

# Does Covid 19 Infections Have a Significant Risk on Children With Cancer? Single Centre Experience and Recommendations

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## Abstract

**Objectives:** The aim of this study is to evaluate the Covid-19 infection among pediatric oncology patients diagnosed in our centre in 15 months period starting January 2020, to assess their clinical characteristics, laboratory findings, treatment outcomes, and to address the department and hospital strategies for management of such cases during the pandemic. Our study included 29 subjects.

**Setting:** It is a single centre study at King Fahad Specialist Hospital in Dammam which is 400 beds tertiary referral hospital with 27 beds pediatric oncology Ward, 4 beds bone marrow transplant and 18 bed pediatric oncology day care services.

**Methods and Results:** We retrospectively reviewed all the patients with different types of pediatric malignancies diagnosed with Covid-19 infection from January 2020 to March 2021, from both inpatient and outpatient settings. Data about their type of malignancies, current treatment course, pattern of presentation, and the impact of their Covid -19 infection on their therapy while addressing on the same time the effects of their malignancy pattern and the therapy provided on the severity and morbidity of their Covid-19 infection. The study was approved by the ethics committee with IRB number: ONC0373-dated 14/12/2020.

**Conclusion:** During the COVID-19 pandemic, children from different age groups caught COVID-19 infection without any significant age or gender preference; however, fortunately, the clinical manifestations of children's COVID-19 disease were less severe than those of adult's patients. In this study, despite the small number of cases and being single institute experience, we found that there is no significant impact of covid-19 infection on children with cancer under therapy in term of significant delays to their treatment, the clinical outcome or for increased complications or fatalities that known to be associated with Covid-19 infection.

**Keywords:** Covid-19 infection • Pandemic • Children cancer • Pediatric malignancy

## Introduction

The world was not familiar with the COVID-19 infection until last December 2019, when some cases of pneumonia of unknown origins started to appear first in Wuhan, Hubei province, China. The disease has then rapidly spread at the national level of China and globally, to involve other countries across other continents. Not after much time when they were able to identify the coronavirus in samples of bronchoalveolar lavage fluid from a patient in Wuhan in early January 2020 and subsequently confirmed as the cause.

Shortly later, on February 11<sup>th</sup>, 2020, WHO named the illness associated with 2019-CoV as the 2019 coronavirus disease (COVID-19) [1]. Due to soaring numbers of cases that appear subsequently all over the world on March 11<sup>th</sup>, WHO has declared the COVID-19 as a pandemic. There is no doubt about the great pressure that the COVID-19 pandemic put on society, especially at health and economic levels with serious global efforts to contain the disease were run including certain measures of lockdown, social distancing and restrictions on traveling, and so on, with the WHO emphasizes on the four key areas as the followings: First, to prepare and be ready. Second to detect, protect and treat. Third, to reduce transmission, and finally, the Fourth, is to innovate and learn [2].

As the infection rate of the COVID-19 pandemic starts to curve up, most of the children's cancer-treating faced an unprecedented global threat to safe and effective care for children with cancer. Multiple centers adopted new policies

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that were balancing between reasonable and safe approaches to their services to continue in providing cancer treatment while protecting the health and safety of staff, patients, and families on the other hand [3]. In this study, we addressed the impact of Covid-19 infection among our pediatric oncology patients and to evaluates if it influences their course of therapy and clinical outcome.

## Method

This is a retrospective study in a single institute King Fahad Specialist Hospital Dammam, in which we reviewed all of the children below 16 years old who diagnosed with cancer and under pediatric oncology and hematopoietic stem cell transplant (HSCT) service from January 2020 to March 2021 and who were diagnosed with COVID-19 infection by PCR. In Our study, we assessed the impact of the COVID-19 pandemic on this group of cancer pediatric patients with regards to their infection course and its effects on their course of therapy, the medical service provided, and the clinical outcome. We also evaluate the hospital and department strategies for management of those cases during the pandemic period. Our inclusion criteria were all children between the ages of 0 to 16 years diagnosed with or recently diagnosed with cancer who acquired Covid-19 infection between January 2020 till March 2021.

## Results

A total of 29 patients diagnosed with various types of pediatric malignancies were found to have Covid-19 infection during the period between January 2020 and March 2021. 18 cases (62%) were males, and 11 cases (37.9%) were females; only 2 cases (6.8%) were non-Saudi. Most of our patients diagnosed with Covid -19 were below or equal to 5 years old since we had 13 cases for this group (44.8%), while we had 7 cases (24.13%) their ages are above 5 years to 10 years. And further 9 cases (31%) are between 10 years to 16 years. With median age is 7.7 years. We noted that 8 cases (27.5%) had increases BSA for their norms as per gender, age, and height; however, the majority were within the normal ranges (**Table 1**).

**Table 1:** The relation of the age with mean body surface area (BSA).

Age group	Mean BSA
< 5 YEARS	0.68
5-10 YEARS	0.87
>10 YEARS	1.49

Acute leukemia, both lymphoid and, to a lesser extent, myeloid, was the primary malignancy in 17 cases (58.6%), and all the solid tumors and central nervous system tumors were occurred in 12 cases (41.4%). We noted that most of our patients were standard risk about 12 cases (41.3%), while both intermediate risk and high risk diagnosed in 7 cases for each (24.1%), and fortunately, only 3 cases were having a very high-risk disease (1.03%) (Figure 1).

Twenty-two patients (75.8%) were on an active treatment course, and seven patients (24.1%) were off-therapy in remission status on a follow-up plan. Considering those cases on active therapy, we found that 5 cases out of the 22 subjects (22.7%) were on their induction or initial treatment courses, another 6 cases were on the middle treatment courses (27.2%), while the majority who are 11 cases (50%) were on maintenance or continuation phases. Analyzing the causes of screening of Covid-19 infection among our sample patients (Table 2), we had 15 patients (51.7%) presented with symptoms needed screening while just less than half which are around 14 cases (48.2%) diagnosed with Covid-19 as a result for elective testing and they denied any symptoms.

Evaluating the causes for elective testing on those 14 cases, we got about 42.8% (6 patients out of the 14) were due for the need of pre-appointment testing before visiting the outpatient department (OPD) as they are coming from outside Dammam city. Other causes are mentioned in (Table 3).

While obtaining a clinical history and tracing the infection transmission pattern on our sample patients, we found that more than half about 15 out of the 29 patients (51.7%) had a history of contact with positive Covid-19 infection family member; 3 cases (10.3%) caught the infection while they are admitted as in-patients with no history of contact previously. And finally, the transmission source was unknown in 11 patients (37.9%). Fever was the main complaint in 13 cases out of 29 patients (44.8%), followed by a cough that occurred in 12 patients (41.3%). Other complaints were like a picture of upper respiratory tract infection with rhinorrhoea and sore throat; none of them presented with low oxygen saturation; however, some degree of tachycardia and tachypnoea were noted on around 31% Gastrointestinal tract complaints of nonspecific abdominal pain occurred in 4 cases, and 3 cases presented with watery diarrhea, which was negative for common stool pathogens. Headache was reported only in one patient, and it was persistent and annoying to the child (Table 4). Preliminary blood workup done in 24 cases (82.7%) at an initial presentation at the time of testing. Low absolute lymphocyte counts were noted in 11 patients out of the 24 patients (45.8%), while low absolute neutrophil counts were observed in 10 cases (41.6%); C-reactive protein CRP was noted to be elevated in 2 cases out of the 24 cases (8.3%). Coagulation profile was not noted to have significant abnormalities in our sample patients; only mild low fibrinogen was noted in 4 cases (16%) without changes in the PT, PTT. Chemistry testing for the renal and liver functions was not significant for almost all of them.

Baseline chest X-ray imaging (CXR) done in 11(37.9%) patients out of the total 29 cases and 72.7% (8 patients out of those 11 imaged cases) were reported as normal, other two patients (18%) had unilateral lung changes in their CXR, and only 1(9%) patient showed bilateral lung changed in the CXR. Most of the patients who diagnosed with Covid-19 infection were having very mild disease course, that they were managed and monitored as out-patients in around 23 cases (79.3%) while only 6 (20.6%) cases managed as inpatients either due to their significant clinical presentation or being as inpatients already at the time of diagnosis (Table 5).

Antibiotics were administered to 12 (41.3%) cases out of the 29, with four patients (33.3%) out of them given single-agent while the rest 8 cases (66.6%)

given more than one agent, especially for those presented with significant concomitant neutropenia. Steroids were used during the course of Covid-19 infection in 3 patients as part of their chemotherapy protocol phase and not as part of Covid-19 directed therapy plan. None of our patients given any anti-viral agent, and fortunately, none of them needed Pediatric intensive care admission nor higher supportive care.

Nasopharyngeal swab for Covid-19 PCR was repeated to prove negative results in 19 out of 29 patients and not done in 10 patients. We obtained a minimum time to get the first negative swab from the initial diagnostic positive test was six days, and the maximum time was 63 days with the mean of 25 days in our patients' sample. Our data showed that similar percentages for those turned into negative in less than 14 days and that swab remained positive for more than 30 days. Assessing the impact of Covid-19 infection on the planned treatment course, we found that 14 cases (48.2%) out of the 29 had some delay on their planned chemotherapy schedule, while the other 15 patients managed without delay. Addressing that only 22 of those 29 were on active therapy, that correcting the delay ratio to 14 cases out of 22 (63.6%).

In this study, we defined the delay days as the difference time between the scheduled time of chemotherapy as per chemotherapy protocol and the actual time we gave it after in our study. We got seven days as minimum delay days up to 35 days as maximum with a mean of delay days around 14 days. Such long delays that reached several weeks found in the few patients acquired the infection in the earlier period of the pandemic. Like other health centers at that time, the mechanism to deal with and contain the pandemic was still not sharply defined initially. On the other hand, the cases that had their infection later in the year 2020, when the department adopted many new strategies and policies, had much less delay in their course of therapy to almost none. Evaluating the causes of delay in therapy in those 14 cases, we found that the primary reason was the need to obtain negative swab result before admission or given OPD-based chemotherapy (Table 6). Fortunately, all of the sample patients recovered smoothly and completely with no further morbidities or fatalities from the covid-19 infection so far.

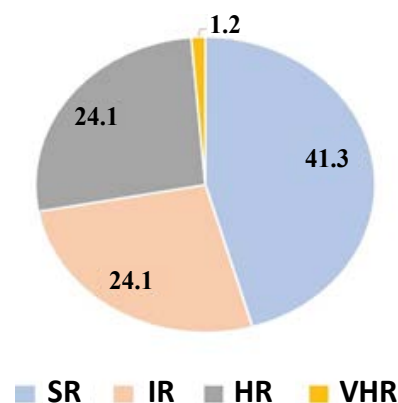


Figure 1. The disease risk distribution percentages.

Table 2: Cause of screening (COS).

COS	Number of cases	Percentage
symptoms	15	51.7%
elective testing	14	48.2%

Table 3: Causes of elective testing (COET) in the 14 subjects.

COET	Number of patients	Percentage
PRE-OPD appointment	6	42.8%
Pre imaging under aesthesia	4	28.5%
Pre aesthesia for procedure	2	14.2%
pre admission	2	14.2%

**Table 4:** Frequencies of symptoms at presentation.

Symptom	Number of patients	Percentage (out of 29 cases)
Fever	13	44.8 %
Cough	12	41.3%
Rhinorrhoea	9	31%
Tachycardia	9	31%
Tachypnoea	9	31%
Sore Throat	6	20.6%
Nonspecific Abdominal Pain	4	13.7%
Diarrhoea	3	10.3%
Vomiting	2	6.8%
Headache	1	3.4%

**Table 5:** Time to obtain first negative swab and frequencies.

Time in days	Number of patients	Percentage
1-14 days	7	36.8%
15-30 days	5	26.3%
>30 days	7	36.8%

**Table 6:** Causes of delay of chemotherapy and frequencies.

Cause of delay	Number of patients	Percentage
need to get negative swab result for admission or OPD visit	8	57%
clinical condition	5	35.7%
city lock down	1	7.1%

## Discussion

The majority of Covid-19 diagnosed cases are from the adult population while incidence is still remarkably less in the pediatric population, with children accounting, for about 1-5% of diagnosed cases, fortunately enough despite considering the children with cancer as a high- risk group. Still, most of the data available in publications up to date (though they are relatively limited) indicates that children tend to have a less aggressive disease course and better prognosis than adults. Mortalities were extremely uncommon [4]. In our study, none of the 29 cancer pediatric patients diagnosed with Covid-19 infection suffered from major morbidities, necessitated admission to intensive care units, and no reported deaths as well.

The clinical presentation of Covid-19 in our pediatric oncology patients was almost like a picture of mild to moderate upper respiratory tract infection in most of the symptomatic cases, with only a marginal number had lower respiratory tract serious infection or significant chest X-ray imaging findings.

Initially, unfortunately, few numbers of our patients remained testing positive for coronavirus for such a long period. However, they became completely free of symptoms; as a result, their scheduled chemotherapy was delayed; later on, after discussion with infectious diseases doctors, we learned that testing positive in asymptomatic subjects is not a reason to hold the planned course of therapy; similarly, that issue was tackled by other health workers that they mentioned that the positivity for weeks and months of coronavirus testing and viral RNA presence could not be used as evidence of ongoing replication," especially when the patients have nothing wrong with them. according to Amesh Adalja of the Johns Hopkins Center for Health Security in Baltimore who thought that it could be just viral debris [5].

Health workers were especially concerned that the Covid-19 infection in patients on chemotherapy may be associated with major complications and difficult course due to their immunity being already suppressed by chemotherapy, but Minotti et al. In a systematic review suggested that this myelosuppression could be one of the protective mechanisms against the cytokine release syndrome that is known to be part of the pathogenesis of the mortalities due to Covid-19 infection [6]. As the infection rate of the COVID-19 pandemic starts to curve up, most of the children's cancer-treating

faced an unprecedented global threat to safe and effective care for children with cancer. Parents and families of children with cancer were very concerned that the management of their children will be compromised or marginalized during the COVID-19 crisis. The challenging situation that occurred nearly in most cancer-treating centers all over the world at that time of emerging of the pandemic was magnified by the crucial need for an emergent, wise and sensible plan that was balancing between providing the best care for children with cancer while not increasing the risk of disease exposure and transmission.

A similar burden was faced in the King Fahad Specialist Hospital Dammam, which considered as the only referring tertiary center that provides service to treat childhood cancer in the whole eastern province, especially Early at pandemic with city lockdown and the very strict isolation rules we noticed that the delay in planned therapy reached in some of our cases to about more than a month, however, the situation improved later after implementing and improving the department and hospital policies and strategies of confining the pandemics. This was reflected on narrowing the delay period to become shorter or none. In this study, we reported that 63.6% of the affected patients had a delay in their course of therapy which is exactly the same findings in a similar national study reported by our colleagues in Riyadh that out of 204 studied cases, 63% of patients reported a delay in treatment received during the COVID-19 pandemic [7].

Several different policies and strategies were established and implemented by the hospital in general and the department of pediatric hematology-oncology and stem cell transplantation to improve the delivered service while keeping the safety measures against disease transmission.

They included the following:

- Protective measures, including hand hygiene, medical waste proper management, wearing masks by all medical staff, patients, and their caregivers, and keeping the social distancing were all enforced strictly.
- Activate the role of effective Triage at hospital entry points and patient's reception to explore and identify the risk of disease and exposure among patients and accompanying family members
- Strict isolation for all the suspected cases and refer the infected patients to specific specialized isolation centers with quarantine in the eastern province.
- Establishing satellite small treating centers in AL-Hassa and ALQatif during the lockdown period to continue providing chemotherapy and supportive care for the patients residing in those areas, the centers operated by trained pediatric oncology staff recruited from King Fahad Specialist Hospital Dammam. They worked in an excellent, highly organized way during the period of city lockdown.
- Improve the pharmacy services to provide a home delivery option to patients to minimize bringing them to the hospital
- They were establishing the service of Virtual OPD clinics, depending on telemedicine concept and augmentation of the role of the clinical coordinators to call the patients and addressed their clinical condition and concerns, and guiding them with proper documentation. Consultants and clinical coordinators ran the clinics.
- Restrictions over the visiting times and the allowed accompanied person number to a maximum of one family member with the patient.
- Enhance the education material about Covid -19 infection, mode of transmission, symptoms, and how to ask for help through simple educative handouts explaining the features and the risks of the disease was distributed at the reception desk or near the elevators so many families can quickly access them,
- Continuous broadcasting of the education information and short representative shows on all the hospital TV screens in the lounges, corridors, and patient rooms.
- Pre anesthesia for imaging or procedures elective testing for Covid -19 to minimize the risk of disease transmission

- We have increased the efficacy of communications among hospital staff on the one hand and with patients and families on the other hand.
- Routine daily virtual meetings for monitoring the situation study and decide about the best plan for care during the pandemic for the patients.
- Emphasize the importance of the COVID-19 vaccine as a top priority issue for the global control of the pandemic. And encourage all the medical staff to be vaccinated.
- Postpone all the elective appointments to OPD and replace them with telephone calls.
- Individual evaluation of the case by case to assess the risk of giving therapy vs. holding them, considering that some patients may remain testing positive for an extended period despite that they are clinically free, such cases should be offered their therapy without delay

## Conclusion

During the COVID-19 pandemic, children from different age groups caught COVID-19 infection without any significant age or gender preference; however, fortunately, the clinical manifestations of children's COVID-19 cases were less severe than those of adult patients. In this study, despite the small number of cases and being single institute experience, we found that there is no significant impact of covid-19 infection on children with cancer under therapy in terms of major delays to their therapy or for increased complications or fatalities. Oncology professionals should continue to make plans not only for the pandemic crisis but even for the post-Coronavirus period, which is critically important for planning the future. The lesson learned from the Pandemic period lay behind knowing early planning, teamwork, and effective communication are the keys to success during the crisis period.

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