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COVID-19 Infection in Children and Adolescents with Cancer in Bangladesh Shishu Hospital and Institute

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Abstract **Original Research Article**

Introduction: Children with cancer are frequently immunocompromised. While children are generally thought to be at less risk of severe SARS-CoV-2 infection than adults, comprehensive population-based evidence for the risk in children with cancer is unavailable. We aimed to produce evidence of the incidence and outcomes from SARS-CoV-2 in children with cancer attending at Bangladesh Shishu Hospital and Institute in Dhaka, Bangladesh. ***Objective:*** This study aimed to determine the rate of COVID-19 infection in children with cancer. ***Methods:*** This was a prospective observational study done in Bangladesh Shishu Hospital and Institute. We include the patients of leukemia and other malignancies attending our Hematology department for treatment. We have 400 cases of acute leukemia and other malignancies. All patients who fulfilled the inclusion criteria were screened for eligibility and were enrolled in the study and who do not have any exclusion criteria and parents provide informed consent. At enrollment detailed history was taken, thorough clinical examination performed and findings was recorded in a questionnaire. For all enrolled cases, Complete blood count, RT PCR for COVID-19 or Rapid antigen test for COVID-19, CXR, LFT, RFT, was performed. After 10 days of COVID positive cases, 2nd sample of RT PCR for COVID-19 or Rapid antigen were done. ***Results:*** Among the 400 patients COVID positive was found 32 patients. Remaining 368 patients are COVID negative. Among the 32 positive patients 18 needs hospitalization. Pulmonary infection was found in 10 patients. 12 patients need oxygen therapy. Two patients need respiratory support. Among 32 patients 2 patients was expired. Chemotherapy was interrupted in 20 patients. ***Conclusion:*** Children with cancer with SARS-CoV-2 infection appear at increased risk of severe infection compared to the general paediatric population, it may be due to their low immunity in compared to healthy children.

Keywords: Acute leukemia, Prospective observational study, SARS-CoV-2 infection, RT PCR, Rapid antigen test.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) caused by the new β-coronavirus severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) currently constitutes the leading and overwhelming health issue worldwide. SARS-CoV-2 can replicate in different tissues, with the respiratory system and gastrointestinal tract being the most important systems involved. SARS-CoV-2 infection has two different phases. In the first phase, viral replication occurs, and in severe cases, it is followed by a second phase characterized by a dysregulated immune response with tissue damage [1, 2]. Mechanisms underlying lung injury in both phases are different but can result in irreversible lung damage and death due to respiratory failure. COVID-19 severity clearly depends on the age of the individual—children present milder symptoms in comparison with the adult population. Mortality among children with COVID-19 is currently estimated at less than 0.03% [3]. Furthermore, the death rate is low in the youngest age group, but age below 1 month, male sex, pre-existing medical conditions, and presence of lower respiratory tract infection signs or symptoms at presentation are associated with higher complication rates [4-6], for immunocompromised children, as many as 77% show an asymptomatic course of SARS-CoV-2 infection [7]. This study was performed to assess the course of SARS-CoV-2 infection among Bangladeshi children with hematological or oncological malignancies who have been actively treated with systemic therapy and its impact on the timing of cancer therapy. We

hypothesized that COVID-19 infection increases nonrelapse mortality and have a negative impact on the continuation of chemotherapy.

MATERIALS AND METHODS

Study Site

This was a prospective observational study done in Bangladesh Shishu Hospital and Institute, Sher-e-Bangla Nagar, Dhaka-1207, Bangladesh over 24 months from 1st July 2020 to 30th June 2022.

Study Population

We include the patients of leukemia and other malignancies attending in Hematology department of BSH&I for treatment. We excluded the patient with acute leukemia getting irregular treatment. Our sample size was 400.

Study Procedure

All leukemia and other malignancies patients who fulfilled the inclusion criteria were enrolled in the study and who do not have any exclusion criteria and parents provide informed written consent. At enrollment detailed history was taken, thorough clinical examination performed and findings was recorded in a questionnaire. For all enrolled cases, Complete blood count, RT PCR for covid 19 or Rapid antigen test for covid 19, CXR, LFT, RFT, was performed. After 10 days of covid positive cases, 2nd sample of RT PCR for covid 19 or Rapid antigen were done.

Data Analysis

The data was analyzed according to standard procedure. SPSS version 16.0 for Windows (SPSS Inc, Chicago, IL, USA) software was used for data entry and analysis. Results of the findings were verified by conducting standard tests for significance (p-value < 0.05), including unpaired student T-test and Chi-square (χ^2) tests, as appropriate.

Ethical Issue

After explaining the procedures of the study to the parents/caregivers, informed written consent was taken. Assurance was given to the parents about the investigations that have no risk & treatment strategy would not be hampered during this study period. All financial cost was paid by the researcher. Permission from ethical board of Bangladesh Shishu Hospital & Institute was taken prior to the work.

RESULTS

Table 1: Age distribution of study population.

Age	Number	Percentage
2-3 years	185	46.25%
3-6 years	150	37.5%
6-9 years	45	11.25%
>9years	20	05%
Total	400	100%

** Among all 400 cases 185(46.25%) were within 2 to 3 years age group, 150(37.5%) were 3-6 years age and 45(11.25%) were 6-9 years age and 20(5%) were >9 years age.

Table 2: Gender distribution of study population.

Sex	Number	Percentage
Female	196	49%
Male	204	51%
Total	**400**	**100%**

** Among all 400 patients, 204 (51%) male & 196(49%) female patients, which indicate male predominant. The ratio is M: F-1.04:1.

Table 3: Characteristics of study population.

Patient characteristics		Number of patient	Percentage
Fever during admission	**Present**	240	60%
	Absent	160	40%
Bone pain	**Present**	135	33.75%
	Absent	265	66.25%
Bleeding	**Present**	155	38.75%
	Absent	245	61.25%
Lymphadenopahy	**Present**	175	43.75%
	Absent	225	56.25%
Splenomegaly	**Present**	186	46.50%
	Absent	214	53.50%
Hepatomegaly	**Present**	176	44%
	Absent	224	56%
Jaundice	**Present**	24	06%
	Absent	376	94%
Vomitting	**Present**	24	6%
	Absent	376	94%

**Among all 400 patients, Fever present in all 240 cases(60%), bone pain present in 135 cases(33.75%), bleeding present in 38.75% cases, lymphadenopathy present in 43.75% cases, splenomegaly in 46.50%,hepatomegaly in 44% cases, jaundice present in 6% cases and vomiting also in 6% cases.

Table 4: Hemoglobin (Hb) concentration among study population.

Hb%	Number	Percentage
< 6 gm/dl	200	50%
6-10 gm/dl	175	43.75%
>10 gm/dl	25	6.25%
Total	**400**	**100%**

**In this study 200(50%) patients Hb% was <6 gm/dl, 175(43.75%) Hb% 6-10 gm/% at the time of diagnosis and remaining 25(6.25%) cases Hb% was >10 gm%.

Table 5: Total Leucocyte count in study population during admission.

Total Leucocyte count	Number of patients	Percentage
<2500/cumm	60	15%
2501-5000/cumm	85	21.25%
5001-10000/cumm	75	18.75%
10001-20000/cumm	130	32.50%
20001-50000/cumm	30	7.50%
> 50000/cumm	20	05%
Total	**400**	**100%**

**Most commonly TC of WBC was 10000-20000/cumm in 130(33.50%) cases at diagnosis, marked leucopenia (<2500/cumm) was found only in 60(15%) cases.

Table 6: Level of SGPT in study population during COVID infection.

Level of SGPT(U/L)	Number of patients	Percentage
10-100	150	37.50%
100-200	175	43.75%
200-300	40	10%
>300	35	8.75%

**In this study 175(43.75%) patient's SGPT was 100-200 U/L, 150(37.5%) patients SGPT was within 100 U/L during treatment.

Table 7: Level of S creatinine in study population during COVID infection.

Level of S creatinine	Number of patients	Percentage
40-80 µ mol/lit	350	87.50%
80-110 µ mol/lit	48	12%
>110 µ mol/lit	02	0.5%

**In this study majority patients,350(87.50%) patients S creatinine was 40-80 µ mol/lit and only 2(0.5%) patients S creatinine was >110 µ mol/lit during treatment.

Table 8: Level of S.bilirubin in study population during COVID infection.

Level of S.bilirubin	Number of patients	Percentage
<1 mmol/L	375	93.75%
1-2 mmol/L	15	3.75%
2-3 mmol/L	08	02%
>3 mmol/L	02	0.5%

**In this study 375(93.75%) patients S.bilirubin was <1 mmol/L,15(3.75%) patients S.bilirubin was 1-2 mmol/L during treatment.

Table 9: Type of malignancy among study population.

Type of malignancy	Number of patients	Percentage
ALL	199	49.75%
AML	33	8.25%
Wilms tumor	68	17%
Neuroblastoma	34	8.50%
NHL	25	6.25%
Hodgkin lymphoma	19	4.75%
Germ cell tumor	09	2.25%
Rhabdomyosarcoma	07	1.75%
Hepatoblastoma	06	1.50%

**Majority patients 199(49.75%) was ALL, 68(17%) were wilms tumor and only 6(1.5%) were Hepatoblastoma.

Table 10: Number of covid 19 positive in different malignancy.

Type of malignancy	Number of patients	Covid 19 positive	Percentage
ALL	199	10	5.02%
AML	33	4	12.12%
Wilms tumor	68	6	8.82%
Neuroblastoma	34	3	8.82%
NHL	25	3	12%
Hodgkin lymphoma	19	1	5.26%
Germ cell tumor	09	1	11.11%
Rhabdomyosarcoma	07	2	28.57%
Hepatoblastoma	06	2	33.33%

**Among study population 10(5.02%) ALL patients develop covid 19 infection and in Germ cell tumor and Hodgkins lymphoma 1 patient form each group found covid 19 positive. The overall incidence rate of covid 19 in our study population was 8%.

Table 11: Pulmonary infection among COVID-19 positive (32) patients.

Pulmonary infection	Number of patients	Percentage
Infection present	20	62.50%
Infection absent	12	37.50%

**In this study among 32(8%) COVID-19 positive patients, pulmonary infection found in 62.50% cases.

Table 12: Death rate among COVID-19 positive (32) patients.

Characteristics of patients	Number of patients	Number of death	Percentage
COVID positive	32	2	6.25%
COVID negative	368	0	0

**In this study among 32(8%) COVID-19 positive patients, 2 patients died due to COVID-19 infection, the rate was 6.25%.

DISCUSSION

Among all 400 cases 185(46.25%) were within 2 to 3 years age group, 150(37.5%) were 3-6 years age and 45(11.25%) were 6-9 years age and 20(5%) were >9 years age. Fever present in 240(60%) patients.The duration of fever ranged from 7 days to 96 days. Among them 20(8.25%) were less than 10 days, 175(73%) were 10-50 days & 45(18.75%) were more than 50 days. Bone pain present in 135(33.75%) cases and absent in 265(66.25%), which coincide with previous study where it was 65.6% [7]. But in western study it was 25% [8]. Site of bone pain mostly were in multiple site 38 (28.15%) predominantly in lower limbs 97(71.85%) which coincide with previous study. Bleeding manifestation was present in 155(38.75%) case only. Bleeding sites involved mostly in the gum & skin in about 125(80.64%) it is always secondary to severe thrombocytopenia, caused by marrow failure. Highest risk of bleeding in patient with platelet count <20,000/cumm. Duration of bleeding in most case was less than 5 days (40%). Pallor was present in 375(93.75%) of case but severity varied. Anemia was due to marrow failure which was almost due to direct reduction in stem cells and may associate with ineffective erythropoiesis [9]. There was no patient found where there was H/O cancer in the family.

Lymphadenopathy was present in 175(43.75%) & absent in 225(56.25%) patients. In majority of the patients cervical lymph nodes were involved in 143(81.71%) others were generalized (13.3%), which coincide with Western study where Lymphadenopathy was in 50% of cases [10]. Splenomegaly was found in 186(46.50%) cases & absent in 214(53.50%). It didn't coincide with the previous study where it was 68.8% [8]. Most of the spleen measured within 3-4 cm of the 66(76.74%) cases and below 2cm in 20(23.26%). In this study, 200 (50%) patients Hb% was <6 gm/dl (40%) at the time of diagnosis, Hb% was >10 gm% in 25(6.25%) cases. In our study among 400 patients majority205 (51.25%) total leucocyte count during admission was between 5000 to 20000/cumm. In our study among 400 patients only 24(12%) having jaundice and vomiting. Our study not correlated to previous study [11-13] as they found a rare presentation of leukemia is jaundice. Chemotherapeutic agent's causes increase hepatic enzymes. However, an increasing number of evidence indicates that it has risk of elevation of the liver enzyme, cholestatic abnormalities and liver injury as adverse effect [14, 15] and the mechanism of its hepatotoxicity appears to be immunologically mediated [16].

The serum bilirubin, AST, ALT, and ALP are the most sensitive biochemical markers employed in the diagnosis of hepatic dysfunction [17]. In our 400 patients, 215(53.75%) having SGPT within 100-300 U/L during treatment, but S. bilirubin was increased only in 25(6.25%) patients. It correlated to previous study by *Ishak and Zimmerma* [18]. In this study we found that chemotherapeutic agents produced a less significant increase bilirubin. The obtained results were not similar to those obtained by others [19]. In our 400 patients, 350(87.50%) having S creatinine within 40-80 µ mol/lit, but only 2 patients having S creatinine >110 µ mol/lit during treatment. It is not correlated with previous study by Liezl Du Plessis, Shahrad Rod Rassekh and Cherry Mammen [20], they found s creatinine high in 43.4% AML children during chemotherapy. In our 32 COVID-19 cases, 20(62.50%) having pulmonary infction evidenced by CxR/Chest CT. Our result is correlated with previous result by Gustavo Nino, Jose Molto, Hector Aguilar *et al.*, [21], they found pulmonary infection in COVID-19 infection patients is 68%. In our study among 400 patients majority, 232(58%) was acute leukemia either ALL or AML. Among 232 leukemia patients 14(6.03%) become covid 19 positive. From these 14 affected cases 2 patients expired, the percentage of death was 14.28%. Dong *et al., [22] study* of 2143 children identified by laboratory tests using a combination of clinical symptoms and exposure status revealed that 34.1% had laboratory- confirmed disease, while the remainder had clinically suspected disease. Contrary to our observation, all children were diagnosed positive on the basis of the RT-PCR laboratory test. The proportion of asymptomatic children found in the literature [23] and observed in our study, extinguishes the thesis of a milder evolution of the disease and a better prognosis in children. Our overall COVID-19 infection rate was 8% and overall death rate was 6.25%.

CONCLUSION

The incidence of COVID-19 infection among children with cancer in Bangladesh Shishu Hospital and Institute is 8% and death rate was 6.25%.Children with cancer with SARS-CoV-2 infection have increased risk of severe infection compared to the general pediatric population, it may be due to their low immunity in compared to healthy children.

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CONFLICT OF INTEREST

The Author has no conflict of interest.

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