Epidemiology of a Hospital-Based Pediatric Cancer Registry - An Experience at a Major Tertiary Care Center in Pakistan

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Abstract

Background: Cancer is a prominent non-communicable disease, responsible for more than 8 million deaths each year worldwide. Globally, 400,000 children and daily 1000 children are diagnosed with cancer.

Objective: The current study aims to analyze retrospective childhood cancer registry data from IHHN since 2016 and provide the Age Standardized Incidence Rates (ASIR) for children having different types of malignancies.

Method: A retrospective study was conducted through a chart review of the childhood cancer registry, data retrieved from the Indus Paediatric Oncology Database (IPOD) software. Only patients with behavior code/3 for positive malignancy, as defined in the International Classification of Disease for Oncology, 3rd edition (ICD-O-3) were included in the dataset.

Results: A total of 4631 children diagnosed with cancer were enrolled, with 2951 (63.7%) males and 1680 (36.3%) females. Overall median age and Interquartile range were 7(3.3-11) years. Leukemia was the predominant cancer in both genders, the second highest being lymphoma. Central Nervous System (CNS) tumors were the third highest cancer in males and soft tissue sarcomas in females. Hepatic tumors are the least common among genders.

Conclusion: In conclusion, the childhood cancer registry at the Indus Hospital and Health Network (IHHN) reported standard quality data including patients mostly from Sindh and Baluchistan along with other provinces and neighboring countries. Moreover, at the national level, there is an essential need for the formulation of an effective childhood cancer registration system by policymakers to determine the true incidence rate and etiology of common cancers.

Keywords: *Cancer, non-communicable disease, oncology, leukemia, etiology.*

INTRODUCTION

A dramatic increase in childhood cancer survival was noted in high-income countries with over 80% of children surviving 5 years after cancer diagnosis [1]. Unfortunately, these numbers are largely undocumented at the population level in most low- and middle-income countries (LMIC) [2]. In Pakistan, known figures of childhood cancer survival currently reside between 25-35%, overall. Multiple studies have identified that this survival gap can be reduced through efforts focused on improved public awareness, early diagnosis, access to quality care, and provision of timely supportive care [3] To address the described inequity, the World Health Organization launched the Global Initiative for Childhood Cancer (GICC) in 2018, giving LMIC's a target to reduce disparity in survival and health status by 2030.

Clinical data is an essential resource within healthcare systems to deliver quality clinical care, initiate research and clinical trials, create holistic policies, and boost public health. Despite the plethora of existing evidence, even large healthcare economies are struggling to construct comprehensive data systems to fulfill these functions [4]. Many countries use cancer as a benchmark for data integration and linkage across various sections of healthcare systems. This may be because cancer requires multidisciplinary care at different points of the treatment journey. Cancer is also a gateway to personalized and targeted medicine owing to the strong links between incidence and genetic susceptibilities of the individual [5].

An evolution of informal registries into a national registry can be seen in the National Cancer Registration Service (NCRS) of the United Kingdom, collecting timely data on each cancer patient. This population-level NCRS now delivers a single cancer data service, at the population level, a quality-assured data source of clinical data not maintained in real time [6]. From analyzing incidence, abandonment, and overall survival, population-based childhood cancer registries (PBCR) around the world have managed to expedite research and development processes for improved diagnostic and therapeutic techniques. PBCRs are now an essential need in LMICs to achieve improvement of an overall survival rate of 60% following the Global Initiative of Childhood Cancer (GICC).

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The Indus Hospital & Health Network (IHHN) is one of the largest centers for childhood cancer in Pakistan, registering over 1000 patients annually and offering free-of-cost quality care to each patient. IHHN, under the My Child Matters (MCM) grant awarded for holistic improvement in childhood cancer by the Sanofi Espoir Foundation in 2009, created a multi-hospital-based cancer registry software in 2016. This study aims to analyse retrospective childhood cancer registry data entered into the IHHN in 2016.

METHODOLOGY

A retrospective study was conducted through a chart review of the childhood cancer registry, data retrieved from the IPOD software developed by the Department of Electronic Medical Record (EMR), IHHN, and the Pakistan Society of Paediatric Oncology (PSPO-CR) software. All 4631 records of children diagnosed with cancer at IHHN from January 2016 to December 2021 were included. Patient variables contained basic demographics (age, gender, and province) information regarding the tumor (date of diagnosis, site, and morphology), and follow-up status (date of last follow-up and patient outcome status).

Only patients with behavior code/3 for positive malignancy, as defined in the International Classification of Disease for Oncology, 3rd edition (ICD-O-3) were included in the dataset. Cancers were segregated into 12 main diagnostic groups as per the International Classification of Childhood Cancer, 3rd edition (ICCC-3). Whereas, all non-malignant or borderline central nervous system tumors including craniopharyngioma, meningioma, ganglioglioma, benign teratoma, and pilocytic astrocytoma were excluded.

STATISTICAL ANALYSIS

Data was analyzed using Microsoft Excel and Statistical Package for Social Sciences (SPSS) version 23.0 software. Frequencies and percentages were reported for all the categorical data. Median and Interquartile range (IQR) were calculated for age as data was not normally distributed.

Patients were divided into four age groups: (0-4, 5-9, 10-14, and 15-19) years. For the calculation of the Age-Standardized Incidence Rate (ASIR) for each cancer site in each age group, the incidence of cancers reported in Globcan 2021 was used for Pakistan. Direct standardization method was selected for ASIRs estimation using the World Standard of Segi as the standard population, all the cases were presented as per 100,000 population.

RESULTS

A total of 4631 children diagnosed with cancer were enrolled in this study, with 2951 (63.7%) males and 1680 (36.3%) females, *i.e.* male to female ratio of 2:1. Overall median age and Interquartile range were 7(3.3-11) years. Patients were segregated into the four age groups 0-4 years included 1626 (35.1%), 5-9 years included 1454 (31.4%), 10-14 years included 1280 (27.6%) and 15-19 years included 271 (5.9%).

Table 1: Demographic characteristics.

Age Median (Inter Quartile Range)	**7.0 (3.3-11.0)**	
	n	**%**
Age Categories (in years)		
0-4	1626	35.1
5-9	1454	31.4
10-14	1280	27.6
15-19	271	5.9
Gender		
Male	2951	63.7
Female	1680	36.3
Types of Cancers		
Leukemia	1892	40.9
Lymphomas	830	17.9
Soft Tissue Sarcomas	319	6.9
CNS and Intraspinal	297	6.4
Malignant Bone Tumors	229	4.9
Retinoblastoma	291	6.3
Renal Tumors	188	4.1
Neuroblastoma	172	3.7
Germ Cell Tumor	169	3.6
Epithelial Neoplasms and Melanomas	126	2.7
LCH/HLH	55	1.2
Hepatic Tumors	46	1.0
Others	17	0.4

The majority of the patients originated from the IHHN home province of Sindh 3627 (78.3%) with the second highest frequency seen from Balochistan 725 (15.7%) and 68 (1.5%) patients hailing from neighboring countries of Pakistan. There were 1363 (29.4%) patients from Karachi and 3268 (70.6%) patients from other cities of Sindh outside of Karachi.

The most common cancer among children was: blood cancer, namely Leukemia with 1892 (40.9%) followed by Lymphomas with 830 (17.9%) patients. The remaining distribution of cancer types is shown in Table **1**.

Curative and palliative treatment was given to 3085 (66.6%) and 938 (20.3%) patients respectively. While 608 (13.1%) children were abandoned and left before initiation of treatment. 2595 (84.1%) were alive and 490 (15.8%) had died. The main causes of mortality were treatment-related 318 (64.8%) and disease-related 165 (33.6%) and the remaining 7 (1.42%) are the minor causes of mortality.

Fig. (1) Shows the distribution of cancer morphology according to age categories. Rising trends of all malignancies are depicted for the age group 0-4 years. Whereas, declining peaks are illustrated in the 15-19 years category.

Fig. (2) Depicts the gender-wise segregation of cancers. Leukemia was the predominant cancer in both genders, the second highest being lymphoma. Central Nervous

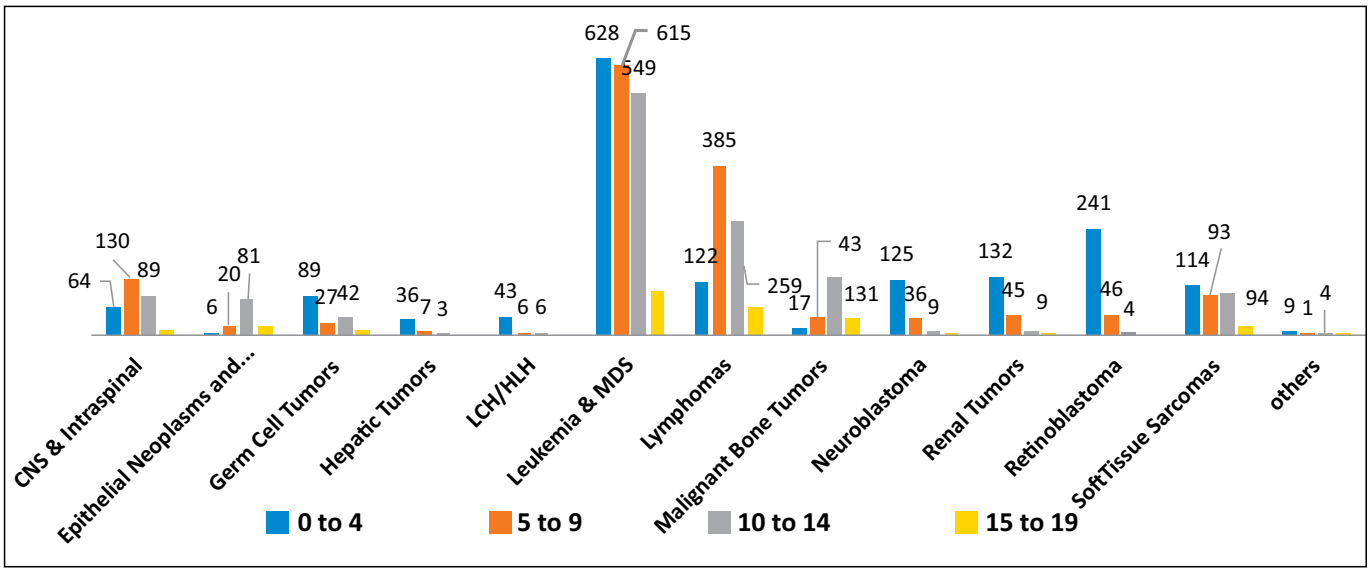

Fig. (1): Age wise frequency distribution of cancer types.

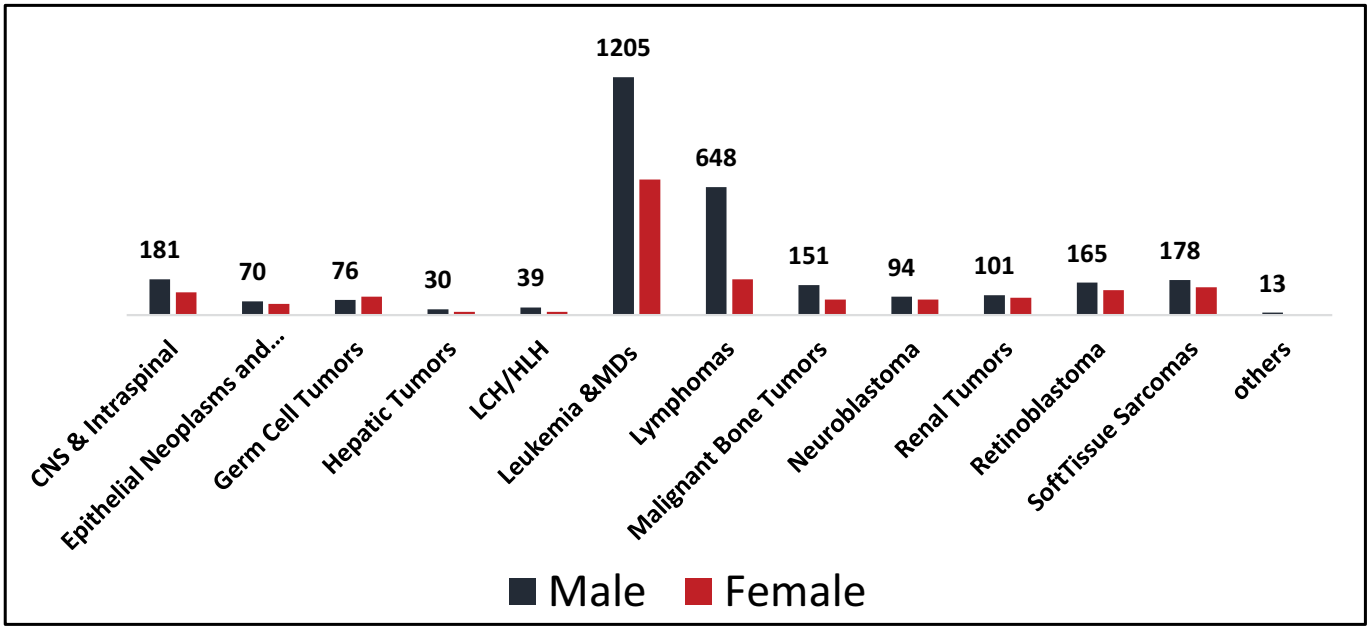

Fig. (2): Gender wise frequency distribution of cancer types.

Table 2: Age-standardized incidence rate by age groups.

Age Categories (Years)	0-4		5-9		10-14		15-16	
Cancer Sites	**Count**	**ASIR**	**Count**	**ASIR**	**Count**	**ASIR**	**Count**	**ASIR**
Lip & Oral Cavity	4	0.02	2	0.01	3	0.01	0	0
Esophagus	0	0	0	0	3	0.02	5	0.04
Colorectum	1	0.01	2	0.02	23	0.25	7	0.07
Stomach	0	0	1	0.01	3	0.04	2	0.02
Lung	4	0.04	0	0	0	0	0	0
NHL	62	1.11	116	1.74	90	1.21	18	0.24
Liver	42	0.94	8	0.15	4	0.06	1	0.01
Brain, Nervous System	83	2.08	138	2.89	100	1.88	19	0.35
Ovary	1	0.02	16	0.36	31	0.64	06	0.12
Hodgkin Lymphoma	54	3.90	247	1.48	149	8.07	37	2.00
Prostate	0	0	2	0.04	1	0.01	0	0
Small Intestine	5	2.54	10	4.23	10	3.81	2	0.76
Salivary Gland	0	0	7	0.77	8	0.80	2	0.20

Age Categories (Years)	0-4		5-9		10-14		15-16	
Cancer Sites	Count	ASIR	Count	ASIR	Count	ASIR	Count	ASIR
Nasopharynx	1	0.14	11	1.32	24	2.59	6	0.64
Pharynx	1	0.83	1	0.69	1	0.62	0	0
Bone	34	1.47	49	1.77	127	4.14	37	1.20
Anal Canal	0	0	0	0	2	0.31	0	0
Omentum, Mesentery	18	1.66	14	1.07	3	0.20	1	0.69
Testis	40	6.36	4	0.53	4	0.47	5	0.59
Pancreas	3	0.30	0	0	3	0.23	0	0
Skin	6	1.43	12	2.39	13	2.33	1	0.17
Leukemia	645	9.31	617	7.42	546	5.91	100	1.08
Orbit	257	2.54	54	0.44	14	0.10	0	0
Vagina	4	1.72	1	0.35	1	0.32	1	0.32
Kidney	220	1.01	66	2.52	17	0.58	5	0.17
Urinary Bladder	8	0.20	7	0.14	1	0.01	0	0
Oropharynx	0	0	0	0	1	0.07	1	0.07
Others	137	0.31	68	0.12	95	0.16	15	0.02

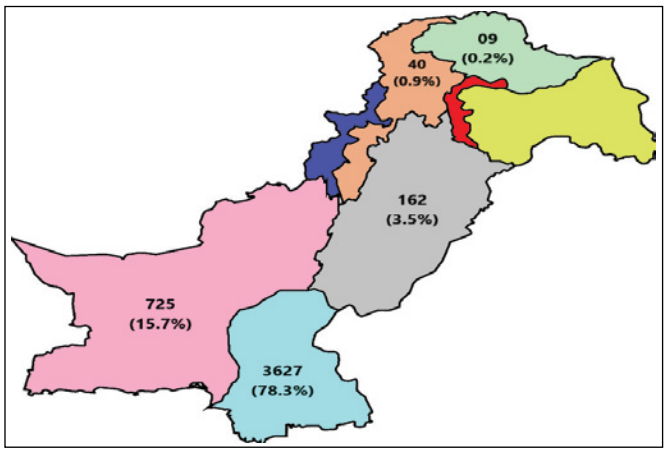

Fig. (3): Province wise burden of cancer.

System (CNS) tumors were the third highest cancer in males and soft tissue sarcomas in females.

Table **2** Shows the Age-Standardized incidence rate (ASIR) per 100,000 populations in four categories of age (0-4, 5-9, 10-14, and 15-19 years) in different cancer sites. Leukemia, Hodgkin Lymphoma, Orbit Brain, and CNS malignancies are the topmost malignancies according to their ASIR in 0-4 year age groups. In 5-9 years leukemia, the small intestine, and Brain, CNS are the most common. Whereas, in the 10-14 and 15-19 age groups leukemia, Hodgkin lymphoma, and bone are the predominant sites.

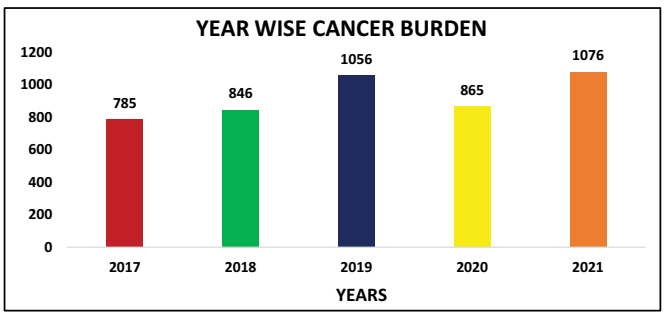

Fig. (4): Year wise burden of cancer.

DISCUSSION

Even though paediatric cancer is rare, the annual rate of new cancer cases reported among children is steadily increasing. In Pakistan, there is a dire need for holistic PBCR for better collection and analysis of childhood cancer data. These registries serve as a bridge between healthcare facilities and local and national governmental institutes. Moreover, registries also enable a deeper understanding of etiology and prognosis, assisting in the development of effective and future pathways for improved survival.

From January 2016 to December 2021, the median age was 7.0 years which was in concordance with the previously published studies by Innocent and Zhang *et al.* [1, 2].

We have reported male preponderance which was statistically significant, in a similar fashion was accounted by Zhenqiu Liu, Jasim N Al Asadi, and Raza MR [3, 4], that males were more susceptible to cancer than females. Additionally, an epidemiological review that was led in Pakistan by Farhana Badar likewise shows that the ratio of cancer among males was higher in comparison with females [5].

Most of the international and national studies reported that leukemia was the prevailing pediatric cancer for both genders [3, 6-8]. Our study likewise reported a striking pattern of leukemia in children. One of the studies conducted by Dr Eva in which data from 2001-2010 were collected represents that Leukemia is the most aggressive cancer among children followed by CNS tumors and lymphoma [9]. Lymphoma shows the second highest cancer and the third highest was soft tissue sarcomas. However, the least common cancer that was detected in our review was hepatic tumors. A comparative study was also reported [4].

Overall, we report the highest ASIR of leukemia in all age categories. A high prevalence of leukemia in children of Pakistan has been reported in other regional studies as

well [10, 11]. In comparison with other registries that are operated in Pakistan shows that the profile of cancer from the registry is by and large similar. Data from the Karachi Cancer Registry (KCR) also estimates leukemia as the top most common malignancy in children [12].

There was an upward ASIR trend of cancers in the age groups 0-4 years. Consistent findings are seen in earlier studies. Comparative patterns were also accounted for in studies by Al-Mutlaq, Hiroyuki Ishihara, and Wiangnon [13-15]. Nationally, the same trends are reported.

Most of the published international studies estimate OS of >80% in children with cancer [16-21]. Similar findings accounted for in our study. The current study reported the highest survival in Retinoblastoma which is in concordant with previous studies [16, 22].

CONCLUSION

In a nutshell, the childhood cancer registry operated at IHHN reported standard quality data which incorporates patients from every province of Pakistan and even patients outside Pakistan, as IHHN provides free of cost and quality services. Moreover, at the national level, there is an essential need for the formulation of an effective childhood cancer registration system by policymakers and higher authorities where all cancer cases should be reported. This effective registration system at the National level also helps in the depiction of the true image of childhood cancer incidence, prevalence, and mortality. For childhood Cancer presentation cancer control programs and awareness sessions should also be conducted.

LIST OF ABBREVIATIONS

ASIR	Age Standardized Incidence Rates
CNS	Central Nervous System
CR	Cancer Registry
EMR	Electronic Medical Record
GICC	Global Initiative of Childhood Cancer
ICCC-3	International Classification of Childhood Cancer, 3rd edition
ICD-O-3	International Classification of Disease for Oncology, 3rd edition
IHHN	Indus Hospital & Health Network
IPOD	Indus Paediatric Oncology Database
IQR	Interquartile range
KCR	Karachi Cancer Registry
LMIC	Low- and Middle-income Countries
MCM	My Child Matters
NCRS	National Cancer Registration Service
OS	Overall Survival
PBCR	Population-based Childhood Cancer Registries
PSPO	Pakistan Society of Paediatric Oncology
SPSS	Statistical Package for Social Sciences

ETHICAL APPROVAL

Ethical exemption was obtained from the Institutional Review Committee of, Indus Hospital, Karachi (REF letter No. (IHHN_IRB_2022_04_009). All procedures performed in studies involving human participants were following the ethical standards of the institutional and/or national research committee and with the Helsinki Declaration.

CONSENT FOR PUBLICATION

Written informed consent was taken from the participants.

AVAILABILITY OF DATA

The data set may be acquired from the corresponding author upon a reasonable request.

FUNDING

Declared none.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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AUTHORS' CONTRIBUTION

NY- contributed to the conceptualization and design of the study. MF-organized, integrated, maintained data, analyzed, and interpreted the results of the study. WF-reviewed and edited the original version of the paper. SM- shared his valuable comments and reviewed the manuscript. RR and SJ reviewed the final submitted version of the manuscript and provided their intellectual output and approved the final submitted version.

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