Predictors of poor outcome in covid-19 infection, in a cohort of pediatric cancer patients, during the second wave in India.

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Abstract

The second wave of COVID 19, far outnumbered the first, in cases and deaths. We report outcome of pediatric cancer patients with COVID-19 during the second wave, from a tertiary center in India. Out of 41 patients who tested positive; 51% were asymptomatic, 36% had mild symptoms, 12 required admissions in ward and 4 in intensive care. Mechanical ventilation, systemic steroids, Remdesivir and IVIG were required in those admitted to intensive care unit. Out of 4 deaths (9.7%), 3 occurred in adolescent age and 2 had superimposed bacterial/viral infections. Other contributors to mortality were: cachexia, airway obstruction, disease relapse.

Predictors Of Poor Outcome In COVID-19 Infection, In A Cohort Of Pediatric Cancer Patients, During The Second Wave In India

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Abbreviations

COVID-19	Coronavirus disease 2019
CBNAAT	Cartridge-based nucleic acid amplification test
HSCT	Hematopoietic stem cell transplant

IVIG	Intravenous immune globulin
MIS-C	Multisystem inflammatory syndrome in children

Abstract : The second wave of COVID 19, far outnumbered the first, in cases and deaths. We report outcome of pediatric cancer patients with COVID-19 during the second wave, from a tertiary center in India. Out of 41 patients who tested positive; 51% were asymptomatic, 36% had mild symptoms, 12 required admissions in ward and 4 in intensive care. Mechanical ventilation, systemic steroids, Remdesivir and IVIG were required in those admitted to intensive care unit. Out of 4 deaths (9.7%), 3 occurred in adolescent age and 2 had superimposed bacterial/viral infections. Other contributors to mortality were: cachexia, airway obstruction, disease relapse.

Introduction : The second wave of COVID 19, that hit India from April-June 2021, had far outnumbered the first in terms of cases and deaths; resulting in 17 million cases and 0.2 million deaths (1). Children with a pre-existing systemic disease might be at risk of getting severe COVID-19 (2) (3). Data from various regions of the world has demonstrated variable mortality rates in childhood cancer patients contracting the virus. While the data from UK (4) reported 0% mortality, that from regions of USA (5) and Saudi Arabia (6) has reported 4.1% and 2.5% mortality respectively. A systematic review (7) of 33 various studies from USA, Italy, Egypt found that out of 6.6% COVID-19 deaths in 226 patients, 4.9% were attributable to the disease, while in others, patients were incidentally COVID positive.

At the time of writing the manuscript, there was scarcity of literature on the clinical spectrum and outcome of the novel viral infection in childhood cancer patients from Indian subcontinent. We report the outcome of patients with COVID-19 during the second wave, from the pediatric oncology unit of a tertiary center in India and highlight some of the factors contributing to higher COVID -19 deaths in childhood cancer patients in developing nations as compared to developed western countries.

Methods : This was a single institutional observational study. Pediatric cancer patients, tested positive for SARS-CoV-2 by RT-PCR or CBNAAT or Rapid Antigen Test or CT- severity score during the period of second wave of COVID 19 were included. Patient data regarding symptoms, treatment, hospitalization, outcome, hematologic and inflammatory markers was collected. The severity of the disease was classified as asymptomatic, mild, moderate, and severe/critical based on the criteria by Dong et al (9). All patients were followed up till they tested negative. Data analysis was done using MS-office excel.

Results : Forty-one patients (23 ALL, 5 Ewing sarcoma, 3 retinoblastoma, 2 each of AML/Neuroblastoma/Non-Hodgkin lymphoma and 1 each of Hodgkin lymphoma/LCH/ Rhabdomyosarcoma/Nasopharyngeal carcinoma) tested positive for SARS-CoV-2 by RT-PCR/ CBNAAT/Rapid Antigen Test/CT- severity score. While more than half were asymptomatic, 36% had mild symptoms (TABLE 1). In the study population, 38 patients were without any co-morbidity. One patient was relapsed ALL post HSCT, one Hodgkin lymphoma relapse and one was CNS relapse of rhabdomyosarcoma. Hematological parameters were normal in majority, but the median values of CRP, Ferritin, IL-6 and D-dimer were elevated i.e., 11.7 mg/dl, 1024 ng/ml, 37.5 pg/ml, 1050 ng/ml respectively.

Twenty-five (60.9%) patients were sent on home isolation, 12 were admitted in COVID ward and 4 in intensive care.Out of 5 patients that required supplemental oxygen, 4 needed mechanical ventilation. Systemic steroids, IVIG and Remdesivir were given in 4, 2 and 2 patients respectively. Out of the 4 deaths (9.7%) one was a case of rhabdomyosarcoma with CNS relapse admitted for end-of-life care, the cause of death not attributed to the virus. Rest 3 deaths (7.3%) occurred in adolescent age group with cancer cachexia, oncologic emergencies and post HSCT period being additional risk factors for death (TABLE 2).

The mean time to negativity was 18±11 days. While 8 patients tested negative after 3 weeks, 5 did so only after one month. Maximum time to negativity was 46 days found in a case of nasopharyngeal carcinoma.

Discussion :

Based on our observation 51% of cases were asymptomatic and 60% improved with home isolation. Out of those who were symptomatic, only 80% had manifested fever, while classical symptom of anosmia was reported by none. Meena JP et al. (8) in their systematic review had analyzed data from 33 studies (226 patients) from various countries and reported 6.6% COVID-19 positive deaths, of which 4.9% were attributable to the disease itself, while in the rest SARS-CoV-2 was an incidental finding, not contributing to death. Due to widespread infection by the virus during the second wave in India, we made a similar observation where incidental positive tests were evident, by the finding that, half of the cases were asymptomatic.

Pre-existing co-morbidities might increase the risk of severe COVID in children. Graff et al report that, age 0–3 months or >20 years, preterm birth or comorbidities including immunocompromise, gastrointestinal condition, diabetes, asthma and raised CRP were predictors for hospitalization and severe outcome (3). Out of three COVID attributed deaths in our study population, while severe bacterial sepsis was a major contributory cause of death in one patient, another had Adenoviral infection, with MIS-C being a common contributor for deterioration in both. This observation highlights that COVID deaths in LMICs could be compounded by superimposed bacterial and viral infections. Recent IDSA finding also suggest that bacterial superinfections were evident at postmortem examination in 32% of COVID-19 deaths (12). Musuuza JS et al. (13) in their meta-analysis also found that 19% of patients with COVID-19 have co-infections and 24% have superinfections. The presence of either co-infection or superinfection was associated with increased mortality.

Though UNICEF India enlists malignancy as one of the risk factors (2) for getting severe COVID 19 in children, data from various regions of the world are quite variable. Data from United Kingdom published by Millen GC et al. reports 0% mortality with 28% asymptomatic, 63% mild and 10% moderate, severe or critical infections in a cohort of 54 pediatric cancer patients. They concluded that children with cancer who contract COVID-19 are not at any additional risk of serious infection than general children (4). Registries from regions of USA (5) and Saudi Arabia (6) have reported 4.1% and 2.5% mortality respectively in pediatric cancer patients with COVID-19, which is more than the general population (10) (11). Although the rate of severe COVID 19 in our study (10%), is somewhat similar to other developed countries, 7.3% COVID related death in our cohort is higher than those of the above-mentioned developed nations. However, the mortality and severity rates were similar to that in adult cancer patients reported by another apex cancer hospital in the country (14). Ramaswamy et al. from TMC, Mumbai reported 11% severe COVID and 10% death in 230 adult cancer patients, but no death was encountered in pediatric population that comprised 14% of their cohort. While our patient population comprised of patients from 7 months to 17 years, deaths attributable to COVID were mostly in adolescent age groups. Additional co-morbidities were present in these patients. While one patient had severe thinness, another one had airway obstruction due to superior mediastinal syndrome. One patient also died of Adenoviral infection plus COVID MIS-C, who was one-year post-HSCT. Hence patients with cancer cachexia, oncologic emergencies and those who are less than one year post HSCT, might be at increased risk of severe disease and death.

In our study while the mean time to negativity was 18 days, 5 patients became negative only after one month, with maximum time to negativity being 46 days. A Ramaswamy et al from TMC, Mumbai have also reported similar median time to negativity of 17 days (14). Using viral culture, Teresa Aydillo etal (15) had reported that viral RNA was detected for up to 78 days after the onset of symptoms during immunosuppressive therapy in adult cancer patients. This prolonged period of viral shedding in these cancer patients emphasizes the need for extending the period of isolation in this population.

Conflict of Interest statement: The authors declare no conflict of interest.

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Legends:

TABLE 1: Clinical characteristics of the pediatric cancer patients with COVID- 19.

TABLE 2. Risk factors in COVID positive deaths

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