

# The impact of COVID-19 pandemic on pediatric oncology

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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<sup>1</sup>. However, the true impact of COVID-19 infection on children with cancer remains unknown<sup>2</sup>.

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)<sup>3</sup> and more severe outcomes following SARS-CoV-2 infection (39% vs. 8%; Fisher's exact  $p=0.0003$ )<sup>4</sup> than those without cancer. However, in these studies cancer patients were also more likely to be of older age, smokers, and have other comorbidities<sup>3,4</sup>. 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<sup>5</sup>.

Nearly 90% of children with COVID-19 present with mild or moderate symptoms<sup>6</sup>. However, in other coronaviruses, immunocompromised children are known to have more severe symptoms including life-threatening respiratory failure<sup>7</sup>. Reports of post-transplant patients with COVID-19 suggest that T-cell immunosuppression predisposes patients to more severe outcomes<sup>8,9</sup>. Even in

previously healthy patients, severity of disease is correlated with T-cell lymphopenia<sup>10</sup>. This suggests that functional T-cells may be vital to control the COVID-19 infection<sup>11</sup>.

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<sup>12-15</sup>. 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<sup>12</sup>. Three of these patients had newly diagnosed cancers with extremely severe presentations, one dying within days of admission<sup>12</sup>.

Regarding infection prevention, many have referred to the efforts of the pediatric hematology-oncology and transplant center in the Lombardy region in Northern Italy<sup>16</sup>. 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<sup>16</sup>. 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<sup>15,16</sup>. In the out-



patient setting, many of these same measures were untaken, patient visits were managed remotely when possible [telemedicine], and strict patient isolation procedures were put into place<sup>16,17</sup>.

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 pandemic<sup>15</sup>. 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 workers<sup>15</sup>. Overall, they recommend all children suspected of having a newly diagnosed malignancy undergo immediate workup and proceeding with treatment when possible<sup>15</sup>. 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 testing<sup>15</sup>. Similarly, there is no current evidence to support an elective reduction in cancer treatments<sup>15</sup>. 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<sup>15</sup>. Deferring elective high-risk treatments (such as cellular and stem cell therapies) may be important to patient safety and preserving hospital services<sup>15,16</sup>.

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 resources<sup>15</sup>. 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 resources<sup>18,19</sup>. Lack of government safety net programs<sup>5,18,20</sup>, and suspended funding from non-governmental organizations (NGO) will exacerbate and prolong the burden of the COVID-19 pandemic in LMIC<sup>21</sup>.

Due to a paucity of data of SARS-CoV-2 infection, a global COVID-19 childhood cancer registry has been established<sup>15</sup>. This information will be vital to inform not only present decisions, but similar challenges in the future.

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