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Second wave of COVID-19 – Not a matter of great concern for pediatric hematologist/oncologist



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ABSTRACT

Objective: Coronavirus disease-19 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has become a global pandemic and is giving rise to a serious health threat globally. SARS-CoV-2 infection ranges from asymptomatic carrier state to severe illness requiring intensive care unit (ICU) management. It is postulated that with COVID-19 infection, children are less prone to develop severe symptoms as compared with adults. The data on immunocompromised children affected with COVID-19 infection is limited and not many publications are there on the effects of 2nd wave of COVID-19 infection in pediatric hematology/oncology patients till date.

Methods: Retrospective data analysis of patients under the age of 18 years with underlying hematological and oncological conditions including those who underwent stem cell transplantation. All SARS-CoV-2-positive cases were included in the study.

Results: In our experience during second wave, 17 patients were found to be positive for SARS-CoV-2 with a male: female ratio of 2.4: 1 and median age of 8 years (range 1 – 18 years). Out of these 17 patients, 10 (58.8%) patients required hospital admission whereas the remaining were managed at home. Only 1 patient required ventilatory support and there was no mortality.

Conclusion: Though the number of pediatric patients with COVID-19 infection were more during the second wave but majority had mild to moderate symptoms and were easily managed.

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1. Introduction

COVID-19, caused by SARS-CoV-2, has become a global pandemic and is giving rise to a serious health threat globally. Most of the countries have already seen a two-wave pattern of reported cases. SARS-CoV-2 infection ranges from asymptomatic carrier state to severe illness. Approximately 15% of patients progress to severe pneumonia, and 5% require ICU management [1].

As of October 2021, around 244 million confirmed cases of COVID-19 have been reported worldwide including around 4.9 million deaths. Case fatality rate reported is around 2%, but this varies widely by location. In India, from January 2020 till October

2021, more than 34 million confirmed cases have been reported and around 0.45 million patients have lost their lives with a case fatality of around 1% [2].

From the beginning, it is known that the severe COVID-19 infection mostly affects the elderly population and is rare among children and young adults because of the comorbidities like diabetes and hypertension which are associated with age and a weaker immunity of the elderly leading to a dismal outcome [3].

Another postulation as to why children are less prone to have a complicated course compared with adults includes the possibility of differences in the distribution of their angiotensin-converting enzyme 2 (ACE 2) receptors which may limit viral entry and subsequent inflammation, hypoxia, and tissue injury [4].

Relatively unaffected during the 1st wave of COVID-19 last year, a high number of children and adolescents contracted the novel coronavirus during the 2nd wave in India. In the 1st wave of COVID-19, those children who had infection were asymptomatic, but in the 2nd wave, they were showing symptoms such as fever, diarrhea, cold, and cough [5].

Experts in India believe that the double mutant COVID-19 variant alongside a cocktail of other strains has a higher tendency to infect

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children. Other explanations for children getting infected more in the 2nd wave can be lack of precautions taken, more exposure to vulnerable areas, and non-approval of vaccination for children.

There is also a higher concern for children with underlying hematological and oncological conditions, who, because of their suppressed immunity, are thought to be at high risk for an unfavorable course of infection.

Although data on the clinical features and outcome of COVID-19 infection in immunocompromised children is limited, data on adults with cancer suggest increased susceptibility and more severe clinical course [6].

We are sharing our experience of pediatric hematology/oncology patients affected with COVID-19 infection during the 2nd wave.

2. Methods

Retrospective data analysis of patients under the age of 18 years with underlying hematological and oncological conditions including those who underwent stem cell transplantation. All SARS-CoV-2-positive cases confirmed with the presence of viral RNA in respiratory swabs by reverse transcription-polymerase chain reaction (RT-PCR) were included in the study. Demographics included were age, sex, type of underlying disease and disease status at the time of infection, symptoms, neutrophil status, treatment required as well as clinical outcomes.

3. Results

A total of 17 patients were found to be positive for SARS-CoV-2 during the period from April 1, 2021 to May 15, 2021. All patients

were tested for SARS-CoV-2 by RT-PCR because they were symptomatic except one who had a strongly positive contact history. Demographics of the patients are shown in Table 1. Male: female ratio was 2.4: 1. The median age was 8 years (range 1–18 years).

Sixteen out of 17 patients had fever at presentation and 5 patients had cough along with it. None of the patients had gastrointestinal symptoms.

Out of these 17 patients, 10 (58.8%) patients required hospital admission whereas the rest 7 were managed at home with proper isolation measures. Eight out of ten patients, though had mild symptoms, required admission as they were neutropenic and were initially managed with broad-spectrum antibiotics. The remaining two non-neutropenic patients were admitted as they had high-grade fever with high inflammatory markers.

CT scan of the chest was done in 6 (35.2%) patients. The reason for performing CT was high inflammatory markers (serum ferritin and C-reactive protein). Two patients had normal chest CT scan study while three patients had diffuse ground glass opacities involving bilateral lung fields with CT severity score of 7/25, 13/25 and 22/25.

Only one patient required ventilatory support. He was a case of ALL on chemotherapy and had superimposed pseudomonas infection. CT scan of the chest showed large confluent air space consolidation in the apical and posterior segment of the right upper lobe with scattered areas of air space consolidation in the rest of the lung fields along with underlying COVID-19 changes suggesting superadded bacterial infection. CT score could not be calculated due to underlying bacterial consolidation. He was given a course of remdesivir along with steroids and antibiotics. No other patient required oxygen support.

Steroids were given in 7/17 (41.1%) patients. Six patients were given steroids as the inflammatory markers were high whereas one

Table 1
Demographics of patients.

Age (yr)/ Sex	Underlying illness	Disease status	Symptoms	Neutropenia	CRP (mg/l)	Ferritin (ng/ml)	Hospital admission	CT scan score	Treatment	Outcome
18/M	SAA post IST	PR	Fever Cough	No	29	2871	Yes	7/25	Steroids	Recovered
12/M	ALD post HSCT	CR	Fever	No	ND	ND	No	ND	Supportive	Recovered
1/M	Medulloblastoma	PR	Fever	Yes	<5	ND	Yes	ND	Supportive Antibiotics	Recovered
3/F	ALL	CR	Fever	No	ND	ND	No	ND	Supportive	Recovered
2/M	Neuroblastoma	PR	Fever	No	ND	ND	No	ND	Supportive	Recovered
9/M	SCD post HSCT		Fever	Yes	20	4308	Yes	N	Steroids Antibiotics	Recovered
11/M	Thalassemia post HSCT		Fever	Yes	35	3562	Yes	N	Steroids Antibiotics	Recovered
17/M	PMBCL	CR	Fever Cough	No	ND	ND	No	ND	Supportive	Recovered
10/F	Medulloblastoma	CR	Fever	Yes	<5	ND	Yes	ND	Supportive Antibiotics	Recovered
8/M	Medulloblastoma	PR	Fever	Yes	ND	ND	No	ND	Supportive Antibiotics	Recovered
8/M	ALL	Active disease	Fever	Yes	8	552	Yes	ND	Steroids Antibiotics	Recovered
4/M	ALL	CR	Fever	Yes	7	437	Yes	ND	Supportive Antibiotics	Recovered
5/F	ALL	CR	No	No	<5	ND	No	ND	Supportive	Recovered
8/F	ALL	CR	Fever Cough	No	<5	ND	No	ND	Supportive	Recovered
14/M	ALL	CR	Fever	Yes	130	7233	Yes	Could not be calculated	Remdesivir Ventilator Steroids Antibiotics	Recovered
15/M	MDS	Active disease	Fever Cough	No	64	1486	Yes	13/25	Steroids	Recovered
5/F	ALL	CR	Fever cough	No	82	2534	Yes	22/25	Steroids	Recovered

Abbreviations: SAA – Severe Aplastic Anemia; IST – Immunosuppressive therapy; ALD – Adrenoleukodystrophy; HSCT – Hematopoietic stem cell transplantation; PMBCL – Primary Mediastinal B-cell lymphoma; ALL – Acute Lymphoblastic Leukemia; SCD – Sickle cell disease; MDS – Myelodysplastic syndrome; PR – Partial Response; CR – Complete response; ND- Not done; N - normal.

patient was given steroids as a part of acute lymphoblastic leukemia (ALL) induction chemotherapy protocol.

All 17 patients recovered successfully from COVID-19 infection and are currently on follow-up and are doing well.

4. Discussion

There is limited data from developing world of COVID-19 infection in pediatric hematology and oncology patients. According to the experts from India, the preliminary data from the country has not shown much of a difference in the age-wise distribution of COVID-19 infection during the 1st and 2nd wave, the increase in pediatric cases seems to be because of the sharp rise in the total number of cases during this second wave of the pandemic. This sharp rise is attributable to the reopening of most public places and the double mutant virus which follows the escape phenomenon. In our study, the total number of patients during the 2nd wave was more as compared to the 1st one (only 4 cases were seen during the 1st wave) and a majority of them had mild symptoms this time.

There are a few publications on the effect of the 2nd wave in children which have been reported in the literature and even fewer publications describing the effects in children with blood and cancer disorders.

Itimie et al. from Spain compared reported cases of COVID-19 infection during the 1st and 2nd wave and found that in the 2nd wave there were a greater number of children, pregnant and postpartum women but the duration of hospitalization and the case fatality rate was lower than that in the 1st wave. The total number of patients admitted during the 1st and 2nd wave were 204 and 264 respectively and age-wise distribution showed that the cases during the 2nd wave were younger as compared to the 1st wave (58 ± 26 vs. 67 ± 18 years; $p < 0.001$). Out of the total 264 patients during the 2nd wave, 21 were of the age between 0–9 years and 12 were less than 1 year. Duration of hospital stay was also significantly shorter in the 2nd wave (14 ± 19 vs. 22 ± 25 days; $p < 0.001$). A total of 49 and 35 deaths occurred during the 1st and 2nd wave respectively and the case fatality rate came down from 24.0% to 13.2% [7].

Brookman et al. from King's College Hospital, London reported the effect of the new SARS-CoV-2 variant B.1.1.7 on children and young people during the 2nd wave, and found a high prevalence of this variant accounting for 70% of infections in this group but there was no evidence of a severe or complicated course of illness in this younger population, thus suggesting that infection with this variant during 2nd wave was not different as compared to the original strain. Therefore, severe acute respiratory COVID-19 remains an uncommon occurrence in children and young people [8].

Banerjee et al. published their data last year on 1st wave of COVID-19 in children from India, found that the clinical course of COVID-19 in children was less severe than in adults, which was consistent with other reports published in children from the world [9].

Pediatric patients with underlying hematological and oncological conditions constitute a group of patients who are predicted to be at high risk for COVID-19 but different studies from various countries in the world have reported a mild course of the disease.

Millen et al. conducted an observational study in the United Kingdom on cancer patients with age less than 16 years and found that of a total of 54 cancer patients with COVID-19 infection, 15 (28%) were asymptomatic, 34 (63%) had mild infections and 5 (10%) had severe or critical infections [10].

Hrusak et al. conducted a survey from 25 different countries on SARS-CoV-2 infections in pediatric patients on anticancer treatment, where almost 10,000 patients at risk were followed up and around 200 children with cancer were tested, only 9 were found to be positive for COVID-19 and had asymptomatic to mild course of

the illness. They concluded that most of the children receiving anti-cancer therapy had a benign course of the disease presenting mostly with mild symptoms [11].

Hamdy et al. from National Cancer Institute, Cairo University, Egypt, followed up their pediatric cancer patients over 3 months and found that out of 75 patients only seven were tested positive for COVID-19, and of these, three patients showed a severe infection with ICU admission and unfavorable outcome [12].

Boulad et al. conducted a study in which a total 178 pediatric patients with cancer who were tested for COVID-19, only 20 had shown positive results, and only four patients required hospitalization while the remaining had mild symptoms and were managed at home [13].

There is a limited number of publications on the effect of COVID-19 in pediatric hematology and oncology patients from India and other developing countries. Radhakrishnan et al. showed their experience of COVID-19 in children with cancer and found that 15 patients, 8 caregivers, and 8 staff tested positive for SARS-CoV-2 during the study period. Out of the 15 cancer patients, only 5 (33%) were symptomatic while the rest were detected incidentally while before admission. Only one patient (7%) had respiratory distress and required respiratory support [14].

In another report from India by Yadav et al., reinfection with SARS-CoV-2 was seen in two children after recovering fully and developing immunoglobulin G (IgG) antibodies against it [15]. In our center, we did not see any case of reinfection in pediatric hematology and oncology patients.

In our study, only 1 patient (5.88%) out of a total of 17 had a complicated course of the illness and that too was because of co-existing bacterial sepsis, while the rest had mild symptoms. We conclude that, though the number of patients with COVID-19 were more during the 2nd wave but the outcome of the children remained excellent. Thus we feel that 2nd wave of COVID-19 infection was not a matter of great concern for the Pediatric Hematologist/Oncologist in the developing world.

Declaration of competing interest

The authors report no conflict of interest and no disclosures.

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Ethical approval

Not applicable.

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