Clinical profile of pediatric oncology patients treated with radiation therapy – An institutional experience from Pakistan

Bilal Mazhar Qureshi[1], Yumna Ahmed[2], Ayesha Arshad Ali[1], Maria Tariq[1], Sehrish Abrar[1], Asim Hafiz[1], Nasir Ali[1], and Ahmed Abbasi[1]

[1]The Aga Khan University
[2]Cyberknife & Tomotherapy Center

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Abstract

Background: This study aims to improve practices in pediatric radiation oncology in LMIC by sharing an institutional experience of radiation therapy (RT) for pediatric cancer at the Aga Khan University Hospital. *Methods:* All patients from January 2009 to December 2020 who received radiation therapy at Aga Khan University Hospital were included. Records were retrospectively reviewed from hospital information management system (HIMS) and radiation oncology information system were searched to identify children aged up to 19 years of age who received RT based on the pediatric protocol. Data was reviewed for frequencies and percentages were calculated for demographics, clinical characteristics, and treatment-related variables. *Results:* A total of 496 patients were offered RT for soft tissue and extra osseous sarcomas (n=115 patients, 23.2%), lymphomas and reticuloendothelial neoplasms (n=88 patients, 17.7%) and CNS and miscellaneous intracranial and intraspinal neoplasms (n=86 patients, 17.3%) and malignant bone tumors (n=77, 15.5% patients). The most common regions for radiation were head and neck (n=144, 29%) and CNS (n= 123, 24.3%). General anesthesia was used for radiation planning and/or execution of treatment in 122 (26.8%) patients. More than half the patients (n=261, 53.16%) received RT in the postoperative setting, 89 (18.13%) had RT as consolidative treatment. 30 (6.1%) leukemia patients received prophylactic radiation therapy and 103 (20.98%) received RT as a definitive treatment modality. *Conclusions:* Our study reinforces the use of radiation therapy in multidisciplinary management of different pediatric tumors. A multi-level pediatric cancer registry is required to assess the utilization of radiotherapy for different pediatric tumors. This will help in planning systems to cater to the needs of pediatric oncology management and survivorship.

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Bilal Mazhar Qureshi[1,], Yumna Ahmed[2], Ayesha Arshad Ali[3], Maria Tariq[1], Sehrish Abrar[1], Asim Hafiz[1], Nasir Ali[1], Ahmed Nadeem Abbasi[1]

[1] Radiation Oncology Section, Department of Oncology, Aga Khan University, Pakistan.

[2] Cyberknife & Tomotherapy Center, Jinnah Postgraduate Medical Center, Pakistan.

[3] Global Health & Development, Aga Khan University, Pakistan.

Corresponding author: Bilal Mazhar Qureshi

Address: Radiation Oncology Section, Ibn-e-Zuhr Building, Aga Khan University, Karachi, Pakistan

Email: bilal.mazhar.qureshi@gmail.com

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Abbreviations

LMIC	*low and middle-income countries*
RT	*radiation therapy*
HIMS	*hospital information management system*
WHO	*World Health Organization*
HIC	*Higher income countries*
ICCC-3	*International Classification of Childhood Cancer, Third Edition*
CNS	*Central Nervous System*
SEER	*Surveillance, Epidemiology, and End Results*
AML	*acute myeloid leukemia*
ALL	*Acute lymphoblastic leukaemia*
NHL	*Non-Hodgkin Lymphoma*
GA	*General anesthesia*
AVATAR	*Audiovisual-Assisted Therapeutic Ambience in Radiation Therapy*
CCSS	*Childhood Cancer Survivor Study*

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Abstract

Background: This study aims to improve practices in pediatric radiation oncology in LMIC by sharing an institutional experience of radiation therapy (RT) for pediatric cancer at the Aga Khan University Hospital.

Methods: All patients from January 2009 to December 2020 who received radiation therapy at Aga Khan University Hospital were included. Records were retrospectively reviewed from hospital information management system (HIMS) and radiation oncology information system were searched to identify children aged up to 19 years of age who received RT based on the pediatric protocol. Data was reviewed for frequencies and percentages were calculated for demographics, clinical characteristics, and treatment-related variables.

Results: A total of 496 patients were offered RT for soft tissue and extra osseous sarcomas (n=115 patients, 23.2%), lymphomas and reticuloendothelial neoplasms (n=88 patients, 17.7%) and CNS and miscellaneous intracranial and intraspinal neoplasms (n=86 patients, 17.3%) and malignant bone tumors (n=77, 15.5% patients). The most common regions for radiation were head and neck (n=144, 29%) and CNS (n= 123, 24.3%). General anesthesia was used for radiation planning and/or execution of treatment in 122 (26.8%) patients. More than half the patients (n=261, 53.16%) received RT in the postoperative setting, 89 (18.13%) had RT as consolidative treatment. 30 (6.1%) leukemia patients received prophylactic radiation therapy and 103 (20.98%) received RT as a definitive treatment modality.

Conclusions: Our study reinforces the use of radiation therapy in multidisciplinary management of different pediatric tumors. A multi-level pediatric cancer registry is required to assess the utilization of radiotherapy for different pediatric tumors. This will help in planning systems to cater to the needs of pediatric oncology management and survivorship.

Keywords: pediatric cancers; radiation oncology; radiotherapy; oncology

Introduction

According to the World Health Organization (WHO), 400,000 children and adolescents develop cancer each year. More than two-thirds of the world's pediatric cancers are diagnosed in low and middle-income countries (LMIC). [1] Pakistan is a lower middle-income country and no such data is available. Our country's lack of population-based cancer registries results in an underestimation of the burden of childhood cancer. In Pakistan, a regional cancer registry estimated that about 7000 to 7500 children are diagnosed with cancer every year.[2] Radiation therapy is an integral part of cancer treatment in the pediatric population and its utilization faces multiple and unique barriers in countries with limited resources due to lack of data regarding pediatric RT service and the clinical profiles of children requiring radiation therapy. All these factors contribute towards a poorer survival chance than those in high income countries (HIC).

There is limited data available on radiotherapy experience for pediatric tumors in our part of the world. We present the clinical profile of pediatric cancer patients who received radiation, either alone or as an adjuvant to surgery and chemotherapy; in prophylactic, radical, or palliative clinical settings.

Improvement in pediatric oncology care can only be achieved through national cancer control program which begins with establishing cancer registries. This study aims to improve practices in pediatric radiation oncology in LMIC by sharing an institutional experience of radiation therapy for pediatric cancer at the Aga Khan University Hospital, a tertiary care hospital accredited by Joint Commission International. This data may further identify and help reduce the disparity in outcomes between HIC and LMIC.

Material and Method

Hospital information management system (HIMS) and radiation oncology record system were searched to identify children aged up to 19 years of age and received RT based on the pediatric protocol. All patients from (January 2009 to Dec 2020) who received radiation therapy were retrospectively reviewed. All adult cancer patients (>19 years) were excluded from the study. Data was collected for age, diagnosis, general anesthesia for radiation planning, site, dose, and other parameters related to RT. All pediatric tumors were classified based on the International Classification of Childhood Cancer, Third Edition (ICCC-3).[3] All the patients who fulfilled the inclusion criteria were reviewed to fill the performa in a de-identified manner. After collecting information for each patient, data was compiled using Microsoft Excel 2020. Data was analyzed using IBM SPSS version 25.0. Frequencies and percentages were calculated for demographics, clinical characteristics, and treatment-related variables.

RESULTS

A total of 496 patients under the age of 19 received radiation therapy as part of their cancer treatment at the Aga Khan University between 2009 and 2020. All patients received radiation therapy after discussion in a pediatric tumor board meeting\sout. These patients' constitutes about 5 % of the total 9,920 patients who received RT during the same time period at Radiation Oncology facility of Aga Khan University. A total of 269 out of these 496 were referred to our hospital for radiation therapy only. Among the study group, 326 patients (65.72%) were male and 170 (34.27%) were female. There were 104 patients (21%) less than 5 years. The most common age group was 5-9 years (166 patients, 32.7%) followed by those between the ages of 10-14 years (121 patients, 24.2%). There were 129(26%) patients treated with general anesthesia. However, the most frequent utilization of general anesthesia was found in children with age group 1-5 years (88 patients). The age-wise distribution of all the patients included is shown in Figure 1.

The most common diagnoses for which patients were given RT were soft tissue and other extra osseous sarcomas (n=115 patients, 23.2%), specifically rhabdomyosarcomas (n=93, 18.7%) followed by lymphomas and reticuloendothelial neoplasms (n=88 patients, 17.7%) specifically Hodgkin's lymphomas (n=84, 16.9%), CNS and miscellaneous intracranial and intraspinal neoplasms (n=86 patients, 17.3%) and Malignant bone tumors (n=77, 15.5% patients). The most common sites for radiation were head and neck (n=144, 29%) and CNS (n= 123, 24.3%). Tumor-wise and site-wise distribution of patients are shown in Figure 2 and 3, respectively.

The use of general anesthesia was required for radiation planning and/or execution in 122 patients (26.8%) and were all under the age of 13 as shown in Figure 2. 118 patients had unplanned gap in treatment, with 36 patients having a break of more than 7 days with the longest gap of 15 days.

Almost half the patients (n=261, 53.16%) received RT in the postoperative setting, 89 (18.13%) for consolidative treatment, and 5 (1%) patients received radiation therapy as palliative treatment. 103 (20.98%) received RT as part of definitive treatment and 30 (6.1%) leukemia patients received prophylactic radiation therapy to CNS. This study showed that the use of radiation therapy as part of pediatric cancer treatment has consistently increased over the last few years as evident in figure 04.

Discussion

The actual burden of childhood cancer in lower middle income countries is unknown due to lack of population-based cancer registries. According to GLOBOCAN's 2020 estimates, South-central Asia and Eastern Asia have the highest incidence of cancers in children (<19 years) with over 143,000 new cases annually. The exact incidence and prevalence of pediatric cancer cases in low and middle-income countries like Pakistan are unknown due to a lack of resources needed to establish and maintain a centralized national cancer registry; however, it is estimated that around 8000 new pediatric cancer cases and diagnosed in Pakistan each year accounting for almost 10% of the total reported cancer cases in the country.[4] Overall survival of childhood cancer patients has improved fairly over the last few decades, from less than 30% to about 80% in high-income countries owing to the introduction of aggressive multimodal treatment protocols which include a combination of chemotherapy, radiation, and surgery.[5] However, the overall survival is much lower in Pakistan and other low and middle-income countries due to a number of intrinsic hurdles negatively affecting outcomes such as poor nutrition, lack of capital to build and maintain proper facilities and train personnel as well as a lack of infrastructure to gain access to healthcare. Radiation therapy is a critical component of childhood cancer worldwide yet access, in terms of equipment as well as geographic location, is limited in LMICs like Pakistan where only few hospitals are treating pediatric cancer patients in the entire country and only our institute utilizes general anesthesia for planning and treatment of pediatric patients.[6] The availability of expert manpower for pediatric radiation therapy remains limited.

The Surveillance, Epidemiology, and End Results (SEER) registry of the National Cancer Institute reported a decline in the use of RT for ALL, NHL, and retinoblastoma from 1973 to 2008 as new prognostic groupings lead to treatment with surgery alone or intensified chemotherapy for certain patients instead of RT. However, the use of RT for neuroblastoma, Wilms tumor, brain and bone cancer has declined slightly over the years, but remained proportionately stable for AML, Hodgkin's lymphoma and soft tissue cancers.[7-9] Trends observed in our data showed an increase in RT use for bone tumors, soft tissue tumors, and Wilms tumor and a decrease in ALL patients as shown in Figure 3.

Improving pediatric oncology care can be achieved by determining the actual burden of childhood cancer so that specific demands will be put on the management of childhood cancer in an environment with limited resources. The number of patients receiving RT at our institution has increased steadily over the years, almost doubling over the 10-year period, possibly reflecting the collaboration with pediatric oncologist resulting in patient's referral to radiotherapy and increase in incidence of cancer cases as well as improvement in prompt identification and treatment of such patients.

For safe and effective delivery of radiation, patients' immobility for 15-20 minutes is required which can be difficult for children especially in an unfamiliar environment of the radiation suite without parents or caregivers around. Hence, anesthesia is routinely used for patients under the age of 3, and sedation requirements decrease with increasing age. Anesthesia use carries a major risk for complications including 'failure to rescue' from cardiopulmonary collapse, respiratory depression or airway obstruction, or the need for emergent procedures like intubation. However, we did not have any such adverse event reported for our patients. Also, the long-term effects of repeated GA on neurocognition are unknown and is a question for future research in our region.[10] Equipment and drugs to safely deliver anesthesia are costly and require a dedicated medical team including anesthesiologists, pediatric nurses, and respiratory therapists.[11] A recent analysis reported

better tolerability of daily RT without anesthesia with the use of AVATAR (Audiovisual-Assisted Therapeutic Ambience in Radiation Therapy) during RT delivery. This unique approach has potential to minimize the burden of health care staff and health care cost needed in LMIC.[12]

Advances in multimodal therapy for childhood cancer have led to more than 80% cure and survival rates for pediatric solid tumors but the adverse effects of therapy may cause debilitating events and sometimes poor quality of life beyond the primary disease process. The Childhood Cancer Survivor Study (CCSS) estimated that 1 in 5 childhood cancer survivors died after 30 years of survivorship with 1 in 10 deaths due to treatment-related factors.[13] Radiotherapy-related late effects include cardiac dysfunction, cognitive deficits, hypopituitarism, cataracts, ototoxicity, spinal and bone growth abnormalities, pulmonary fibrosis, bowel fibrosis, etc. A noteworthy point for pediatric cancers remain the long term radiation induced effects which may adversely impact the quality of life among childhood cancer survivors. These late effects might be compromised neurocognitive functions, memory loss, cataract formations, endocrine problems, bone weakness, and other primary tumors. Subsequent neoplasms due to radiation exposure are the major cause of no relapse-related mortality with the CCSS reporting a 20.5% 30-year cumulative incidence. Hence, it is important to screen and monitor childhood survivors for late toxicity according to standard guidelines and deliver a lower cumulative dose for fewer treatment-related side effects. Our study reported different aspects of radiation practices including age at treatment, body site(s) affected, and radiation delivery with time has a potential to work on survivorship issues of children treated with RT. This guides us on planning survivorship program for these children tailored according to the common body sites irradiated.

The World Health Organization's Global Initiative for Childhood Cancer goal to reach 60% survival rate for pediatric cancer by 2030 can only be done with a special focus on cancer care in LMICs. This includes establishing specialized pediatric RT units to alleviate the burden on existing facilities. For a sustainable system, suitable equipment including pediatric-specific immobilization devices, anesthesia machines, etc. should be acquired, and adequate, trained staff including radiation oncologists, clinical medical physicists, radiation therapy technologists, and technical machine engineers should be hired.[14] Staffing ratio and competency can improve over time to build capacity in terms of patient numbers and RT techniques. Exchange of ideas between experts at different institutions at combined forums such as tumor board meetings, etc. could also help develop appropriate treatment protocols for the maximum benefit of the patients. Clinical research and studies on RT practices from LMIC are needed for the development of new treatment strategies in children with cancer specifically applicable to our region who do not enroll in clinical trials. To overcome the challenges faced by LMIC, sharing our radiotherapy experience will help in collaboration, and assistance from international organizations, societies, and institutions to make an appreciable difference.

Conclusion

Our study has showed that pediatric population maintains a significant proportion of cancer patients receiving RT in an LMIC based population. Therefore, our study reinforces the need of a multi-level pediatric cancer registry to determine the exact frequency of pediatric cancer that would further help in tailoring the RT facilities. However, the data remains subtle as it represents population from a single center only. Further studies with a multi-centered approach is advocated.

Conflict of interest: None

Acknowledgment: None

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