The impact of COVID-19 pandemic on pediatric oncology

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Keywords: COVID-19, Coronavirus, Pediatric oncology, Childhood cancer, SARS-CoV-2.

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus responsible for the ongoing coronavirus disease 2019 (COVID-19) pandemic, has posed an unprecedented threat to the global healthcare system. Children with cancer stand to be amongst the most vulnerable populations given their immunocompromised state and high reliance on hospital-based or clinic-based care. However, the true impact of COVID-19 infection on children with cancer remains unknown.

Emerging research suggests that adults with cancer and adult cancer survivors have a higher risk of SARS-CoV-2 infection (OR, 2.31; 95% CI, 1.89-3.02) and more severe outcomes following SARS-CoV-2 infection (39% vs. 8%; Fisher’s exact p = 0.0003) than those without cancer. However, in these studies cancer patients were also more likely to be of older age, smokers, and have other comorbidities. While these additional risk factors do not apply to the pediatric oncology population, we can expect a similar or greater impact of COVID-19 due to the more myelosuppressive and immunosuppressive nature of pediatric cancer treatments.

Nearly 90% of children with COVID-19 present with mild or moderate symptoms. However, in other coronaviruses, immunocompromised children are known to have more severe symptoms including life-threatening respiratory failure. Reports of post-transplant patients with COVID-19 suggest that T-cell immunosuppression predisposes patients to more severe outcomes. Even in previously healthy patients, severity of disease is correlated with T-cell lymphopenia. This suggests that functional T-cells may be vital to control the COVID-19 infection.

Children with cancer are also susceptible to become indirect victims of the COVID-19 pandemic due to delayed diagnosis, limited access to care, interruptions in treatment, blood shortages, and suspensions of clinical trials for promising new therapies. A small case series of the Italian Pediatric Hospital Research Network described delayed presentations to the pediatric emergency room during a week at the height of the COVID-19 outbreak. Three of these patients had newly diagnosed cancers with extremely severe presentations, one dying within days of admission.

Regarding infection prevention, many have referred to the efforts of the pediatric hematology-oncology and transplant center in the Lombardy region in Northern Italy. Despite being embedded in a designated COVID-19 hospital within the most affected region in Italy, there were no reported positive cases of COVID-19 in pediatric hematology-oncology or transplanted inpatients. This was attributed to the implementation of aggressive anticipatory infection prevention measures. The crux of these measures were clear clinical leadership, limiting non-urgent admissions, isolating staff and patients from COVID-19 areas, nucleic acid testing for staff and patients prior to elective procedures and admissions (if symptomatic with a negative test, a second nasopharyngeal swab should be performed), supervised handwashing and use of personal protective equipment (PPE), and restricting visitors. In the out-
patient setting, many of these same measures were untenable, patient visits were managed remotely when possible [telemedicine], and strict patient isolation procedures were put into place15,17.

Recently, leadership of the International Society of Pediatric Oncology (SIOP), Children’s Oncology Group (COG), St Jude Global program, Childhood Cancer International (CCI), and others came together to put forth a framework for caring for children with cancer during the COVID-19 pandemic15. Although informed by collective expert opinion and not evidenced-based, these guidelines provide advice on adapting diagnostic and treatment protocols to protect children and healthcare workers15. Overall, they recommend all children suspected of having a newly diagnosed malignancy undergo immediate workup and proceeding with treatment when possible15. If diagnostic modifications are necessary due to resource constraints (i.e. lack of flow cytometry and molecular diagnostics, neuroimaging, etc.), judgement should proceed based on available clinical information and testing15. Similarly, there is no current evidence to support an elective reduction in cancer treatments15. However, if complex surgeries or radiotherapy are unavailable, administering chemotherapy prior to or in absence of these agents may be safe in children who meet the appropriate clinical criteria. Deferring elective high-risk treatments (such as cellular and stem cell therapies) may be important to patient safety and preserving hospital services15,16.

These guidelines also acknowledge that the burden of this pandemic may inequitably fall on low- and middle-income countries (LMIC) and protocols should be modified based on regional resources15. Pediatric oncology patients in LMIC face additional unique challenges of COVID-19 ranging from scarce financial resources, limited testing and PPE, drug shortages, and insufficient skilled healthcare professionals and hospital resources18,19. Lack of government safety net programs3,18,20, and suspended funding from non-governmental organizations (NGO) will exacerbate and prolong the burden of the COVID-19 pandemic in LMIC21.

Due to a paucity of data of SARS-CoV-2 infection, a global COVID-19 childhood cancer registry has been established15. This information will be vital to inform not only present decisions, but similar challenges in the future.

**Funding:** The authors have no funding related to the content of this manuscript.

**Acknowledgements:** The authors of this article have no conflicts of interest or financial interests to disclose. All authors have contributed to the manuscript in significant ways, have reviewed and agreed upon the manuscript content. This article is not under consideration at another journal.

**Conflict of Interest:**

The authors declare that they have no conflict of interest to disclose.

**References**

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