Pediatric Hemato-Oncology Care Amid the COVID-19 Pandemic

Puneet Kaur Sahi¹ • Jagdish Chandra²

Received: 8 August 2020 / Accepted: 20 November 2020 / Published online: 9 January 2021
© Dr. K C Chaudhuri Foundation 2021

The Coronavirus disease (COVID-19) pandemic has created a parallel world of neglected non-COVID patients, especially, children with cancer and chronic blood disorders with several barriers to continuing care.

Challenges to Continuing Care

1. *Hospital resource* (e.g., hospital staff, hospital beds, ventilators, blood components) re-allocation to manage COVID-19 infection has severely curbed services to pediatric hematology-oncology patients. Several tertiary-care hospitals have been designated as exclusive COVID-19 treatment centres without any suitable alternative centres being allotted for pediatric hemato-oncology patients [1, 2].
2. *Interrupted drug supply chains* have resulted from travel restrictions and shutting of several pharmacies in high-risk areas.
3. *Blood component shortage* has resulted from reduced voluntary blood donations due to restricted travel and fear of getting exposed to COVID-19 during hospital visit. Transmission of SARS-CoV-2 via blood product transfusion is controversial. Despite insufficient data, certain International organizations advise deferral of blood donation for 28 d after symptom resolution in a COVID-19 positive case and for 21 d after exposure to a confirmed case of COVID-19 [3].
4. *Fear of contracting COVID-19* during hospital visits may reduce access of healthcare by patients during ‘seemingly stable’ clinical condition.

5. *Restricted travel* may result in treatment default by outstation patients receiving treatment from pediatric hemato-oncology centres concentrated in major cities in India.
6. *Financial crisis* may cause significant treatment defaults in low-income groups due to redirection of limited money to provision of basic necessities (food/clothing/house rent) and inability to afford private local treatment.
7. *Hampered Non-Governmental Organisations (NGOs) functioning* may impact fund-raising and organizing care in LMICs.
8. *Un-lockdown* would bring challenges of increased COVID-19 cross-infection rates in patients and doctors, sudden cumulative surge of newly diagnosed hemato-oncology patients (likely in more advanced stages of disease), pending chemo-radiotherapy and surgery patients, and complicated cases (tumor relapses, treatment failures). COVID-19 testing strategy and quarantine prior to intense therapy especially for outstation patients will need attention.

Addressing the Challenges

Apart from the universal infection prevention practices such as screening of patients and caregivers, isolation of patients, ensuring ‘social distancing’ and use of masks, the following measures may help:

1. *Patient education and training* regarding hand hygiene, respiratory etiquette and use of mask done telephonically/ by sharing videos/ social media platforms [4]
2. *Continuum of care* [4–7]
 - i) Tele-consultation as substitute for follow-up visits for stable patients
 - ii) Patient tracking for those lost to follow-up by dedicated hospital staff and treatment advise per feasibility
 - iii) Courier methods to deliver oral chemotherapy for home administration.

✉ Puneet Kaur Sahi
puneetsahi@gmail.com

¹ Department of Pediatrics, Maulana Azad Medical College and associated Lok Nayak Hospital, New Delhi, India

² Department of Pediatrics, Lady Hardinge Medical College and KSCH, New Delhi, India

- iv) Follow-up visits in person should be limited, drugs should be dispensed in buffer amounts to cover for delays in scheduled visit

Conversion of our centre at the pandemic-onset, to an exclusive COVID-19 care hospital, entailed coordinated *transfer of hemato-oncology patients to other hospitals*. Listing of all patients with stage and phase of treatment, stratification on the basis of urgency of treatment continuation and feasibility of transfer to other nearby government/private hospitals was worked upon. *Networking* was done with all pediatric hemato-oncologists in Delhi, and with involvement from the NGO's, the patient transfer was implemented. Outstation patients were additionally *tagged with local healthcare facilities*. Throughout, treatment from other centres, regular *tele-consultation* was ensured between the primary and transfer-center hemato-oncologists as well as the patient. Transport, residence and medical finances were *supported by NGOs*. In return, a large number of COVID-19 positive hemato-oncology patients were treated at our centre.

3. *Dissemination of hospital policy* using social media platforms, email, personal communication to update patients of available services and working days, avoiding unnecessary visits [4].
4. *Blood donations/transfusion may be continued as follows:*
 - i) Facilitation of blood transfusion at nearby healthcare facility
 - ii) Mobile unit services for facilitating blood donation at doorstep
 - iii) Special social media drives to encourage blood donations
 - iv) Special travel passes for donors, issued by e-mail or WhatsApp to facilitate travel to the blood banks
 - v) Advertise safety of blood collection areas

Cancer-Specific Measures

The following principles may be applied with local modifications:

1. Diagnostic investigations and response evaluation may be adapted to available resources. For example: If sincere attempts to get baseline flow cytometry/ molecular genetics in an acute leukemia child significantly delays treatment, initiation of therapy may be based on morphology. If possible, standard protocols for diagnosis and treatment of cancer patients “unmodified” should be continued. If resource constraints mandate treatment modification, a whole-service approach over individual clinical decision-making should be preferred [5]. This should be

done after discussion with the family explaining proposed modifications/ alternatives and possible consequences. Documentation should be done on the case records with a revised consent.

2. A triage system may be used to tailor treatment per patient disease, stage, phase of treatment and prognosis [6]. For example: *very-low-risk* patients (cancer survivors) may be advised to stay home and tele-consult regularly, *low-risk* patients (receiving less intense chemotherapy like acute lymphoblastic leukemia maintenance, Hodgkin lymphoma, etc.) may be given chemotherapy at a nearby hospital and monitored with necessary investigations via teleconsultation. *Intermediate-risk* patients (those requiring surgery/radiation/stem-cell transplant) may be given an additional chemotherapy cycle awaiting the deferred procedure. *High-risk* patients (like induction/ consolidation of acute leukemia, Non-Hodgkin lymphoma) should be given chemotherapy via in-house admission/day-care facility [6].
3. Measures like drug-dose reductions, delay of intensive chemotherapy regimens, increased duration between cycles and conversion to oral agents may be adopted to reduce patient visits [5, 7]. Following disease-specific modifications may be made [7]:
 - a). Acute lymphoblastic leukemia (ALL)
 - i) Deferral of Intrathecal chemotherapy during maintenance
 - ii) Capizzi interim maintenance instead of high dose methotrexate therapy
 - iii) Pegylated L-asparaginase instead of *Escherichia coli-asparaginase*
 - b). Acute myeloid leukemia (AML):
 - i) Interim oral chemotherapy instead of upfront induction for new patients
 - ii) Consolidation chemotherapy instead of BMT in high-risk disease
 - iii) Reduction of intensive cycle cytarabine dose from 18 to 12 g/m²
 - c). Non-Hodgkin lymphoma: Less myelosuppressive regimen (Ex: MCP842 for non-CNS disease)
 - d). Solid tumors:
 - i) Oral metronomic therapy (palliative intent) for advanced stage
 - ii) Dose compressed three weekly chemotherapy cycles for Ewings sarcoma
 - iii) Use of non-high dose methotrexate protocols in osteosarcoma

- iv) Switch from ifosfamide to cyclophosphamide for rhabdomyosarcoma reducing inpatient admission by 24 h
 - v) Use of prophylactic pegylated G-CSF
4. Consider surgical delays if tumor is benign/low grade [5].
 5. Consider disease-specific modified radiotherapy protocols to minimize treatment duration and complications [8], like hypofractionation of radiotherapy for brain tumors
 6. Enlist cases with treatment modification and review on priority on return of normal service capacity.
 7. Febrile neutropenia – Administer antimicrobials near place of patients stay and consider early switch to oral antimicrobials to reduce hospital visits. Avoid throat examination and aerosol generating procedures.
 8. Undertake interdepartmental teleconsultation to help shared decision-making without in-person meetings

With phased un-lockdown, catching-up on delayed diagnosis and acute treatment may become priority, and treatment modifications and deferrals may be needed in fewer cases. The above-mentioned triage system may be modified to resume treatment for both high-risk and intermediate-risk patients while deferred high-risk transplants, essential surgeries and radiotherapy sessions may be resumed.

Blood Disorder Specific Measures [9]

1. Monitor thalassaemia patients with crucial tests like hemogram and serum ferritin as usual
2. Emphasize extra-caution in thalassemia children with comorbidities such as good glycemic control in patients with secondary diabetes
3. Postpone annual routine monitoring tests like Ferriscan in stable patients
4. Continue low-dose hydroxyurea in sickle cell children as it prevents stroke, acute chest syndrome and vaso-occlusive crisis in under-transfused SCD [9]
5. Defer stem-cell transplantation
6. Ensure up-to-date vaccinations

COVID-19 Disease in Children with Cancer and Blood Diseases

COVID-19 in children is milder with lower mortality and predominance of gastrointestinal and respiratory manifestations. Limited data show SARS-CoV-2 infection is mild in children with cancer and chronic blood disorders except when associated with co-morbidities (splenectomized, iron

overload, etc.) [9–11]. In SCD, COVID-19 infection may act as a trigger for acute chest syndrome [9].

Testing Policy for COVID-19 in pediatric hemato-oncology patients is the same as that for the general population [10, 12], although certain centers may prefer a cautionary test prior to invasive procedures.

Treatment

Chemotherapy/radiotherapy/surgery may be deferred for symptomatic COVID-19 positive patients [13]. For COVID-19 positive asymptomatic patients, chemotherapy may be continued in the intensive phases (e.g., induction of ALL) but may be withheld in less intense phase of chemotherapy (like maintenance of ALL) [13, 14]. Hydroxychloroquine prophylaxis has been used in asymptomatic COVID-19 positive patients [14]. Azithromycin has been used in patients with mild respiratory disease. Broad-spectrum antibiotics and anti-viral drugs like remdesivir have been used in COVID-19 positive moderately to severely symptomatic lymphopenic patients [13, 14]. Stringent monitoring for disease progression and check on drug contraindications, interactions and side-effects are required. For symptomatic COVID-19 positive thalassemics, deferiprone (side effects – lymphopenia and agranulocytosis) may be withheld [15]. During an acute febrile episode, chelation should be stopped until detailed patient evaluation [15]. No changes in transfusion thresholds have been advised.

Conclusions

All-in-all, strategies for care of pediatric hemato-oncology patients need to be adapted locally in line with available resources, updated researches and the dynamic nature of the pandemic.

Authors' Contributions PKS: Conceptualized and drafted the manuscript; JC: Conceptualized, drafted and critically appraised the manuscript. JC will act as guarantor for this paper.

Compliance with Ethical Standards

Conflict of Interest None.

References

1. Pramesh CS, Badwe RA. Cancer management in India during Covid-19. *N Engl J Med*. 2020;382(20):e61.
2. LNJP hospital will function as dedicated COVID-19 one: Union health minister. 2020 April 4. Available at: <https://timesofindia.indiatimes.com/city/delhi/lnjp-hospital-will-function-as-dedicated-covid-19-hospital-union-health-minister/articleshow/74984186.cms>. Accessed 6 July 2020.

3. Chang L, Yan Y, Wang L. Coronavirus disease 2019: coronaviruses and blood safety. *Transfus Med Rev.* 2020;34(2): 75–80.
4. Tata Memorial Centre COVID-19 Working Group; Tata Memorial Centre COVID-19 Working Group comprises the following: the COVID-19 pandemic and the Tata Memorial Centre response. *Indian J Cancer.* 2020;57(2):123–8.
5. Sullivan M, Bouffet E, Rodriguez-Galindo C, et al. The COVID-19 pandemic: a rapid global response for children with cancer from SIOP, COG, SIOP-E, SIOP-PODC, IPSO, PROS, CCI, and St Jude Global. *Pediatr Blood Cancer.* 2020;e28409 <https://doi.org/10.1002/pbc.28409>.
6. Seth R, Das G, Kaur K, et al. Delivering pediatric oncology services during a COVID-19 pandemic in India. *Pediatr Blood Cancer.* 2020;67(12):e28519. <https://doi.org/10.1002/pbc.28519>.
7. Saroha M, Moulik NR. COPING with CORONA: a developing country perspective on managing children with cancer during COVID-19 pandemic. *Cancer Res Stat Treat.* 2020;3:97–101.
8. Simcock R, Thomas TV, Estes C, et al. COVID-19: global radiation oncology's targeted response for pandemic preparedness. *Clin Transl Radiat Oncol.* 2020;22:55–68.
9. Eleftheriou A. The COVID–19 pandemic and haemoglobin disorders. *Thalassaemia & Sickle Cell Disease: Classification of Risk Groups & Other Considerations. Guidance for Patients, Parents & Healthcare Professionals.* Thalassaemia International Federation. 2020 May 11. Available at: <https://thalassemicsindia.org/images/pdf/202005131231380.pdf>. Accessed 3 July 2020.
10. Ferrari A, Zecca M, Rizzari C, et al. Children with cancer in the time of COVID-19: an 8-week report from the six pediatric oncology centers in Lombardia, Italy. *Pediatr Blood Cancer.* 2020;67(8):e28410. <https://doi.org/10.1002/pbc.28410>.
11. Rosenzweig JD, McThenia SS, Kaicker S. SARS-CoV-2 infection in two pediatric patients with immune cytopenias: a single institution experience during the pandemic. *Pediatr Blood Cancer.* 2020;67(9):e28503. <https://doi.org/10.1002/pbc.28503>.
12. Strategy for COVID-19 testing in India (Version 5). Indian Council of Medical Research. 2020 May 18. Available at: https://www.icmr.gov.in/pdf/covid/strategy/Testing_Strategy_v5_18052020.pdf. Accessed 3 July 2020.
13. Iehara T, Manabe A, Hosoi H. Statement on the prevention and treatment of COVID-19 in patients with pediatric cancer in Japan. *Pediatr Blood Cancer.* 2020;67(9):e28440. <https://doi.org/10.1002/pbc.28440>.
14. Bisogno G, Provenzi M, Zama D, et al. Clinical characteristics and outcome of Severe acute respiratory syndrome coronavirus 2 infection in Italian pediatric oncology patients: a study from the Infectious Diseases Working Group of the Associazione Italiana di Oncologia e Ematologia Pediatrica. *J Pediatric Infect Dis Soc.* 2020;9(5):530–4. <https://doi.org/10.1093/jpids/piaa088>.
15. Roy NBA, Telfer P, Eleftheriou P, et al. Protecting vulnerable patients with inherited anaemias from unnecessary death during the COVID-19 pandemic. *Br J Haematol.* 2020;189(4):635–9.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.