Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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COVID-19 in children with blood and cancer disorders: An experience from India

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To the editor:

Coronavirus disease-2019 (COVID-19) is caused by severe acute respiratory syndrome corona virus-2 (SARS-CoV-2) and has been declared as a pandemic due to rapid global spread. Children and young adults usually have milder course of illness & good outcome in comparison to adults who are elderly or have co-morbidities [1,2].Children with blood and cancer disorders are at high-risk of getting COVID-19 due to frequent visits to the hospital to get chemotherapy or supportive care [1]. Children with cancer are immunosuppressed and even after completion of chemotherapy, the immune dysfunction may persist for several months [3]. Severe infections due to human coronaviruses (HCoV) in immunocompromised children have been reported [4] and a similar impact was expected in children on chemotherapy due to SARS-COV-2. But so far, we are still learning about impact of COVID-19 in children with blood & cancer disorders [1]. A strong association of cycle threshold (Ct) values of virus by the polymerase chain reaction (PCR) test with the severity of disease, mortality & laboratory parameters has been reported [5]. In one study it was observed that replication of SARS-CoV-2 in older children leads to similar levels of viral nucleic acid as in adults, but significantly greater amounts of viral nucleic acid are detected in children younger than 5 years [6]. In India, although government of India has provided a treatment protocol to manage COVID-19 but for children with COVID-19; no specific treatment has been recommended [7]. Increased morbidity and mortality have been reported in adult cancer patients with COVID-19 and also delivery of cancer care has also been affected [8–14]. We report here our experience of diagnosing and managing COVID-19 in children with blood and cancer disorders in India.

We retrospectively studied outcome of children with blood & cancer disorders diagnosed with COVID-19 between February to October 2020. All were screened with nasopharyngeal swab for SARS-CoV-2 by RT-PCR prior to inpatient admission or if child had symptoms of COVID-19. Ct values were noted. Positive patients were isolated for atleast 14 days and retested as per hospital policy.

A total of 55 patients were tested for SARS-COV-2 prior to 252 in-patient admissions. COVID-19 was detected in 13 patients. Results are shown in Table 1. COVID-19 was detected in 13 patients (leukemia-3, solid tumors-7, thalassemia major-2 and aplastic anaemia-1). All were male and had median age of 8 years. SARS-COV-2 PCR was tested 369 times in these 55 patients; test positivity rate was 8.1% (30/369). Five patients who were tested by labgun kit had median Ct value of 12.74 (7.24–25.38) for N gene and 13.82 (11.38–26.34) for RDRp gene. By TaqPath kit, 5 patients were tested had median Ct values of N gene −30.90 (19.25–32.52) & for ORF1 gene-30 (29.30–32). One patient tested with FTD kit had Ct value of 22.9. Two patients were tested by different kit so Ct values are not comparable. All except 3 children were managed at home. One child with aplastic anemia needed multiple admissions for transfusions. He died 3-weeks later due to Klebsiella sepsis. One child with Wilms tumor with Mulibrey-Nanism syndrome with atrial flutter needed intensive care but recovered fully 2 days later. Third child with brain stem glioma on ventilator got infected during radiotherapy. He restarted radiotherapy after clearance of the virus. There was mean treatment delay of 21.6 days (14–39 days). Three children had reactivation after administration of further chemotherapy.

In our study, 3 children had asymptomatic reactivation during further chemotherapy and few had PCR positivity for more than 2 weeks. Out of the three children with reactivation we have previously reported 2 children [15]. In one child with neuroblastoma who had reactivation we did whole genome sequencing of the virus in samples taken from both episodes and found that it is reactivation of same virus and not a new infection [16]. As per WHO guidelines, the chances of culturing virus decline to 6% after 10 days from onset of symptoms [17]. Similar results were observed with smaller studies that recognized infectious virus can shed for 8 or 9 days [18] and others signifying correlation between Ct value/viral load and cultivable virus ([18,19]). Previous studies have reported the correlation between Ct value and disease severity ([20–22]). Lower Ct values from respiratory samples were associated with more severe disease & viral load determined via Ct values correlated with disease severity ([23,24]). Our study showed that all immunocompromised patients were mostly asymptomatic irrespective of the Ct values. In contrast to previous studies, we found no significant correlation between Ct values and severity of disease in children with hemato-oncological conditions. Ct values were highly variable.

In our study, a patient with case of CNS relapse of ALL treated on BFM REZ protocol and Rituximab had persistent PCR positivity and also had reactivation after next course of chemotherapy. Rituximab

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Table 1
Details of children with blood and cancer disorders diagnosed with COVID19.

SN	Age Yr.	Sex	Dx	Delay in Rx (days)	PCR +ve (time)	Start Day	Labgun kit Ct values		Taqpath Ct values			FTD kit Ct values	Outcome	Symptoms	Rx	Phase of Rx before COVID19 diagnosis
							N	RdRp	N	ORF1ab	S					
1a	14	M	ALL	14	1	0	NA	NA	32.52	32	34.66	NA	Alive	None	No	BFM95- IB phase
1b	14	M	ALL	21	2	71	NA	NA	19.25	18.7	18.02	NA	Alive	None	HCQ	BFM95-HDMTX
2	8	M	ALL	14	1	0	NA	NA	NA	NA	NA	22.92	Alive	None	No	HD-ARAC
3	3	M	RMS	14	1	0	NA	NA	29.33	29.52	23.37	NA	Alive	None	No	VAC
4a	3	M	NB	21	2	0	NA	NA	14.59	16.84	17.48	NA	Alive	None	No	Post-surgery
4b	3	M	NB	22	3	42	22.37	22.35	NA	NA	NA	NA	Alive	None	No	OJEC
5	2	M	WT	14	1	0	NA	NA	32.48	33.8	35.45	NA	Alive	AF	No	SIOP-WT
6	1	M	TM	39	2	0	NA	NA	30.03	30.51	27.29	NA	Alive	None	No	Hydroxyurea
7	15	M	TM	14	1	0	NA	NA	25.56	29.33	28.03	NA	Alive	None	No	None
8	10	M	HL	14	1	0	24.78	26.22	NA	NA	NA	NA	Alive	None	No	ABVD
9a	6	M	ALL	28	4	0	12.74	13.82	NA	NA	NA	NA	Alive	None	No	R1 block BFMREZ+ R
9b	6	M	ALL	22	3	39	18.92	18.85	NA	NA	NA	NA	Alive	None	No	R2 block BFMREZ+ R
10	10	M	SAA	29	4	0	7.24	11.38	NA	NA	NA	NA	Died	None	No	ATG & CSA
11	15	M	AM	14	1	0	NA	NA	30.38	30.41	28.04	NA	Alive	None	No	None
12	15	M	BSG	30	2	0	13.3	13.6	NA	NA	NA	NA	Alive	Mild	No	Radiotherapy
13	12	M	ES	14	1	NA	NA	NA	*	*	*	NA	Alive	Mild	No	Cycle 4 VDC/IE

SN- Serial Number, Yr.- year, Dx- Diagnosis, Rx-Treatment, PCR- Polymerase chain reaction, +ve-positive, Ct-cycle threshold, M-Male, ALL- Acute lymphoblastic leukemia, NB-Neuroblastoma, RMS-Rhabdomyosarcoma, WT-Wilms Tumor, TM-Thalassemia major, HL- Hodgkin Lymphoma, CR-Complete Remission, SAA- Severe Aplastic Anemia, AM-Atypical Meningioma, BSG- Brain stem glioma, ES-Ewing Sarcoma, NA- Not applicable, *- Ct values not available.

may be the possible cause of prolonged persistence of covid or reactivation of covid. Similar results have been reported in patients treated with Rituximab and getting Covid19 [25–30]. In our study, a child with severe aplastic anemia developed COVID-19 after a course of immune suppressive therapy. During COVID infection, child remained asymptomatic for 28 days. The child expired 5-days after becoming negative for SARS-COV-2 due to sepsis (blood culture positive for klebsiella infection). Child expired due to sepsis but post-covid multi-system inflammatory syndrome (MIS-C) [31] cannot be ruled out.

Post bone marrow transplant, SARS-COV-2 infection similar to HCoV infection can increases the complications, morbidity & mortality [32–34]. In our study, two patients underwent bone marrow transplant (BMT) uneventfully afer recovering from COVID-19 (autologous stem cell transplant for neuroblastoma and allogenic BMT for thalassemia). Viral reactivation was not detected. In our study, we found that planned therapy was delayed by 14–39 days with median value 14 days. Similar rescheduling & delay in chemotherapy has been observed in other centres too due to COVID-19 infection [35].

Varied outcomes of Covid19 in children with cancer has been reported from different parts of the world [15,16,35–40]. Similar to our study most studies suggest that diagnosis of active cancer alone and recent anticancer therapy do not predict worse COVID-19 outcomes [36,37,39,40]. However, few studies showed COVID-19 in paediatric patients with malignancy have reported poor outcomes compared to general population [35,38].

COVID-19 in children with blood & cancer disorders is mostly asymptomatic and can be managed at home. However, it does lead to treatment delays and post covid complications. Ct values have wide variation and do not predict severity.

Disclosure

All authors have nothing to declare.

Conflict of Interest

Nothing to declare

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Nil

Consent

Patient consent has been received

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