ORIGINAL RESEARCH

Profile and outcome of Covid-19 Infections in Pediatric Cancer Patients: A study from a tertiary care centre from North India

[1]Dr. Faisal R Guru, [2]Dr. Anjum Ara Mir, [3]Dr. Taskeen Mehmood, [4]Dr. Shumail Bashir, [5]Dr. Syed Nisar Ahmad, [6]Dr. Saquib Zaffar Banday, [7]Dr. Areez Ahmad, [8]Dr. Haider R Guru, [9]Dr. Ulfat Ara Wani, [10]Dr. Mohmad Hussain Mir

[1,5,6,7,9,10]Department of Medical Oncology, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Jammu & Kashmir, India
[2]Department of Microbiology, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Jammu & Kashmir, India
[3]Department of Radiotherapy, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Jammu & Kashmir, India
[4]Department of Chest Medicine, Govt. Medical College, Baramulla
[8]Department of Cardiology, Sher-i-Kashmir Institute of Medical Sciences, Srinagar, Jammu & Kashmir, India

Corresponding Author
Dr. Shumail Bashir
Department of Chest Medicine, Govt. Medical College, Baramulla
Email: faisal_guru@yahoo.com

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ABSTRACT

Background: SARS-CoV-2, the causative agent of covid-19 infection was detected in China in December 2019 and rapidly spread around the world and was responsible for the ongoing pandemic. Pediatric cancer patients undergoing anti-neoplastic therapy are at a higher risk for Covid- 19 infection related complications owing to their immuno compromised state. This study provides an insight to the factors associated significantly to the Covid -19 infection in the pediatric patients with malignancy and the effect of chemotherapy on the infection in terms of morbidity and mortality. **Methodology:** This retrospective cohort study was conducted in a tertiary care hospital and SARS-CoV-2 infection was diagnosed on the basis of a positive polymerase chain reaction (PCR) test from a nasopharyngeal swab or throat swab. The data on age, gender, symptoms, diagnosis, length of admission and time to negative PCR were collected from the medical files of all pediatric patients treated for cancer who tested positive for COVID 19 from May 2020 to October 2021. **Results:** A total of 300 patients were treated during the study period out of whom 46 patients with diverse pediatric cancers tested positive for SARS-COV-2 .Males accounted for the majority of cases, (60.9%) whereas 19 patients were females. The median age at the time of diagnosis was 5 ± 2years. Acute lymphoblastic leukemia (30.5%) was the most common malignancy followed by Neuroblastoma (10.9%), Wilm'stumor(8.7%) ,Osteosaroma (8.7%), Ewing sarcoma (8.7%), Non- Hodgkin's Lymphoma(6.5%), Giant cell tumor (6.5%), Rhabdomyosarcoma (6.5%), Hodgkin's lymphoma (4.3%),Acute Myeloid leukemia (4.3%), Medullobastoma (2.2%) and Retinoblastoma (2.2%). Among patients suffering from Acute Lymphoblastic Leukemia,53.3% were diagnosed with Covid-19 during induction , 26.7% during maintainance therapy and 20.0% during the consolidation phase. Negative results for RT-PCR were obtained after a mean duration of 15 days ± 1.5 days. Most of the patients maintained an oxygen saturation above 90% whereas the lowest oxygen saturation of 70-75% was seen in 8 patients. **Conclusions:** Our study concluded that although covid-19 affected the treatment course in a significant proportion of patients admitted for anti cancer therapy but the morbidity was low with no mortality recorded in our subset of patients.

Keywords: Covid-19, Cancer, Pediatric, tertiary care.

INTRODUCTION

At the end of 2019, a novel corona virus was identified as the cause of a cluster of respiratory diseases resulting in an epidemic throughout the world and the virus was designated as severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) by the International Committee on Taxonomy of Viruses (ICTV).[1] On December 31, 2019, the outbreak of novel corona virus was initially reported to the World Health Organization (WHO). And On

January 12, 2020, WHO designated this virus as novel coronavirus "2019-nCoV". This viral outbreak was declared as a public health emergency of international concernon January 30, 2020 by WHO and the disease was termed as corona virus disease 2019 (COVID-19) on February 11, 2020.[2]The infection is characterized primarily by fever and lower respiratory symptoms but can the severity may range from asymptomatic infection to critical illness with complications like acute respiratory distress syndrome (ARDS), septic shock, multi organ failure and death occurimg in some cases. Age >65 years is a strong predictor of death. In addition to this, patients with comorbidities at any age have been found to suffer from severe disease more frequently.[3] Cancer patients are regarded as a highly vulnerable group in the COVID-19 pandemic owing to compromised immune systems caused by the tumor growth itself and anti-cancer treatment. In addition to this, the cancer patients are more prone to getting infected by SARS-CoV-2 due to contact with COVID-19 patients or virus-contaminated areas, during their frequent visits to hospitals for anticancer therapy as there is a significant nosocomial transmission of SARS-CoV-2 among patients in healthcare facilities.[4] Age is an important factor that determines the severity of COVID-19 infection and children are known to have milder symptoms once infected with COVID-19 as compared to the adult population and mortality among children is comparatively less. The death rate has been found to be low in the youngest age group, but more complications are associated with age below 1 month, male sex, pre-existing medical conditions, and presence of signs or symptoms of lower respiratory tract infection at presentation. [5] Covid 19 infection is diagnosed by RT-PCR that detects viral ribonucleic acid using flourogenic primers/probes and various steps involving thermal cycling. Other diagnostic modalities include Serology for estimation of sero-prevalence, asymptomatic infections, contact tracing and vaccine effectiveness, Lateral flow immunoassay (LFIA), chemi-luminescence immunoassay or the traditional enzyme linked immunosorbent assay (ELISA) that are point of care (POC) tests with a quick turnaround time but are less sensitive than RT-PCR. [6]

Here, we present a series of forty si xpediatric patients with COVID-19 infection during active antineoplastic treatment for diverse diagnoses in a tertiary medical center in a tertiary hospital in Jammu and Kashmir.

METHODS

This retrospective observational study was conducted in Sher-i-Kashmir Institute of Medical Sciences, a tertiary care hospital in Jammu and Kashmir. All pediatric patients treated for cancer from May 2020 to November 2021 were included in the study. Data on age, gender, symptoms, diagnosis, length of admission and time to negative PCR was collected. The diagnosis of SARS-CoV-2 was based on a positive polymerase chain reaction (PCR) test from a nasopharyngeal swab or throat swab.COVID-19 was categorized according to the US National Institutes of Health (NIH) classification severity index: asymptomatic, mild, moderate, or severe disease.

RESULTS

A total number of 300 patients received antineoplastic treatment during the period of 18 months among which 46 tested positive for SARS-COV-2. 28 patients were males and 18 were females and the male to female ratio was 1:1.5. The median age at the time of diagnosis was 5±2years. Acute lymphoblastic leukemia (n=14 ,30.5%) was the most common malignancy followed by Neuroblastoma (n=5, 10.9%),Wilm'stumor (n=4,8.7%), Osteosaroma (n=4,8.7%), Ewing sarcoma (n=4,8.7%),Non-Hodgkin's Lymphoma(n=3,6.5%), Giantcell tumor (n=3,6.5%),Rhabdomyosarcoma (n=3,6.5%), Hodgkin's lymphoma (n=2,4.3%),Acute Myeloid leukemia (n=2,4.3%), Medullobastoma(n=1,2.2%)and Retinoblastoma (n=1,2.2%) was the least common. Among the ALL patients, 8 (53.3%) were diagnosed with Covid-19 during induction , 4(26.7%) during maintain ancetherapy and 3 (20.0%) during the consolidation phase. The average time to negative PCR was 15 ± 1.5 days and the lowest oxygen saturation of 70 % -75% was seen in 8 patients.

Table 1: Gender wise distribution of patients included in the study

Gender	No. of cases (N)	Percentage (%)
Male	28	60.9
Female	18	39.1
Total	46	100

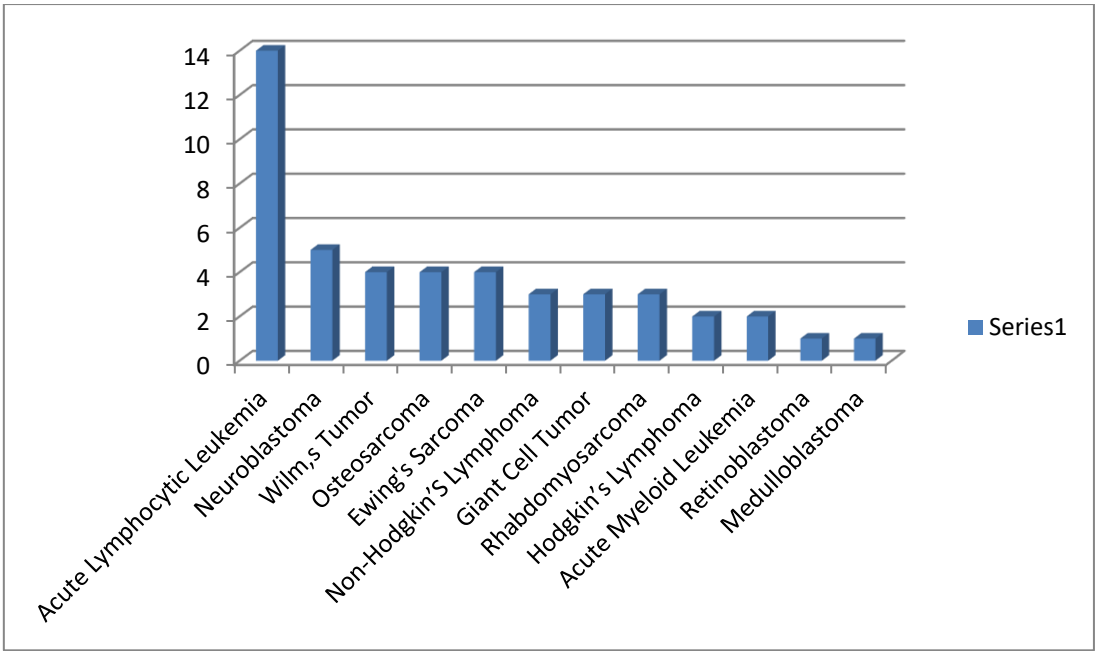

Figure 1: Disease profile of Covid-19 positive patients

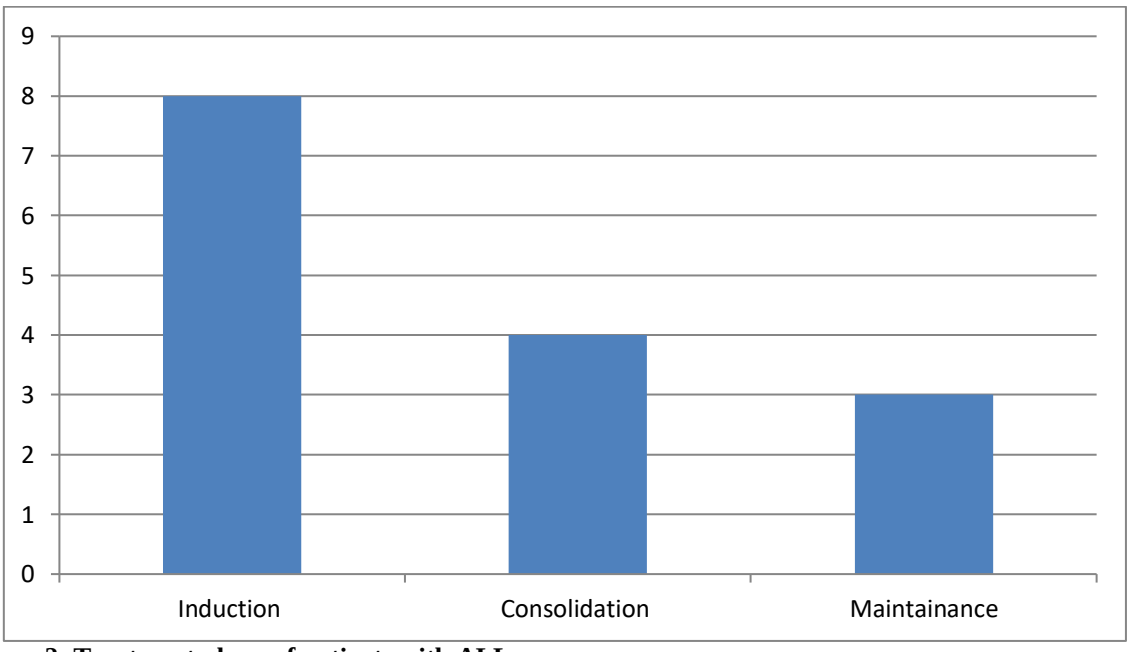

Figure 2: Treatment phase of patients with ALL

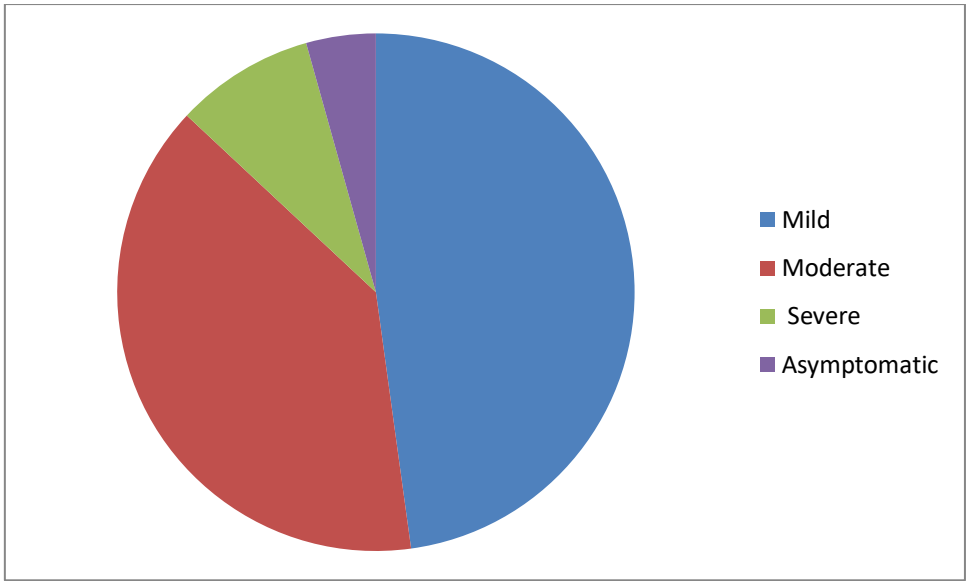

Figure 3: Degree of illness in covid-19 positive cases.

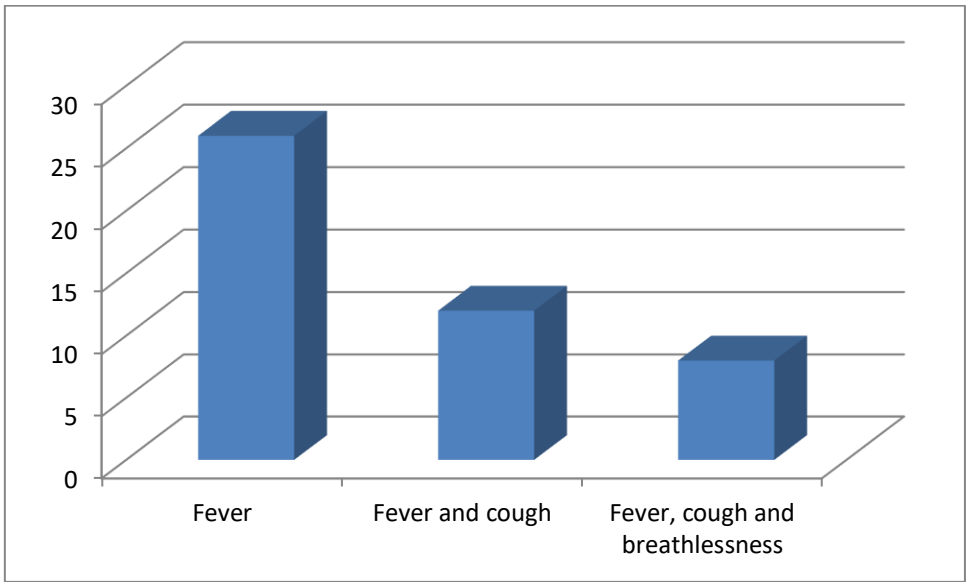

Figure 4: Bar diagram depicting symptoms of the cases.

Table 2: Table showing time to negative PCR in Covid-19 positive patients

Time to negative PCR	No. of cases (N)	Percentage (%)
1-10 days	30	65.2
10-20 days	16	34.8
Total	46	100

DISCUSSION

Severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) is a highly transmissible, an infected individual being able to transmit SARS-CoV-2 virus to an average of 2.2 individuals and virulent corona virus infecting humans that emerged in China. It was found to corona virus disease 2019 (COVID-19), a respiratory disease and had a massive impact on global public health.[7]The fatality rate of COVID-19 patients was initially high and increased constantly owing to the lack of selective therapeutic interventions and potent vaccines.[8] Numerous studies have shown that children are susceptible to SARS-CoV-2 infection, most of them being either asymptomatic or pre-symptomatic or present with mild symptoms and are at a low risk of life threatening complications.[9]In patients with underlying coexisting illness like hypertension, diabetes , coronary heart disease, and chronic obstructive lung disease , Immunocompromising conditions , there is a fairly high chance of severe disease.[10]

In our study, we found that the percentage of delay in antineoplastic treatment was 56.5% and that covid-19 had a significant effect on the therapeutic continuum in patients. Several studies suggest that malignancy subjects the pediatric patients infected with Covid-19 to a higher risk of severe disease with treatment effect playing an important role and such patients have been reported to require intensive care admission with contiined chemotherapy resulting in dismal outcomes.[11] Contrary to this, a study carried out by Minotti S *et al* concluded that immuno suppression in pediatric patients may be associated with a favourable outcome of simultaneous Covid-19 infection as compared to other comorbidities.[12] Another systematic review by Dorantes Acosta E et al suggested that COVID-19 does not have a significant impact on mortality in the pediatric cancer population.[13]

The anti cancer therapy was stopped for sometime in 26 patients. Mukkada S *et al* carried out a study and found that the modifications to cancer-directed therapy occurred in 609 (55·8%) of 1092 patients receiving active oncological treatment. [14]

Most of the patients in our study belonged to the agegroup of 5 years.Hamdy R *et al* in their study found that 71 % chidren belonged to the age group of 1 -9.9 years whereas 29 % beloged to the age group of 10 to 18 years.[15] Higher rates of covid 19 infection in male children (58.69%) than in female children (41.3%) was noted in our study. The results were similar to those found in a study of 44,672 confirmed cases taken from China's Infectious Disease Information System through February 11, 2020, it was found that 51.4% of patients with confirmed cases of COVID-19 were male.[16] On the other hand, Clinical data regarding COVID-19 showed no significant sex differences in susceptibility to COVID-19 infection in an analysis of the public data set from the Chinese Public Health Science Data Center that contained the first 37 fatalities from COVID-19 and 1,109 cases of COVID-19 survivors.[17]

Fever was the most common symptom in 99% of the affected patients. Similar results were found in a study conducted by Węcławek-Tompol*et al* in which the most common manifestation was fever, in 31 patients, followed cough in 13 patients, coryza in 12, gastrointestinal symptoms in 10, and headache in 8 and these symptoms were present in different combinations.[18] In another study conducted by Madhusoodhan PP*et al*, fever was found to be the most common symptom in 82.2%, followed by cough cough (61.6%), or respiratory distress (26%) with fatigue, myalgias, vomiting/diarrhea, anosmia, ageusia, and sore throat being reported less frequently.[19]

Majority of the cases was Acute lymphoblastic leukemia, 30.4% followed by Neuroblastoma 10.8% , Osteosarcoma 8.69% ,Ewings sarcoma 8.69% , Wilms tumour 8.69% , Non Hodgkin Lymphoma 6.52% , Germ cell tumor6.52 % ,Rhabdomyosarcoma 6.52% , Medulloblastoma 2.17%,Acute myeloblastic Leukemia 2.17% and Retinoblastoma 2.17%. Our results are in accordance to what has been reported by Schlage *et al* who reported Acute lymphoblastic leukemia (ALL) as the most common malignancy in 50.1% patients , followed by AML in 10.1% patients whereas 5.1% patients had malignant teratoid rhabdoid tumor and Wilms' tumor, hepatoblastoma or lymphoma.[20]

80 % of the patients had mild symptoms and similar results were seen in a study conducted by who found out that 44% patients were asymptomatic, 50% had mild disease with just one patient developing ARDS.[21]

In our study, 53.3 %patients were diagnosed with Covid-19 during induction, 26.7% during maintainance therapy and 20.0% during the consolidation phase. The same was seen by Schlage who reported 55 patients received first-line intensive chemotherapy or were on oral maintenance therapy (69.6%), 15 patients were in remission (18.9%), 8 patients had progressive disease and received various individual rescue treatment regimens (10.8%), and one patient had refractory malignant diseases and was on palliative oral chemotherapy (1.5%). [20]

The mean time to negative RT-PCR was 15±1.5 days and was comparable to the results of a study conducted by Weclawek- Tompot J et al which showed the median time to be 14 days while ranging from 2 to 133 days.[18] In another study conducted by Yingying Lu, the median duration of SARS-CoV-2 RNA shedding was 15 days with prolonged duration of viral shedding being associated with fever, pneumonia and low lymphocyte counts.[22]

CONCLUSION

Our findings show that although there was an interruption in treatment in majority of patients, however, most of the patients with covid-19 infection showed mild symptoms with no mortality.This clearly indicates that pediatric oncology patients if managed aggressively for covid-19 have excellent outcomes with some delay in treatment protocols.

CONFLICT OF INTEREST

None

REFERENCES

1. Oz-Alcalay L, Elitzur S, Amitai N, Toledano H, Barzilai-Birenboim S, Avrahami G et al. COVID-19 infection in pediatric patients treated for cancer. Int J Clin Oncol. 2022;27(2):448-454.
2. Majumder J, Minko T. Recent Developments on Therapeutic and Diagnostic Approaches for COVID-19. AAPS J. 2021 5;23(1):14.
3. Liu C, Zhao Y, Okwan-Duodu D, Basho R, Cui X. COVID-19 in cancer patients: risk, clinical features, and management. Cancer Biol Med. 2020 15;17(3):519-527.

4. Węcławek-Tompol J, Zakrzewska Z, Gryniewicz-Kwiatkowska O, Pierlejewski F, Bień E, Zaucha-Prażmo A et al. COVID-19 in pediatric cancer patients is associated with treatment interruptions but not with short-term mortality: a Polish national study. J Hematol Oncol. 2021 11;14(1):163.
5. Biswas M, Rahaman S, Bisws TK, Hazaque Z, Ibrahim B.Association of Sex, Age, and Comorbidities with Mortality in COVID-19 Patients: A Systematic Review and Meta-Analysis.Intervirology 2021;64:36-47.
6. Rai, P., Kumar, B.K., Deekshit, V.K. et al. Detection technologies and recent developments in the diagnosis of COVID-19 infection. ApplMicrobiolBiotechnol 2021;105:441–455.
7. Ribeiro da Silva SJ, Frutuoso do Nascimento JC, Mendes RP, Guarines KM, Alves da Silva CT,Gomes da Silva P et al Two Years into the COVID-19 Pandemic: Lessons Learned. ACS Infect. Dis. 2022, 8, 9, 1758–1814
8. Beeraka NM, Tulimilli SV, Karnik M, Sadhu SP, Pragada RR, Aliev G, Madhunapantula SV. The Current Status and Challenges in the Development of Vaccines and Drugs against Severe Acute Respiratory Syndrome-Corona Virus-2 (SARS-CoV-2). Biomed Res Int. 2021 Jun 1;2021:8160860.
9. Nikolopoulou GB, Maltezou HC. COVID-19 in Children: Where do we Stand? Arch Med Res. 2022;53(1):1-8.
10. Chams N, Chams S, Badran R, Shams A, Araji A, Raad M et al. COVID-19: A Multidisciplinary Review. Front Public Health. 2020 Jul 29;8:383.
11. Nadkarni AR, Vijayakumaran SC, Gupta S, Divatia JV. Mortality in Cancer Patients With COVID-19 Who Are Admitted to an ICU or Who Have Severe COVID-19: A Systematic Review and Meta-Analysis. JCO Glob Oncol. 2021 ;7:1286-1305.
12. Minotti C, Tirelli F, Barbieri E, Giaquinto C, Donà D. How is immunosuppressive status affecting children and adults in SARS-CoV-2 infection? A systematic review. J Infect. 2020;81(1):e61-e66.
13. Dorantes-Acosta E, Ávila-Montiel D, Klünder-Klünder M, Juárez-Villegas L, Márquez-González H. Survival and Complications in Pediatric Patients With Cancer and COVID-19: A Meta-Analysis. Front Oncol. 2021,21;10:608282.
14. Mukkada S, Bhakta N, Chantada GL, Chen Y, Vedaraju Y, Faughnan L. Global Registry of COVID-19 in Childhood Cancer. Global characteristics and outcomes of SARS-CoV-2 infection in children and adolescents with cancer (GRCCC): a cohort study. Lancet Oncol. 2021;22:1416-1426.
15. Hamdy R, El-Mahallawy H, Ebeid E. COVID-19 infection in febrile neutropenic pediatrichematology oncology patients. Pediatr Blood Cancer. 2021;68(2):e28765.
16. The Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. The Epidemiological Characteristics of an Outbreak of 2019 Novel Coronavirus Diseases (COVID-19) - China, 2020. China CDC Wkly. 2020 .21;2(8):113-122.
17. Mukherjee, S., Pahan, K. Is COVID-19 Gender-sensitive?. J Neuroimmune Pharmacol 2021;16, 38–47.
18. Węcławek-Tompol, J., Zakrzewska, Z., Gryniewicz-Kwiatkowska, O. et al. COVID-19 in pediatric cancer patients is associated with treatment interruptions but not with short-term mortality: a Polish national study. J Hematol Oncol 2021;14,163.
19. Madhusoodhan PP, Pierro J, Musante J, Kothari P, Gampel B, Appel Bv et al. Characterization of COVID-19 disease in pediatric oncology patients: The New York-New Jersey regional experience. Pediatr Blood Cancer. 202;68(3).
20. Schlage S, Lehrnbecher T, Berner R, Simon A, Toepfner N. SARS-CoV-2 in pediatric cancer: a systematic review. Eur J Pediatr. 2022 ;181(4):1413-1427.
21. Oz-Alcalay L, Elitzur S, Amitai N, Toledano H, Barzilai-Birenboim S, Avrahami G et al. COVID-19 infection in pediatric patients treated for cancer. Int J Clin Oncol. 2022;27(2):448-454.
22. Lu Y, Li Y, Deng W, Liu M, He Y, Huang L, Lv M, Li J, Du H. Symptomatic Infection is Associated with Prolonged Duration of Viral Shedding in Mild Coronavirus Disease 2019: A Retrospective Study of 110 Children in Wuhan. Pediatr Infect Dis J. 2020;39(7):e95-e99.