

CLINICAL ANALYSIS OF COVID-19 INFECTIONS IN CHILDREN WITH CANCER IN A TERTIARY CARE HOSPITAL IN BANGLADESH

ISLAM S¹, AKTER M², AHMMED MT³, ARA Z⁴, RAHMAN SMR⁵ BASHER AKMK⁶, NAHAR K⁷, MORSHED AKMA⁸

Abstract:

Background: Children suffering from cancer are more vulnerable than others. This study performed to outline the clinical characteristics and outcome of children with cancer with severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) infection in Dhaka Medical College Hospital, Dhaka.

Methods: Clinical data and epidemiologic history of 24 children with cancer with laboratory-confirmed COVID-19 infection by real-time reverse transcription-PCR (RNA-PCR) were admitted in the Dhaka Medical College Hospital, Dhaka from May, 2020 to June, 2020. Clinical data and epidemiologic history of these patients were retrospectively collected and analyzed.

Results: Among the 24 cases, 16 (67%) were males and 8 (33%) were females. The median age was 5 years (range 0.11–12 years). The most common symptoms were fever (11 cases, 45%) and runny nose (8 cases, 33%), cough (8 cases, 33%), 6 (24%) were asymptomatic. Acute Lymphoblastic Leukemia were the most common (50%) and second most were Wilms tumor (17%). Among the 24 cases, on admission, 17 (71%) had normal white blood cell counts, while only 2 (8%) more than $10 \times 10^9/L$ and 5 (21%) less than $4 \times 10^9/L$, respectively. 16 cases (67%) had normal neutrophil count and 7 cases (29%) had neutropenia. Lymphocyte counts were normal in 50% cases, lymphocytopenia in 10 (42%). C Reactive protein and serum ferritin raised in 19 (79%) cases, D-dimer raised, prothrombin time, activated partial thromboplastin time raised in 8 (33%) cases. X-ray chest was abnormal in 6 cases (25%). 16 cases (66%) received intravenous antibiotics, 5 cases (21%) needed oxygen therapy and 4 cases (17%) needed corticosteroid. Nineteen (79%) patients were discharged from hospital, 3 cases (13%) were discharged on request and death was 2 cases (8%).

Conclusions: Children at all ages appeared susceptible to COVID-19 and there was significant gender difference. Clinical manifestations of children's COVID-19 cases were generally less severe than those of adult patients. Death rate is more in children with cancer than others.

Key Words: COVID-19, Children, Cancer

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1. Professor Shahnoor Islam, Department of Pediatric Surgery, Dhaka Medical College Hospital, Dhaka.
2. Dr. Mehnaz Akter, Assistant Professor, Department of Pediatric Hematology and Oncology, Dhaka Medical College Hospital, Dhaka.
3. Dr. Md. Tanvir Ahmmmed, Assistant Professor, Department of Pediatric Hematology and Oncology, Dhaka Medical College Hospital, Dhaka.
4. Dr. Zannat Ara, Assistant Professor, Department of Pediatric Hematology and Oncology, Dhaka Medical College Hospital, Dhaka.
5. Dr. S.M. Rezanur Rahman, Assistant Professor, Department of Pediatric Hematology and Oncology, Dhaka Medical College Hospital, Dhaka.
6. Dr. A.K.M. Khairul Basher, Indoor Medical Officer, Department of Pediatric Surgery, Dhaka Medical College Hospital, Dhaka.
7. Dr. Kamrun Nahar, Assistant Registrar, Department of Pediatric Surgery, Dhaka Medical College Hospital, Dhaka.
8. Professor AKM Amirul Morshed, Department of Pediatric Hematology and Oncology, Dhaka Medical College Hospital, Dhaka.

Correspondence: Professor Shahnoor Islam, Department of Pediatric Surgery, Dhaka Medical College Hospital, Dhaka. Mobile No: +8801714497128, Email: shahnoor6989@yahoo.com

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Introduction:

In December 2019, the city of Wuhan in Hubei province which is China's seventh largest city became the center of a pneumonia outbreak of unknown cause with global implications and an ongoing impact. The image depicts severe acute respiratory syndrome (SARS) coronavirus 2 (SARS-CoV-2), previously known as 2019-nCoV, the novel virus that causes coronavirus disease 2019 (COVID-19). World Health Organization declared COVID-19 as a pandemic on March 11, 2020 and till date has attacked almost all (215) the countries and states. As of 29 August, 2020, a total of 24.9 million people affected and 841,290 people killed worldwide.¹

In Bangladesh the first three known cases were reported on March 8, 2020 and first death on March 21, 2020. On 6 May, cases were confirmed in all districts. A total of 306,794 cases affected and 4174 death counted countrywide.¹

Increasing number of children, even infants and newborns, are being infected by SARS-CoV-2 in this COVID pandemic situation.² By comparison with adults, the number of confirmed COVID-19 children is very low. Moreover, children are generally asymptomatic or pauci-symptomatic and their clinical course is shorter than adults. Therefore, children appear to be less susceptible to COVID-19 infection although the reasons are still little known. Hypotheses based on children's vaccines cross reactivity against COVID-19 or on the paucity of angiotensin-converting enzyme-2 (ACE2) cell receptors present on the respiratory mucosa of children as protective factors have not been confirmed.^{3,4} Children are affected around 1 to 5% of diagnosed cases of COVID-19, although children with cancer are considered a high-risk population, data specifically addressing the pediatric oncology population are still limited.^{5,6}

Due to their greater level of immunosuppression patients receiving anticancer treatments can have a higher risk of developing infective complications when compared to healthy people. Even after cessation of their antineoplastic treatment, immunosuppression is reported to last for several months although

its duration is yet to be accurately determined. In addition, it is known that younger children have more persistent immune deficits following chemotherapy, and alterations of the immune system have been reported until 6–12 months following cessation of their antineoplastic treatment.⁷

Current evidence indicates that it is not justified to interrupt or delay pediatric anticancer treatment; however, Cancer Research UK has recently proposed to stop recruiting patients in several cancer clinical trials because clinical staff are being redeployed to frontline COVID-19 care.⁸

Methods*Patients and Methods:*

This retrospective observational study included all 24 children (aged 0-12 years) with cancer with laboratory-confirmed 2019-nCoV infection by real-time reverse transcription-PCR (RT-PCR) from 1st May, 2020 to 30 June, 2020 in the Department of Pediatric COVID unit, Burn and Plastic Surgery Building, Dhaka Medical College Hospital, Dhaka.

The patient's age, sex, symptoms and signs, hematological and biochemical parameter, disease patterns, distribution of diseases, treatment plan and outcome were collected through a review of medical records observed. COVID-19 test done by RT PCR technique in Virology Department of Dhaka Medical College Hospital, Dhaka and test positive was considered as corona virus positive. Hematological and biochemical parameter were observed by standard measurements. All children were admitted for isolation and treatment with ensuring sufficient calories and water intake; maintain water-electrolyte balance and monitoring vital signs and oxygen saturation; keeping respiratory tract unobstructed and inhaling oxygen when necessary. They were in regular follow up. Data were analyzed. Approval was obtained by the local Ethical Committee.

Statistical analysis of data:

Descriptive statistics were used to summarize the data. All statistical analyses were performed using SPSS (statistical Package for the social sciences) version 19.0 software (2010; SPSS Inc., Chicago, IL) , expressed as table and diagram.

Results:

Total 24 COVID -19 positive children (0-12years) with cancer patients were enrolled in this study. All the admitted patients treated as COVID -19 positive.

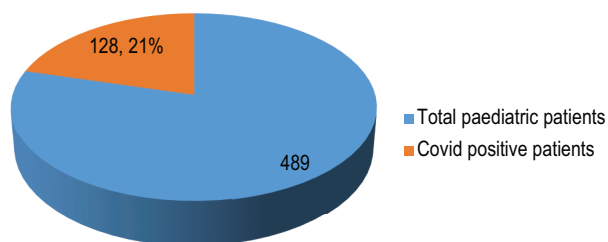


Fig.-1: Number of COVID -19 positive pediatric patients among the total pediatric patients.

Total pediatric patients in the month of May, 2020 and June, 2020 were 489, among them 128(21%) pediatric patients were COVID positive (Figure-1)

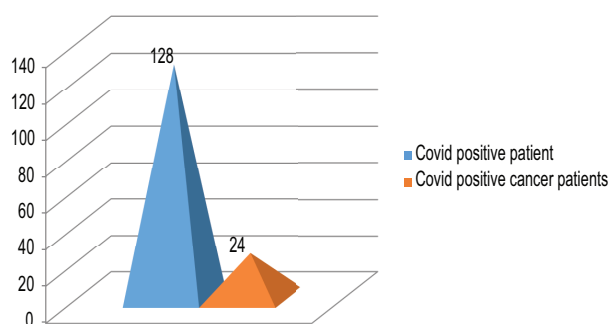


Fig.-2: Number of COVID-19 positive children with cancer among the COVID-19 positive pediatric patients.

Out of 128 COVID-19 positive patients, COVID positive pediatric cancer patients were 24(18.75%) (Figure-2).

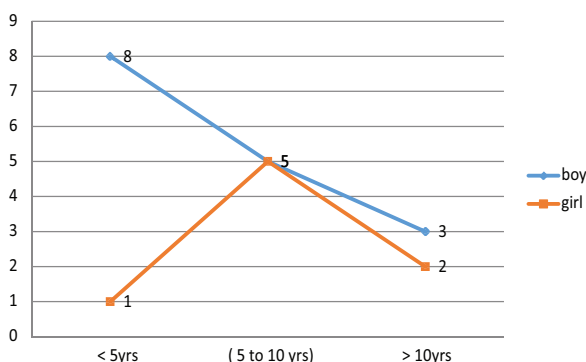


Fig.-3: Age and sex distribution of children with cancer with COVID-19 infection

Age and sex distribution of COVID positive children with cancer showed that maximum number of patients 10 (42%) were in the age group 5 to 10 years, followed by 9 (38 %) in the age group of less than 5years and the range was from 1 years to 12years (Figure- 3).

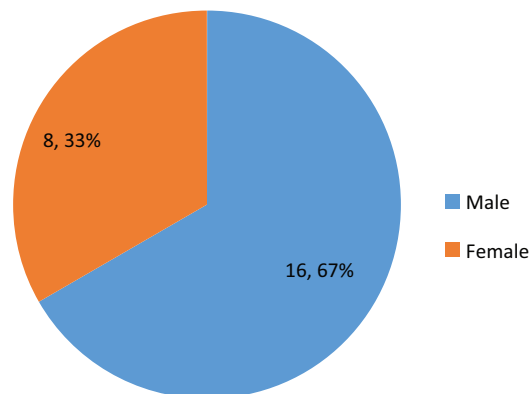


Fig.-4: Sex distribution of COVID-19 infections in children with cancer

Sex distribution of covid-19 positive children with cancer showed that 16 (67%) were male and 8 (33%) were female (Figure-4).

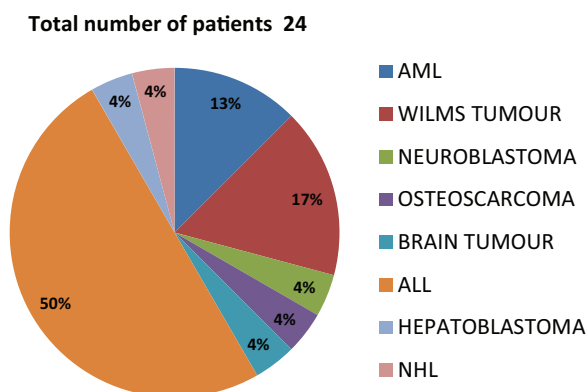


Fig.-5: Disease pattern with percentages of children with cancer with Covid-19 infection.

The distribution of disease pattern with COVID-19 positive pediatric cancer patients showed that 12 (50%) patients were ALL, 04 (17%) patients were wilm’s tumour, 02 (13%) patients were AML and 01 (04%) patients were neuroblastoma, osteosarcoma, brain tumour, hepatoblastoma and other malignencies (Figure - 5)

The distribution of clinical parameters among study population showed that 11 (45%) patients presented with fever, 08 (33%) presented with Running nose and cough, 05 (21%) patients had

difficulty in breathing, 01 (1%) patients had diarrhea and body ache, 06 (25%) patients had asymptomatic (Table I).

Table I

Clinical characteristics of COVID-19 in children with cancer

Symptoms and signs	Total (n=24)	Percentage (%)
Fever	11	45%
Running nose	8	33%
Cough	8	33%
Difficulty in breathing	5	21%
Diarrhoea	1	4%
Bodyache	1	4%
Asymptomatic	6	25%

Table II

Hematological and Laboratory features of COVID-19 positive children with cancer

Investigations	Total n =24	Percentage (%)
White blood cell count, x10 ⁹ /L		
Increased (>10)	2	8
Normal (4-10)	17	71
Decreased (<4)	5	21
Neutrophil count, x10 ⁹ /L		
Increased	1	4
Normal	16	67
Decreased	7	29
Lymphocyte count, x10 ⁹ /L		
Increased	2	8
Normal	12	50
Decreased	10	42
C- reactive protein (1-11mg/L)		
Normal	5	21
Raised	19	79
Serum Ferritin		
Normal	5	21
Increased	19	79
D-Dimer		
Normal	16	67
Raised	8	33
Prothrombin Time(PT)		
Increased	8	33
Normal	16	67
Activated Partial Thromboplastin Time(APTT)		
Increased	8	33
Normal	16	67
Chest X-ray		
Normal	18	75
Abnormal	6	25

In the 24 cases, 17 (71%) cases had normal white blood cell counts, while only 2 (8%) cases had leukocytosis and 5 (21%) cases had leukopenia. Neutrophil counts were normal in 16 (67%) cases, neutropenia in 7 (29%) cases. Lymphocyte counts were normal in 12 (50%) cases, lymphocytosis in 2 (8%) cases, lymphocytopenia in 10 (42%) cases. C-reactive protein (CRP) was raised in 19 (79%) cases, serum ferritin was raised in 19 (79%) cases. D-Dimer, PT and APTT were raised in 8 (33%) cases. X-ray chest normal in 18 (75%) cases, abnormal in 6 (25%) cases. All the children's liver function test, renal function test was normal (Table-II).

Table III

Drugs and supportive treatments with COVID-19 positive children with cancer

Treatment	N=24	Percentage(%)
Azithromycin	8	33%
Intravenous antibiotic	16	66%
Ivermectin	3	13%
Corticosteroid	4	17%
Oxygen support	5	21%
Blood & blood product	15	63%
Zinc and Vitamin C	24	100%

Treatment with drugs and supportive treatment of study populations showed that 08 (33%) patients treated with oral azithromycin, 16 (66%) patients with intravenous antibiotics, 03 (21%) patients with ivermectin, 04 (17%) patients with corticosteroid, 24 (100%) patients with zinc and vitamin C, 15 (63%) patients with blood and blood products, 05 (21%) patients with oxygen support (Table - III).

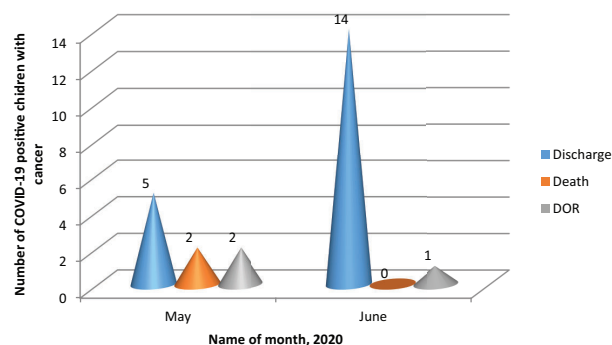


Fig.-6: Outcomes of COVID-19 positive children with cancer

In this study, 19 (79%) patients were cured and discharged after receiving the COVID-19 negative reports, 3 (13%) was discharged on request and there was 2 (8%) deaths. Total 4(3.8%) died who had no malignant disease.

Discussion:

The mortality and morbidity of COVID 19 infection were observed in children was lower than that in adults. It remains a mystery why the mortality and morbidity are lower in children, especially young children, as compared with adults. It is possible that since there are other coronavirus-induced upper respiratory tract infections every year and children are susceptible groups, this may provide some immunity to the COVID 19. However, with increasing of age, this immunity may be gradually lost.

Total pediatric patients in the month of May, 2020 and June, 2020 were 489, among them 128(21%) pediatric patients were COVID positive (Figure-1). Out of 128 COVID positive pediatric patients, COVID positive pediatric cancer patients were 24(18.75%) which were enrolled in this study. Out of 24 patients 22 patients were alive, 02 patients died, 03 patients discharged on request. All the admitted patients treated as COVID -19 positive infection.

Bradley Gampel Alexandre G et al⁹ shown the mean age of COVID-19 patients 10.2 years (range 5 months to 20 years) and Elena Cela et al¹⁰ shown mean age 10.6 yrs(range 0-18). In our study maximum number of patients 10 (42%) were in the age group 5 to 10 years, followed by 9 (38%) in the age group of less than 5 years and the range was from 1 years to 12years. Both the studies were similar to our study.

In this study, sex distribution of covid-19 positive children with cancer showed that a trend toward higher COVID-19 positive infection was observed in males 16 (67%) than females 8 (33%) which is similar with study of Bradley Gampel Alexandre G et al . In Bradley Gampel Alexandre G et al , males appeared three times more likely to have positive test results compared with females and other study in Madrid shown 1(7%) out of 15 patients are female. But the mechanisms underlying the

observed sex discrepancy are still unknown in both studies.^{9,10} Madrid study is far different from our study.

In our study the distribution of disease pattern with COVID-19 positive patients, 14(58%) were haematological malignancy and 10(42%) were solid tumor. Among them 12 (50%) patients were acute lymphoblastic leukemia, 04 (17%) patients were Wilms' tumor, 02 (13%) patients were acute myeloid leukemia and 01 (04%) patients were neuroblastoma, osteosarcoma, brain tumor, hepatoblastoma and other malignancies. In Madrid study 11(73%) patients were hematological cancer and 46% were acute lymphoblastic leukemia. This disease distribution is nearly similar to our study.¹⁰

In this study, the most common symptoms were fever (45%), running nose and cough (33%), asymptomatic (25%), difficulty in breathing (21%), diarrhea and body ache (1%). In Bradley Gampel Alexandre G et al, study showed that the most common symptoms were fever (68%), cough (47%), dyspnea (37%) and Elena Cela et al, shown fever 10(66%), cough 6(40%), both are similar to our study.^{9,10}

In this study neutrophil count normal in 16 (67%) cases, neutropenia in 7 (29%) cases. Lymphocyte count normal in 12 (50%) cases, lymphocytosis in 2 (8%) cases, lymphocytopenia in 10 (42%) cases. But Ke Bai et al shown that 100% patient were normal Lymphocyte count.² CRP raised in 19 (79%) cases in our study but others have 88% were normal which is not similar to our study.² X-ray chest normal in 18(75%) cases, abnormal in 6(25%) cases in this study which is similar to the study of Elena Cela et al (Normal 66%).¹⁰

Treatment with drugs and supportive measures of study population showed that 08 (33%) patients treated with oral azithromycin, 16 (66%) patients with intravenous antibiotics, 03 (21%) patients with ivermectin, 04 (17%) patients with corticosteroid, 24 (100%) patients with zinc and vitamin C, 15 (63%) patients with blood and blood products, 05 (21%) patients with oxygen support. In Madrid study none get ivermectine , they used Hydroxychloroquine (73%), different combinations of azithromycin, corticosteroid and remdesivir(20%) and 29 %

got no treatment. Only 20% patients received Oxygen support. Use of hydroxychloroquine and ivermectin is the basic difference between two studies.¹⁰

In this study, 19 (79%) patients were cured and 2 (8%) patients were died. But in Madrid study there was no death.¹⁰

The case number was too small and study period also limited, these are the limitation of our study.

Conclusions:

Children at all ages appeared susceptible to COVID-19 and there was no significant gender difference. Although clinical manifestations of children's COVID-19 cases were generally less severe than those of adults' patients, young children, particularly infants, were vulnerable to infection. The mortality and morbidity in covid-19 infection in children with cancer is lower than in adults. Death rate is more in children with cancer than others.

Conflict of interest: None.

Acknowledgment:

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References:

1. COVID-19 Coronavirus Pandemic: <https://www.worldometers.info/coronavirus/> Accessed 29th August, 2020.
2. Bai K, Liu W, Liu C, Fu Y, Hu J and Qin Y et al. Clinical Analysis of 25 COVID-19 Infections in Children. *Pediatric Infectious Disease Journal* 2020;39:e100–e103.
3. Yu Y, Jin H, Chen Z, Yu QL, Ma YJ, Sun XL and Wan et al. Children's vaccines do not induce cross reactivity against SARS-CoV. *Journal of Clinical Pathology* 2007;60(2):208–211.
4. Lu R, Zhao X, Li J, Niu P, Yang B and Wu H, Wang et al. Genomic characterization and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet* 2020; 395(10224): 565-574.
5. Bouffet E, Challinor J, Sullivan M, Biondi A, Rodriguez-Galindo C, Pritchard-Jones K. Early advice on managing children with cancer during the COVID-19 pandemic and a call for sharing experiences. *Pediatric Blood & Cancer* 2020:e28327.
6. Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. *Acta Paediatr.* 2020
7. Ruggiero A, Romano A, Attina G. Facing the COVID-19 outbreak in children with cancer. *Drugs in Context* 2020;9: 2020-4.
8. Thornton J. Clinical trials suspended in UK to prioritize covid-19 studies and free up staff. *BMJ.* 2020;368:m1172.
9. Bradley GAG et al. COVID 19 disease in New York city pediatric hematology and oncology patients. *Pediatr Blood Cancer* 2020;67(9): <https://doi.org/10.1002/pbc.28420>. Accessed date 26th August, 2020.
10. Elena Cela, Marta Baragano, Victor Galan, Cristina Mata, Alba Pereto and Luis Madero. *Pediatr Blood Cancer* 2020; e 28397. <https://doi.org/10.1002/pbc.28397>. Accessed date 28th August, 2020.