COVID-19 infection compared to patients with solid tumors.[14,15] Furthermore, patients of COVID-19 with HM have been shown to have remarkably lower percentages of monocytes, double-positive T cells, natural killer cells, and B-cells.[16,17] These patients also have impaired CD4 T-cell and B-cell reaction to SARS-CoV-2 and lower levels of anti-COVID-19 antibodies in comparison to patients suffering from solid cancer.[18] All these factors are likely to contribute to higher hospitalization rates of children with COVID-19 with HM compared to those with solid tumors.

Table 3 Laboratory investigations of pediatric COVID-19 patients at presentation

Parameter	Proportion of children having abnormal values		
"N" observed/ "N" tested	Patients with cancer (group A) ($n = 31$)	Patients without comorbidity (group B) ($n = 66$)	*p*-Value
Anemia	15/23	17/27	0.88
Leucopenia	11/23	2/27	0.003
Leucocytosis	3/23	10/27	0.10
Neutropenia	9/23	1/27	0.003
Neutrophilia	2/23	9/27	0.045
Lymphopenia	11/23	3/27	0.005
Lymphocytosis	1/23	2/27	1.0
Neutrophil: lymphocyte ratio >3.03	4/23	8/27	0.34
Thrombocytopenia	10/23	9/27	0.65
Azotemia	1/17	5/21	0.20
Hyperbilirubinemia	3/19	5/20	0.69
Transaminitis	11/21	11/20	0.89
Hypoalbuminemia	5/13	6/11	0.70
Raised INR	2/4	5/11	1.0
Raised D-dimer	3/5	6/6	0.18
Raised interleukin-6	2/2	4/5	1.0

Abbreviations: COVID-19, coronavirus disease 2019; INR, international normalized ratio.

Table 4 Risk factors for moderate-to-severe COVID-19 disease in cancer patients

Risk factors	Asymptomatic or mild disease $N = 27$	Moderate or severe disease $N = 4$	*p*-Value
1. Age • <2 years • 2–10 years • >10 year	 1 (3.7%) 16 (59.3%) 10 (37%)	 2 (50%) 1 (25%) 1 (25%)	0.06
2. Cancer type • Solid tumors • Hematological	 11 (40.7%) 16 (59.3%)	 2 (50%) 2 (50%)	0.56
3. Cancer stage (solid tumors and lymphomas) • Stage 1 • Stage 2 • Stage 3 • Stage 4	 2 (15.3%) 1 (7.7%) 5 (38.5%) 5 (38.5%)	 1 (33.3%) 0 0 2 (66.7%)	0.49
4. Cancer risk stratification (leukemias) • Standard risk • Intermediate risk • High risk	 3 (21.4%) 7 (50%) 4 (28.6%)	 0 0 1 (100%)	0.53
5. Recent chemotherapy	21 (77.7%)	2 (50%)	0.55
6. Neutrophil: lymphocyte Ratio >3.03	3/19 (15.8%)	2/4 (50%)	0.19
7. Neutropenia	8 (42.1%)	1 (25%)	0.63
8. Presence of coinfection	2 (7.4%)	1 (25%)	0.35
9. Underweight	12 (44.4%)	3 (75%)	0.33

Abbreviation: COVID-19, coronavirus disease 2019.

In terms of severity, most of the patients in both groups were either asymptomatic or had a mild disease that is consistent with data from other studies and larger Registries.[3,12] Higher proportion of patients without cancer had severe disease (12.1%) as compared to patients with cancer (6.2%). However, this difference was statistically nonsignificant. More severe disease in noncancer patients may be explained by the pathophysiology of COVID-19 that involves the host's immune response to the viral antigen leading to cytokine-induced tissue damage.[19] Most of the cancer patients are immunosuppressed, rendering them incapable of mounting an adequate immunological response to infection and hence making them less likely to manifest symptoms.

In both groups, fever, cough, and fatigue were common symptoms among patients. However, noncancer group had significantly a greater number of patients who presented with fever and GI tract manifestations. It has been shown that SARS-CoV2 enters host cells via the angiotensin-converting enzyme receptor 2 and transmembrane protease serine 2 that are found in the type II alveolar cells of the lung, in enterocytes of colon and ileum, and in the glandular cells of the stomach, duodenum, and rectal epithelium.[20] Thereafter, COVID-19 invaded cells release many chemokines and inflammatory mediators causing a cytokine storm and aggregation of immune system cells in the GI tract.[21] Patients with cancer often have chemotherapy-induced mucositis.[22] This may interfere with the entry of the virus into the GI tract. Also as previously stated, patients with cancer are unable to mount a cytokine storm in response to COVID-19 due to their weakened immune responses. These two factors may be responsible for a low prevalence of GI manifestations in children with cancer.

In our study, 47.8% of children with cancer had lymphopenia and 39.1% had neutropenia. This is comparable to the global data which shows that 41.3% of pediatric cancer patients had lymphopenia and 32.3% had neutropenia.[12] In terms of laboratory parameters, COVID-19-infected children with cancer had significantly more leukopenia ($p = 0.003$), neutropenia ($p = 0.003$), and lymphopenia ($p = 0.005$). It has already been shown in previous studies that the most common hematological manifestation of COVID-19 among children is leucopenia.[23] Pediatric cancer patients with COVID-19 may be prone to develop severe leukopenia due to their underlying immunosuppressed state, chemotherapy, and also due to the additive effect of COVID-19.

Both groups received similar treatment as per the prevailing Indian Council of Medical Research protocol. There was no difference with respect to oxygen requirement and outcome. Mean period of hospital stay among cancer patients was higher (11.6 ± 6.8 days) as compared to noncancer patients (9.6 ± 5.4 days), although this difference was statistically non-significant. A higher mean duration of hospital stay among cancer patients reflects increased morbidity in them. As demonstrated in previously published literature, patients with cancer have delayed seroconversion, prolonged viral shedding, and a higher viral load following COVID-19 infection.[14] Since our discharge criteria included RTPCR negativity, hence patients with cancer had a longer mean duration of hospital stay as they took a longer time to become RTPCR negative.

The case fatality rate among cancer patients was 3.2% as compared to 1.5% in noncancer patients. The mortality rate among pediatric cancer patients in this study is similar to that reported in the Global Registry of COVID-19 in childhood cancer (3.62%). Similar to our study, a greater mortality risk in pediatric cancer patients has also been reported in a systematic review.[24] However, most studies have not reported COVID-19 as an exclusive cause of death in cancer patients. An increased risk of mortality among cancer patients may be attributable to the fragile health status of the individuals due to underlying disease, the type and stage of cancer, ongoing immunosuppressive therapy, and poor nutrition.[25]

We also tried to explore the risk factors for moderate-to-severe COVID-19 among cancer patients in terms of cancer type, staging/risk stratification, intensity of chemotherapy, neutropenia, nutritional status, and presence of coinfections. In our study, chemotherapy was continued for all cancer patients except two patients among which one was under palliation and another was a sick newly diagnosed cancer patient. There was no significant difference observed in terms of severity or outcome based on recent chemotherapy use. Similar to our study, recent chemotherapy was not associated with worse clinical outcomes in many other studies including adult cancer patients with COVID-19.[13,26] Contrary to our results, few studies from adult cancer patients who had COVID-19 show that recent chemotherapy was associated with poor clinical outcome.[27] This may be due to the older age group of the enrolled cohort and a higher incidence of other comorbidities such as hypertension and type 2 diabetes in adult patients. However, it is well known that interruptions or delays in starting therapy lead to relapses and an increase in cancer-related mortality among pediatric oncology patients.[28] Also due to a low mortality rate among children with COVID-19, it has been suggested to continue cancer-related therapy in them.[3]

Our results show that among cancer patients with moderate-to-severe COVID-19 disease, a higher proportion of children was less than 2 years of age, was underweight, was in the advanced stage of their cancer, and had the presence of co-infections. Similar to our results, a previously published meta-analysis revealed that infants were at higher risk for severe COVID-19 and at higher risk for admission to critical care units.[29] It has been suggested in previous studies that COVID-19-induced cytokine storm can exacerbate malnutrition by causing muscle protein breakdown and albumin consumption. Malnutrition has also been considered as a risk factor for severe COVID-19 in children.[30] Another risk factor for severe COVID-19 is the presence of a coinfection. Children with coinfections often have a higher need for supportive therapy and have a higher duration of hospital stay.[31] However, these risk factors were not found to be statistically significant. Further large-scale studies are required to investigate these risk factors.

However, ours is one of the few studies to directly compare clinical characteristics and outcomes of pediatric COVID-19-infected patients with and without cancer while exploring risk factors for severe COVID-19 disease among pediatric cancer patients. It has certain limitations as well like small sample size and inability to follow up patients who were discharged. Another limitation is that the following data represents the inpatient population only and misses out on the disease characteristics of outpatient population.

Conclusion

Cancer is a significant comorbidity among pediatric patients with COVID-19. Most children with cancer have asymptomatic to mild symptoms of COVID-19. However, their case fatality rate is higher than in children without cancer. Fever and GI tract manifestations were found to be significantly less common among pediatric cancer patients. Among COVID-19 infected children with cancer, younger age, under-nutrition, advanced stage of cancer, and presence of coinfections predispose to the development of severe COVID-19. It may be reasonable to continue chemotherapy in COVID-19 infected children with cancer except those with identified risk factors for severe disease.

Authors' Contributions

P.K.S. conceptualized, drafted, and critically appraised the manuscript.

V.K. helped in data collection, reviewed literature, and drafted the manuscript. A.G. conceptualized, reviewed literature, and critically appraised the manuscript.

M.D., P.M., and Divyanshi helped in data collection and review of literature.

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Ethical Approval

Ethical approval was taken from the Institute Ethics Committee prior to commencement of this work.

Patient Consent

None declared.

Conflict of Interest

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