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Original Research Article

COVID-19 in PAEDIATRIC ONCOLOGY PATIENTS: INCIDENCE AND SEVERITY OF CLINICAL FEATURES IN CANCER VS. NON-CANCER PATIENTS

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ABSTRACT

Introduction: With the advancements in medical technology, it is now possible to treat deadly diseases like cancer. The drawback of these anticancer treatments is the significantly reduced host's immune response, which makes these individuals more susceptible to infections. In this study, we analyzed the incidence and clinical features of COVID-19 infections among paediatric cancer patients, and the results were compared to those of non-cancer paediatric patients.

Method: This was an observational, retrospective cross-sectional study. For data gathering, patients' charts were retrospectively analyzed from March 2020 to Feb 2021, and the two groups (COVID-19 infections in paediatric cancer and non-cancer patients) were compared to analyze the incidence and severity of SARS-COV-2 infection and severity of clinical features. The Wilcoxon-Mann-Whitney test was used to compare the means of symptoms and severity of symptoms of two groups, keeping the p -value <0.05 as significant.

Result: Out of the total study population (772), 618 patients were diagnosed with cancer. A total of 53 patients (6.8%) were reported positive for COVID-19, with the break of 35 (5.6%) cancer patients, and 18 (11.7%) non-cancer patients. The mean age of cancer patients with COVID-19 was 7.17 years (range 3-17 years) while of non-cancer patients was 10.6 years (range 2-17 years). 22 patients required hospitalization (62.85%) with an average length of stay of 4.45 days. There was a mortality of one cancer patient with COVID-19. In non-cancer patients, no hospitalization was required with zero mortality.

Conclusion: COVID-19 is more common in the general pediatric population while the infection is more severe in pediatric cancer patients.

Keywords: Paediatric Oncology, SARS-COV-2, CA, COVID-19, chemotherapy.

Authors' Contributions

Idea presentation, project supervision, and developed the theory and performed the computations, took the lead in writing the manuscript including abstract, methodology, results, outcomes, discussion, and conclusion BJ. Manuscript writing BJ, QZ, MRJ. Interpreted the results and worked on the manuscript in terms of methodology, discussion, and conclusion MTA, BJ, MRJ, and QZ. Verification of the analytic calculations and the numerical simulations MTA. Conceived the presented idea MRJ, QZ. Designed the model and the computational framework, and analyzed the data BJ, QZ. Designed the figures MTA, BJ, QZ. All authors provided critical feedback and helped shape the research, analysis, and manuscript.

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Conflict of Interest:

Dr. Bakht Jamal declares on the behalf of co-authors that this article entitled "COVID-19 in paediatric oncology patients: Incidence and severity of clinical features in cancer vs. non-cancer patients" has no conflict of interest in publishing our manuscript in the 'Canadian Journal of Applied Sciences'. If any conflicts of interest arise, 'Canadian Journal of Applied Sciences' journal editors will not be made liable.

INTRODUCTION

The paediatric age group comprises 1-2% of cases of COVID-19 worldwide.¹⁻⁴ However, for some unknown reasons, this virus does not lead to serious signs/symptoms in the paediatric population and most of the affected patients remain asymptomatic with a few reported deaths secondary to SARS-COV-2 infection. Studies from China established that only 0.6% of patients developed the severe disease after contracting SARS-COV-2 infection.⁵ In this study, it is tried to analyze the incidence and severity of SARS-COV-2 infection in paediatric patients undergoing active treatment as compared to the immunocompetent population. Secondly, to determine the incidence and severity of clinical features in cancer vs. non-cancer patients.

MATERIAL AND METHODS

This was an observational, retrospective cross-sectional study, conducted in two tertiary care oncology setups of the same organization, the Shaukat Khanum Memorial Cancer Hospital and Research Center (SKMCH&RC), Lahore, and Peshawar, Pakistan. All paediatric oncology patients up to 18 years of age with confirmed COVID-19 infection undergoing active chemotherapy and COVID-19 positive non-cancer paediatric patients from March 2020 to February 2021 were included. The diagnosis was made based on a positive RT-PCR test. Data were obtained through the electronic hospital information system of the hospital. The formal approval was taken from the Institutional Review Board of SKMCH&RC, Lahore, Pakistan.

Patients who had received chemotherapy more than 4 weeks ago or with clinical features suggestive of COVID-19 without a positive nasopharyngeal RT-PCR were excluded. The study variables included age, gender, type of cancer, clinical features on presentation, pre-procedure screening, and severity of disease symptoms during the course of illness. Symptoms were classified as mild, moderate, or severe.

Mild symptoms included occasional cough without any breathing difficulty or saturation drop or no symptoms at all and the diagnosis was made based on routine pre-procedure screening. The moderate disease was defined as children having respiratory signs/symptoms along with fever and radiological evidence of pneumonia with normal saturation. Whereas the severe disease included critically unwell patients, dropping saturation with impending respiratory failure requiring mechanical ventilation and ICU care. As per presenting signs and symptoms, SARS COV-2 infection among the paediatric population was classified as; asymptomatic upper respiratory tract infection (URTI), mild lower respiratory tract symptoms, severe pneumonia, and gastrointestinal symptoms.^{6,7} The expert's consensus statement

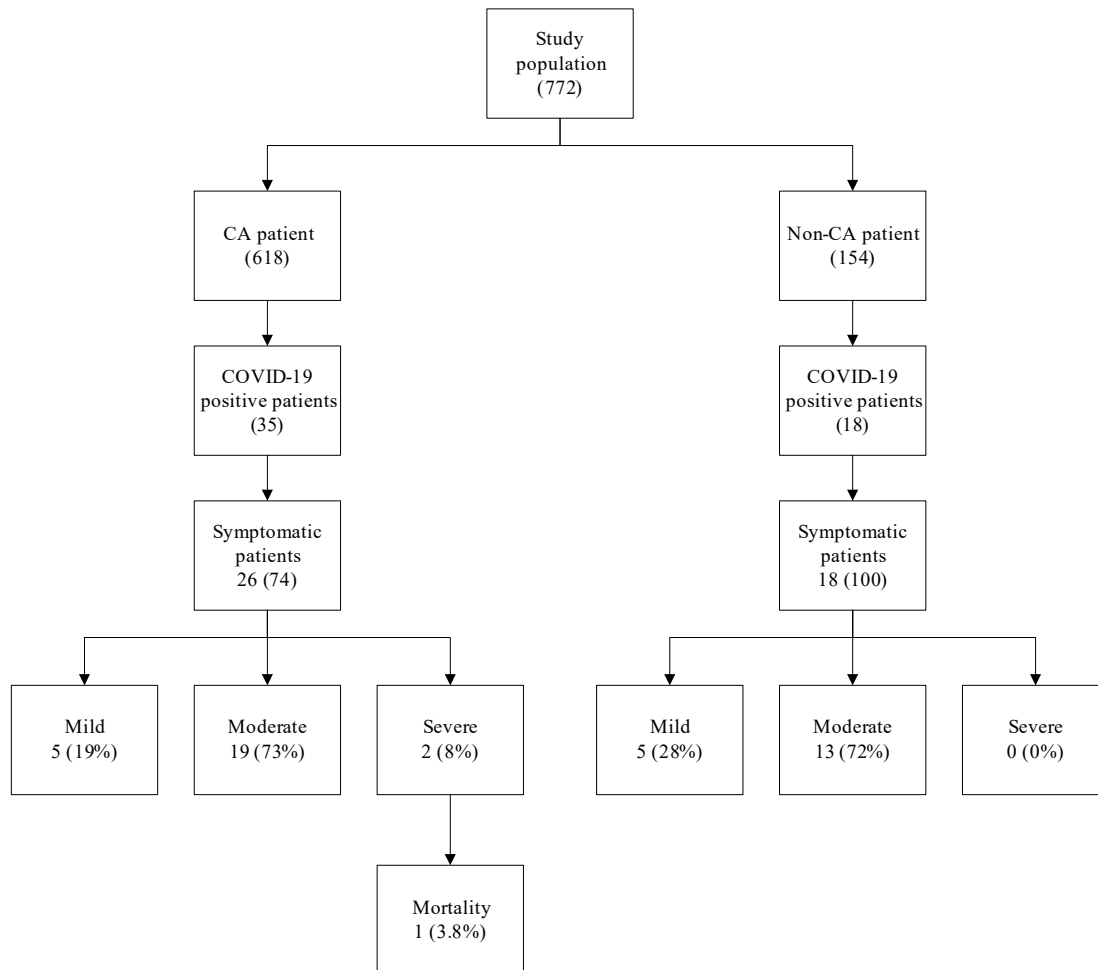
from the National Health Committee on Novel Coronavirus Infection Pneumonia Diagnosis and Treatment Standards were used for clinical classification.⁶

Data were analyzed statistically through SPSS tool version 23. The Wilcoxon-Mann-Whitney test was applied to compare the means of symptoms (symptomatic and asymptomatic) and severity (mild, moderate, and severe) of two independent groups of COVID-19 cancer and non-cancer patients. We did not assume that the COVID-19 non-cancer patient symptoms and severity, our dependent variables, are interval and normally distributed. The significance level was demarcated as a two-tailed p-value <0.05.

RESULTS

The mean age of cancer patients with COVID-19 was 7.17 years (range 3-17 years) while of non-cancer patients 10.6 years (range 2-17 years). Out of the total study population (772), 618 patients were diagnosed with cancer. A total of 53 patients (6.8%) were reported positive for COVID-19, with the break of 35 (5.6%) cancer patients, and 18 (11.7%) non-cancer patients. Please see figure 1.

Twenty-two COVID-19 positive cancer patients required hospitalization (62.85%), an average length of stay of 4.45 days with a mortality rate of 3.8% (one patient only). In non-cancer patients, no hospitalization was required with zero mortality. Common clinical features of our cohort and the underlying cancers are enumerated in table 1.



CA = Cancer; Non-CA = non-cancer

Figure 1: Outlining the selection and severity of symptoms of the study population.

It was observed that 74% of the COVID-19 cancer patients were symptomatic, while all (100%) COVID-19 non-cancer patients had symptoms with a significant difference of a p-value of 0.019. The severity of symptoms in COVID-19 cancer patients varied from 19%, 73%, and 8%, and was categorized as mild, moderate, and severe respectively. A significant difference was found in the 'moderate and 'severe' category (p-value 0.017, 0.019 respectively) in between two groups, while the 'mild' category was insignificant (p-value 0.499) please see table 2.

Table 1: Age and types of cancer in the study population

Intent	Total	COVID-19	
		CA	Non-CA
	(N=53)	(n=35)	(n=18)
	No. (%)		
Age (in years)			
00-06	29 (55)	25 (71)	4 (22)
07-12	10 (19)	3 (9)	7 (39)
13-17	14 (26)	7 (20)	7 (39)
Type of Cancer	-		
Pre-B-ALL		17 (48.5)	
Burkitt's lymphoma		4 (11.4)	
Ewing's sarcoma		3 (8.5)	
Wilms's tumor		2 (5.7)	
Hodgkin's lymphoma		2 (5.7)	
Rhabdomyosarcoma		1 (2.8)	
Hepatoblastoma		1 (2.8)	
T-cell lymphoblastic lymphoma		1 (2.8)	
Germ cell tumor		1 (2.8)	
Osteosarcoma		1 (2.8)	
Brain tumor		1 (2.8)	
Diffuse large B cell lymphoma		1 (2.8)	

Pre-B-ALL = Precursor-B-acute lymphoblastic leukemia; CA = Cancer; Non-CA = non-cancer

Table 2: Comparison of symptoms and severity of COVID-19 cancer and non-cancer patients

Intent	Total	COVID-19		p-value
		CA	Non-CA	
	(N=53)	(n=35)	(n=18)	
	No. (%)			
Symptoms				
Symptomatic	44 (83)	26 (74)	18 (100)	0.019
Asymptomatic	9 (17)	9 (26)	0 (0)	
Severity of Symptoms				
Mild	24 (54)	5 (19)	5 (28)	0.499
Moderate	18 (41)	19 (73)	13 (72)	0.017
Severe	2 (5)	2 (8)	0	0.019
Symptoms				
Chills	3 (6)	1 (3)	2 (11)	0.223
Cough	26 (49)	15 (43)	11 (61)	0.212
Crepts	6 (11)	6 (17)	0	0.065
Desaturation	7 (13)	7 (20)	0	0.044
Fever	32 (60)	21 (60)	11 (61)	0.938
Loose motion	8 (15)	8 (23)	0	0.029
Myalgias	12 (23)	6 (17)	6 (33)	0.188
Respiratory distress	12 (23)	11 (31)	1 (6)	0.035
Sore throat	13 (25)	6 (17)	7 (39)	0.084

CA = Cancer; Non-CA = non-cancer

DISCUSSION

In the present study, the incidence of common symptoms like fever, cough, sore throat, myalgias, chills, and creptation on chest auscultation was the same among cancer and non-cancer patients with a p-value > 0.05. While a few symptoms like loose stools, drop in oxygen saturation, and shortness of breath are seen more frequently in children on active chemotherapy as compared to non-cancer patients partially because these patients were already having some other ongoing infections as well, with immunocompromised state and when contracted SARS COV-2 these symptoms were more evident in cancer patients

A study was conducted in Wuhan, China in which a total of 1391 children were included. Data analysis showed that 65% had developed pneumonia, particularly those with severe SARS COV-2 infection, 19% were found to have URTI and 16% of the population were asymptomatic.⁸ In comparison, we haven't found any major symptoms except fever (60%) and cough (43%), while 26% of the population were asymptomatic. The slightly higher asymptomatic rate (26% vs 16%) in our populations is still unknown. However, another major research with a sample size of 2135 children, revealed that over 90% of them were asymptomatic, mild, or moderately unwell.⁷ Most common symptoms observed among the symptomatic population were cough, body aches, fever, anosmia, irritability, and abdominal pain.⁵⁻¹¹ Whereas fatigue, rhinorrhea, diarrhea, and vomiting are among the less frequently seen symptoms. Mortality and morbidity secondary to covid 19 inaction have largely spared the paediatric

population, including paediatric haematology and oncology patients. Generally immunocompetent paediatric patients with COVID-19 infection experience less severe signs and symptoms than adults.^{7,12}

It has been observed that the degree of illness varied with age with 0.6% critical cases overall and 11% among infants (under one year of age).⁷ Shock, multi-organ failure, and ARDS (acute respiratory distress syndrome) are among the most commonly seen complications.^{5,8,9} However, generally the complications are less common (less than 02% compared to 05%) among the paediatric population than in adults.^{3,5,8,10} The mortality rate among children with SARS COV-2 is significantly low i.e. 0.05% to 0.07%.^{7,8}

It is evident that viral load directly correlates with disease severity¹³. In contrast to viral dynamics, the immune response to COVID-19, remains undefined, however, the decrease in CD8 T cells and B cells in adults has been correlated with severe COVID 19 and poor response to therapy¹⁴. The CD8 T cells and B cell recovery is associated with moderate disease¹³. Similarly, a decrease in regulatory T cells has also been associated with hyperinflammatory responses in adults¹⁵. Unfortunately, no such detailed study is available on paediatric patients. Despite their generally experiencing milder COVID-19 disease, immunocompetent paediatric patients have a high viral load and maybe shed viruses from the upper respiratory tract and gastrointestinal system for weeks after SARS-COV-2 primary infection.^{16,17} This discrepancy between having milder COVID-19 infection despite having a high viral load and prolonged viral shedding suggests that kids may differ from adults in their immune response to COVID-19. One of the major contributory reasons for severe COVID-19 infection in the paediatric cancer population is chemotherapy. And one of the well-known side effects of these chemotherapeutic agents is compromised immunity, anorexia, and decrease physical strength. Generally, patient on chemotherapy is more vulnerable to getting severe life-threatening illness as compared to non-cancer patients.

CONCLUSION

COVID-19 is more common in the general pediatric population while the infection is more severe in pediatric cancer patients. The possible contributory factors that enhance the symptoms of COVID-19 in cancer patients include compromised immunity, psychological stress, anorexia, and decrease physical strength. Hence, the findings of our study encourage the oncologists to offer special care at the maximum possible level and to assure the safety of admitted patients. Further studies with a larger cohort of patients may potentially help to make healthcare more rational.

REFERENCES

1. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. *JAMA*2020;323:1239-42.
2. CDC COVID-19 Response Team. Coronavirus Disease 2019 in Children - United States, February 12-April 2, 2020. *MMWR Morb Mortal Wkly Rep*2020;69:422-6.
3. Ejaz A. Khan. COVID-19 in children: epidemiology, presentation, diagnosis and management. *JPMMA*. 2020 May;70(5). (ours 01-?omit)
4. Shen K, Yang Y, Wang T, Zhao D, Jiang Y, Jin R, et al. Diagnosis, treatment, and prevention of 2019 novel coronavirus infection in children: experts' consensus statement. *World J Pediatr*. 2020;16(3):223-31.
5. Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. *Acta Paediatr*. 2020;109(6):1088–95.

6. Shen K, Yang Y, Wang T, Zhao D, Jiang Y, Jin R, *et al.* Diagnosis, treatment, and prevention of 2019 novel coronavirus infection in children: experts' consensus statement. *World J Pediatr.* 2020;16(3):223-31.
7. Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, *et al.* Epidemiology of COVID-19 Among Children in China. *Pediatrics.* 2020;145(6):e202007
8. Lu X, Zhang L, Du H, Zhang J, Li YY, Qu J, *et al.* SARS-CoV-2 Infection in children. *N Engl J Med.* 2020;382(17):1663–5.
9. Sun D, Li H, Lu XX, Xiao H, Ren J, Zhang FR, *et al.* Clinical features of severe pediatric patients with coronavirus disease 2019 in Wuhan: a single center's observational study. *World J Pediatr.* 2020;16(3):251-9.
10. Su L, Ma X, Yu H, Zhang Z, Bian P, Han Y, *et al.* The different clinical characteristics of corona virus disease cases between children and their families in China - the character of children with COVID-19. *Emerg Microbes Infect.* 2020;9:1:707-713.
11. Li G, Fan Y, Lai Y, Han T, Li Z, Zhou P, *et al.* Coronavirus infections and immune responses. *J Med Virol.* 2020;92(4):424-432.
12. CDC COVID-19 Response team. Severe outcomes among patients with corona virus disease. United states, Feb 12-March 16 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69(12):343-346.
13. Mehta P, McAuley DF, Brown M *et al.* COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet.* 2020;395:1033-1034
14. Wang H, Zhang L. Risk of COVID-19 for patients with cancer. *Lancet Oncol.* 2020;21(4):e181
15. Qin C, Zhou L, Hu Z, *et al.* Dysregulation of immune response in patients with COVID-19 in Wuhan, China. *Clin Infect Dis.* 2020. <https://doi.org/10.1093/cid/ciaa>
16. Xu Y, Li X, Zhu B, *et al.* Characteristics of pediatric SARS-CoV-2 infection and potential evidence for persistent fecal viral shedding. *Nat Med.* 2020;26(4):502
17. Kam KQ, Yung CF, Cui L, *et al.* A well infant with coronavirus disease 2019 (COVID-19) with high viral load. *Clin Infect Dis.* 2020



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