RESEARCH PAPER

Pediatric Cancer Burden in Different Regions of India: Analysis of Published Data From 33 Population-Based Cancer Registries

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Objective: To provide the regional pediatric cancer (age-group 0-14 years) burden and pattern in India utilizing published data of population-based cancer registries established under the National Cancer Registry Programme and Tata Memorial Centre, Mumbai. **Methods:**Based on the geographic locations, the population-based cancer registries were categorized into six regions. The age-specific incidence rate was calculated using the number of pediatric cancer cases and population in the respective age-group. Age-standardized incidence rate per million and 95% CI were calculated.**Results:** In India, 2% of all cases were pediatric cancer. The age-standardized incidence rate (95% CI) for boys and girls is 95.1 (94.3-95.9) and 65.5 (64.8-66.2) per million population, respectively. Registries from northern India reported the highest rate; while the lowest rate was in northeast India. **Conclusion:**There is a need to establish pediatric cancer registries in different regions of India to know the accurate pediatric cancer burden.

Keywords: *Incidence, Leukemia, Lymphoma, Registry.*

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Pediatric cancer, defined here as cancer among children aged 0-14 years, contributes to approximately 1% of the new cancer cases globally [1]. Although, pediatric cancer only represents a small proportion of all cancers, it is a major cause of death in children across the globe [2], and requires evidence-based public health interventions. Furthermore, almost half of the total 2,06,362 globally registered pediatric cancer cases are from low-income and low- and middle-income countries (LMICs) [1]. High-quality population-based cancer registry (PBCR) data, one of the crucial elements for accurate estimation of childhood cancer burden, are required in LMICs like India for better policymaking and planning decisions [3].

With regards to the Indian PBCRs, which cover less than 15% of urban and 1% of rural population [4], data is scarce on the pediatric cancer burden and patterns, especially from different regions of India. This study summarises region-wise incidence of pediatric cancer in India based on the published data of the registries of that region. The study utilized the published data of PBCRs of the National Cancer Registry Programme (NCRP) (period 2012-2016) [5] along with the PBCRs established by Tata Memorial Centre (TMC), Mumbai [6,7] for estimating the burden of pediatric cancer.

METHODS

Based on the geographic position, the PBCRs were categorized into six regions including central, eastern, northern, northeastern, southern, and western India. Three registries including Bhopal, Nagpur, and Wardha are located in the central area, while in the eastern region,there is only one registry (Kolkata). In northern region seven registries (Chandigarh, Delhi, Mansa, Patiala, Sangrur, SAS Nagar, and Varanasi), northeastern region eleven registries (Cachar, Dibrugarh, Kamrup urban, Manipur state, Meghalaya, Mizoram state, Nagaland, Pasighat, Sikkim state, Tripura state, and West Arunachal), southern region five registries (Bangalore, Chennai, Hyderabad, Kollam, and Thiruvananthapuram) and western region six registries (Ahmedabad urban, Aurangabad, Barshi rural, Mumbai, Osmanabad-Beed, and Pune) are present. The

data reported by NCRP registries are for the year 2012-2016, except Bhopal, Kolkata, Mumbai, Osmanabad- Beed (2012-2015), Delhi, Bangalore (2012-2014) and Hyderabad registry (2014-2016). The TMC, Mumbai registries include data from Chandigarh and Punjab registries for period 2013-2016, and Varanasi, Uttar Pradesh state for year 2017.

Statistical analysis: To merge region-wise data of pediatric cancer (age-group 0-14 years), cancer cases for each PBCR for each 5-year age-group were taken as a numerator and population of geographic area from each PBCR was taken as the denominator. The age-specific incidence rate was calculated using the number of pediatric cancer cases and population in the respective age-group. Age-standardized incidence rate (ASIR) per million and 95% CIwere calculated using world standard population [8].

RESULTS

In India, as per the published data of the registries, a total of 4,30,091 cancer cases (male: 2,15,726, 50.2%; female: 2,14,365,49.8%) were reported. The ASIR for males was 105.5 and for females, it was 104.5 per 100,000 population. Of the total cancer cases, 8,692 (2%) were pediatric cancer (Boys: 5,365 (61.7%); Girls: 3,327 (38.3%)). The ASIR of pediatric cancer is 95.1 (95% CI 94.3-95.9) for boys and 65.5 (95% CI 64.8-66.2) for girls per million population. With regards to the region-wise registry locations, registries from northern India shows the highest cancer incidence rate in boys and girls (156.0 and 97.1 per million) followed by southern India (122.0 and 92.4 per million), while registries from northeastern India showed the lowest incidence rate (47.3 and 33.6 per million). The region-wise Indian pediatric cancer incidence rates, depending on the registry location, are presented as ASIR in **Fig. 1**.

Lymphoid leukemia was the predominant site among boys and girls in all the regions of India. The lymphoid leukemia incidence rate in boys ranged from 10.3 to 50.1 and in girls from 5.9 to 28.7 per million population. Moreover, for both boys and girls, brain and nervous system cancers are among the top three leading cancers in most of the regions of India, with incidence ranges from 4.6 to 16.7 and from 3.0 to 13.7 per million population, respectively. Similarly, myeloid leukemia, with incidence rates ranging from 4.3 to 10.9 in boys and 4.0 to 8.1 in girls per million population, was found to be commonly prevalent cancer both in boys and girls.

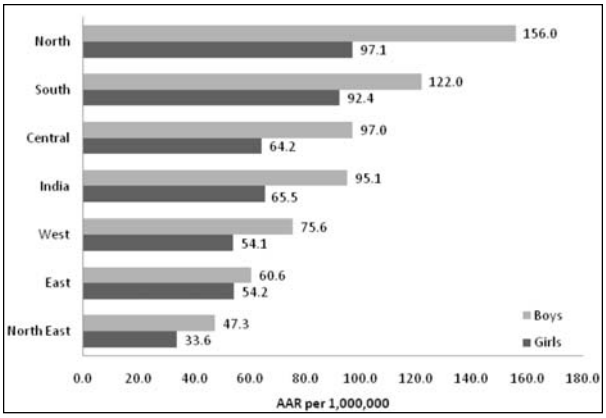


Fig.1 Pediatric cancer burden as per registries from respective regions from India (2012-2016).

The results show that among boys, Hodgkin lymphoma is the third leading cancer in central and eastern region, whereas non-Hodgkin lymphoma is the third leading cancer in northern and western regions of India. It was observed that Hodgkin lymphoma is not among the top ten leading cancer in girls. Among girls, the non-Hodgkin lymphoma ranked seventh with incidence rate ranges from the lowest in northeast region to highest in northern region (1.3 and 5.2 per million population, respectively).

Additionally, malignancies of bone, eye (retinoblastoma) and kidney were the leading cancers both in boys and girls in India; with comparatively higher incidence rate among boys 5.1, 4.7 and 4.5 per million population, respectively. The connective and soft tissue cancers were the ninth leading cancers among boys, with incidence ranging from 1.8 to 6.8 per million population; whereas, it ranked eighth among girls, incidence ranging from 1.7 to 4.6 per million population. Leukemia unspecified was the tenth leading cancer in boys, incidence ranging from 1.3 to 4.9 per million population, while it was the ninth leading cancer in girls, incidence ranging from 0.0 to 3.4 per million population. Furthermore, among girls, ovarian cancer was the tenth leading cancer site with an incidence ranging from 0.8 to 4.1 per million population. The region-wise pediatric cancer burden and the top ten leading cancer sites are presented in **Table I** and **Fig. 2**.

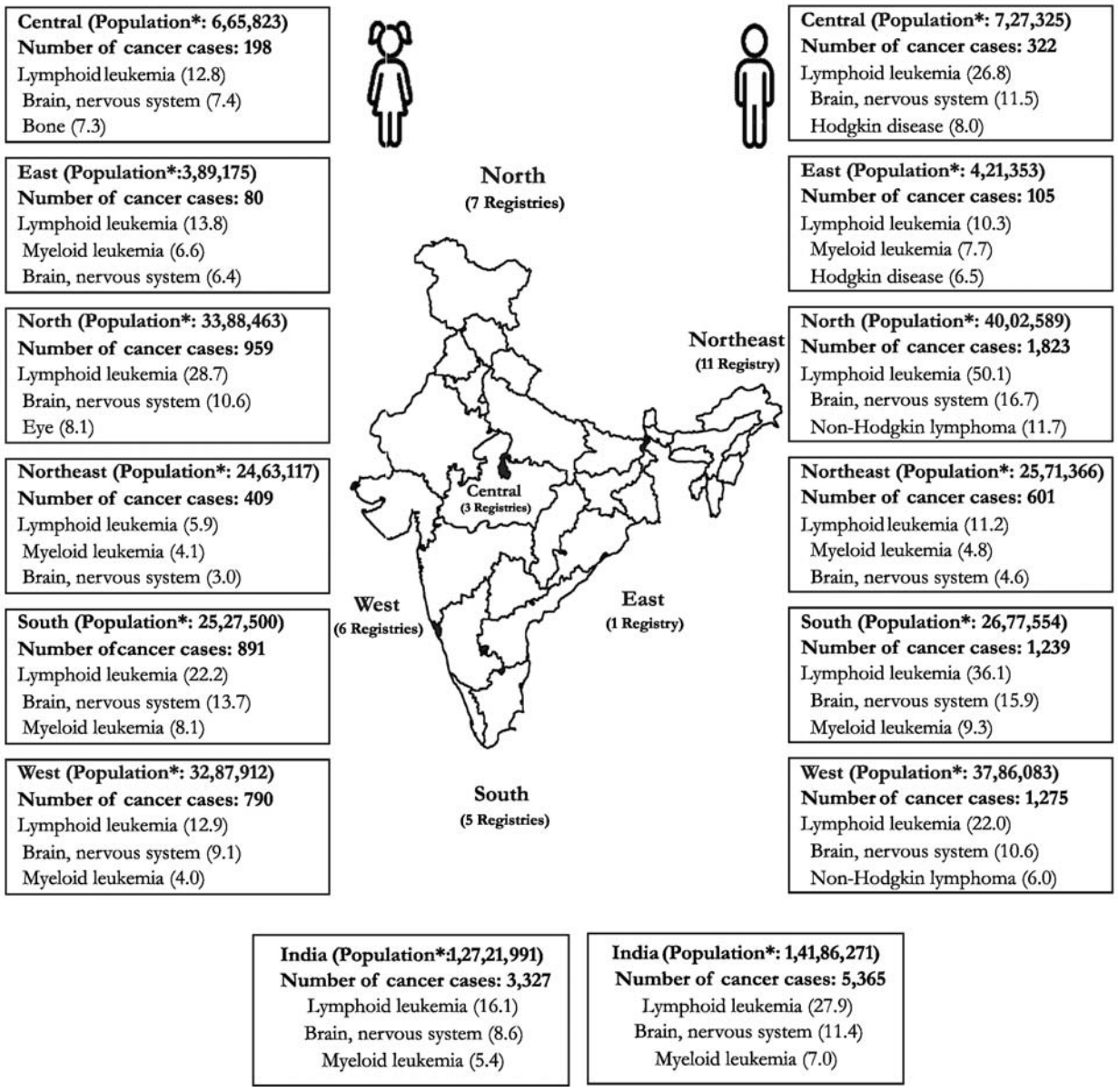
DISCUSSION

We have summarized the pediatric cancer burden in India on the basis of published data on pediatric cancer incidence from33 PBCRs. We observed differences in pediatric cancer incidence region-wise as well as gender-wise. The northern region registries have reported the highest pediatric cancer incidence rate, while the lowest rates are reported by northeastern region registries. Moreover, national and regional data show that boys have a higher pediatric cancer burden than girls. However, it is important to interpret these data cautiously as the regional differences could be due to differences in access to diagnostic and treatment facilities as well as number of PBCRs present in a particular region, the population covered by PBCRs, and cancer registration compliance. It

Table I Age-Standardized Incidence Rate (per million) for Pediatric Cancer in Different Regions of India; 2012-2016

ICD-10	*Site*	*India*	*Central*	*Eastern*	*Northern*	*Northeastern*	*Southern*	*Western*
Boys								
–	All sites	95.1 (94.3-95.9)	97.0 (93.6-100.4)	60.6 (56.8-64.4)	156.0 (153.7-158.3)	47.3 (46.1-48.5)	122.0 (119.8-124.2)	75.6 (74.3-76.9)
C91	Lymphoid leukemia	27.9 (27.5-28.3)	26.8 (25.0-28.6)	10.3 (8.7-11.9)	50.1 (48.8-51.4)	11.2 (10.6-11.8)	36.1 (34.9-37.3)	22.0 (21.3-22.7)
C70-72	Brain and nervous system	11.4 (11.1-11.7)	11.5 (10.3-12.7)	5.3 (4.2-6.4)	16.7 (16.0-17.4)	4.6 (4.2-5.0)	15.9 (15.1-16.7)	10.6 (10.1-11.1)
C92-94	Myeloid leukemia	7.0 (6.8-7.2)	7.4 (6.5-8.3)	7.7 (6.3-9.1)	10.9 (10.3-11.5)	4.8 (4.4-5.2)	9.3 (8.7-9.9)	4.3 (4.0-4.6)
C82-85, C96	Non-Hodgkin lymphoma	6.7 (6.5-6.9)	5.4 (4.6-6.2)	5.5 (4.4-6.6)	11.7 (11.1-12.3)	2.4 (2.1-2.7)	8.4 (7.8-9.0)	6.0 (5.6-6.4)
C81	Hodgkin lymphoma	5.7 (5.5-5.9)	8.0 (7.1-8.9)	6.5 (5.3-7.7)	10.7 (10.1-11.3)	1.4 (1.2-1.6)	6.8 (6.3-7.3)	4.3 (4.0-4.6)
C40-41	Bone	5.1 (4.9-5.3)	5.6 (4.8-6.4)	4.6 (3.6-5.6)	8.9 (8.4-9.4)	2.8 (2.5-3.1)	6.3 (5.8-6.8)	3.4 (3.1-3.7)
C69	Eye	4.7 (4.5-4.9)	3.2 (2.5-3.9)	3.4 (2.4-4.4)	10.7 (10.1-11.3)	2.8 (2.5-3.1)	5.8 (5.3-6.3)	1.9 (1.7-2.1)
C64	Kidney	4.5 (4.3-4.7)	6.8 (5.8-7.8)	2.0 (1.3-2.7)	7.5 (7.0-8.0)	2.7 (2.4-3.0)	4.9 (4.5-5.3)	3.5 (3.2-3.8)
C47+C49	Connective and soft tissue	3.8 (3.6-4.0)	3.1 (2.5- 3.7)	3.6 (2.7-4.5)	6.8 (6.3-7.3)	1.8 (1.6-2.0)	5.3 (4.8-5.8)	2.3 (2.1-2.5)
C95	Leukemia unspecified	3.7 (3.5-3.9)	4.7 (4.0-5.4)	1.3 (0.8-1.8)	4.9 (4.5-5.3)	1.5 (1.3-1.7)	3.2 (2.8-3.6)	4.9 (4.6-5.2)
Girls								
–	All sites	65.5 (64.8-66.2)	64.2 (61.3-67.1)	54.2 (50.3-58.1)	97.1 (95.1-99.1)	33.6 (32.6-34.6)	92.4 (90.5-94.3)	54.1 (52.9-55.3)
C91	Lymphoid leukemia	16.1 (15.7-16.5)	12.8 (11.5-14.1)	13.8 (11.8-15.8)	28.7 (27.6-29.8)	5.9 (5.5-6.3)	22.2 (21.2-23.2)	12.9 (12.3-13.5)
C70-72	Brain and nervous system	8.6 (8.3-8.9)	7.4 (6.4-8.4)	6.4 (5.2-7.6)	10.6 (10.0-11.2)	3.0 (2.7-3.3)	13.7 (13.0-14.4)	9.1 (8.6-9.6)
C92-94	Myeloid leukemia	5.4 (5.2-5.6)	5.9 (5.1-6.7)	6.6 (5.3-7.9)	6.1 (5.6-6.6)	4.1 (3.7-4.5)	8.1 (7.5-8.7)	4.0 (3.7-4.3)
C40-41	Bone	4.8 (4.6-5.0)	7.3 (6.4- 8.2)	3.2 (2.4- 4.0)	8.0 (7.5- 8.5)	2.9 (2.6-3.2)	6.1 (5.6-6.6)	2.9 (2.6-3.2)
C69	Eye	3.9 (3.7-4.1)	1.1 (0.7-1.5)	4.4 (3.2-5.6)	8.1 (7.5-8.7)	2.6 (2.3-2.9)	4.4 (4.0-4.8)	2.2 (1.9-2.5)
C64	Kidney	3.5 (3.3-3.7)	4.1 (3.3-4.9)	0.6 (0.2-1.0)	5.7 (5.2- 6.2)	2.1 (1.8-2.4)	4.5 (4.1-4.9)	2.5 (2.2-2.8)
C82-85, C96	Non-Hodgkin lymphoma	3.3 (3.1-3.5)	3.7 (3.0-4.4)	2.1 (1.5-2.7)	5.2 (4.7-5.7)	1.3 (1.1-1.5)	4.1 (3.7-4.5)	3.3 (3.0-3.6)
C47+C49	Connective and soft tissue	3.1 (2.9-3.3)	3.8 (3.1-4.5)	3.1 (2.1-4.1)	4.5 (4.1-4.9)	1.7 (1.5-1.9)	4.6 (4.2-5.0)	2.3 (2.0-2.6)
C95	Leukemia unspecified	2.3 (2.2-2.4)	3.4 (2.7-4.1)	0.0 (0.0-0.0)	2.3 (2.0-2.6)	1.2 (1.0-1.4)	2.2 (1.9-2.5)	3.3 (3.0-3.6)
C56	Ovary	2.2 (2.1-2.3)	3.2 (2.6-3.8)	3.8 (2.8-4.8)	4.1 (3.7-4.5)	0.8 (0.6-1.0)	3.0 (2.7-3.3)	1.0 (0.8-1.2)

Note: The figure in parenthesis indicates a 95% confidence interval (95% CI).



**Population of respective region registries for the 0-14 age group.*

Fig. 2 Pediatric cancer burden as per registries from respective regions from India (2012-2016).

has also been reported that pediatric cancer incidence is lower among girls compared to boys; however, this area requires further research.

The incidence and mortality of childhood cancer are both inversely correlated with the level of economic development; higher incidence is observed in high-income countries but higher mortality in LMICs. It is evident that in high-income countries, due to easy access to advanced treatment and supportive care, most of the pediatric cancer cases are treated successfully with more than 80% of survival; while in LMICs, the survival rates drop down to 15%-45% as a result of limited accessibility and unaffordable childhood cancer services [9]. The World Health Organization (WHO), along with other collaborators, has launched the Global Initiative for Childhood Cancer (GICC) with the aim of improving outcomes for children with cancer around the world by addressing the gap of non-availability and unaffordable cancer care services in LMICs, and has set the target of achieving at least 60% survival for children with cancer globally [10]. To achieve the target set by GICC-WHO, it is required to utilize accurate population-based estimation of the childhood cancer burden for policy-making and planning and monitoring cancer care services at national and regional levels.

WHAT THIS STUDY ADDS?

- Of the total cancer cases registered in India, 2% were pediatric cancer and there is a difference in pediatric cancer burden as well as pattern in different regions of India.

In India, considering the vastness of the country, the number of PBCRs are less. Based on the NCRP and TMC registry reports, the PBCRs covers only 13% of the total population [5-7]. Aside from the difficulty of ensuring adequate data collection, PBCRs in India confront a number of challenges, including a lack of cancer awareness among parents, a lack of advanced diagnostic facilities, and non-affordable cancer care, which results in low pediatric cancer case registration [11].

The estimated global and country-specific childhood cancer incidence are not adjusted for under-diagnosis. Under-diagnosis may be due to low coverage, poor access to primary care, lack of awareness, and inadequate or delayed diagnosis [12]. It has been estimated that one-in-two pediatric cancer cases is not diagnosed and treated [13]. As a result, even when registries do exist, the burden of childhood cancer is difficult to measure due to limited access to comprehensive diagnosis, and misinterpretation and under-diagnosis. In India, there is under-reporting/ under-diagnosis of pediatric cancer and the estimated pediatric cancer cases in India may be almost double [14]. Additionally, one of the reasons for higher proportion of childhood cancer in LMICs compared to the high-income countries is higher population of age-group <15 years in LMICs compared to the developed world. Nonetheless, demographic factors that affect cancer burden are expected to have only a minimal effect on childhood cancer; whereas, industrialization growth may result in greater exposure to risk factors and, as a result, a larger-than-expected increase in childhood cancers [15].

The limitation of our study is that the data on pediatric malignancies are more commonly classified by morphology, while the incidence reported by PBCRs is on a site-based classification. Moreover, the previously reported gender disparities in childhood cancer registration persist in developing nations. Hence, differences in the incidence of childhood cancer should be interpreted cautiously as they may not necessarily reflect only differences in the underlying occurrence of disease. We recommend that pediatric cancer registries should be established for better interpretation of the pediatric cancer burden.

To conclude, region-wise pediatric cancer incidence is variable across India. There is a requirement for high quality data generated through PBCRs. We suggest that pediatric cancer registries be established widely to know the burden of the disease for better policy-making and strategic interventions.

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