

ORIGINAL RESEARCH

## CHILDHOOD AND ADOLESCENTS CANCER STATISTICS

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### ABSTRACT

**Background:** Hitherto, incidence burden of childhood cancer in India has been derived from GLOBOCAN data. Recent analyses have challenged whether this accurately measures the true incidence of childhood cancer. **Objective:** To use observed data rather than simulation to estimate the number of children (0-14 years), as well as number of children and adolescents (0-19 years), in India who develop cancer every year at the national and state/union territory (UT) level.

**Materials and Methods:** Age-specific (five-year groups), sex-specific, and state/UT specific population data from India Census 2011 was used. Global average incidence rates from the International Incidence of Childhood Cancer 3 (IICC3) report were used. Incidence rates per million person years for the 0-14 years and 0-19 years age groups were age-adjusted using the world standard population to provide age-standardized incidence rates, using the age-specific incidence rates for individual age groups (0-4 years, 5-9 years, 10-14 years, and 15-19 years).

**Results:** The national number of children (0-14 years) and, children and adolescents (0-19 years) that may develop cancer every year based on 2011 census are 52,366 and 76,805 persons respectively. Cancer type specific incidence is provided for each state/UT for these age ranges. This national incidence is approximately double of the GLOBOCAN 2018 estimates of incidence of children diagnosed and registered with cancer and the differential is greater in girls.

**Conclusion:** Our analysis proposes new estimates of incident childhood cancer cases in India for children and adolescents. Future regional, national and international research

**on childhood cancer epidemiology and healthcare accessibility would help further refine these estimates.**

**Keywords: Cancer registry, Epidemiology, Incidence, Population data.**

## **INTRODUCTION**

Defining the local incidence of cancer is a key first step towards developing a comprehensive cancer control strategy.<sup>[1]</sup> In the context of childhood cancer, such information helps to understand disease etiology, improve access to care, plan investments in service delivery, advocate resource allocation, and measure the quality of different components of the health system.<sup>[1]</sup> Estimates of global and country-specific cancer and childhood cancer burden are provided by multiple groups. The recently published GLOBOCAN 2018 study,<sup>[2]</sup> coordinated by the International Agency for Research on Cancer, provides comprehensive global childhood cancer incidence estimates and is commonly used by the World Health Organization and governments for planning cancer control. In 2018, the study estimated that 200,166 new children, age 0-14 years, were diagnosed and registered with cancer globally, of whom 28,712

(14.3%) were from India.<sup>[2]</sup> Recent analyses have questioned the accuracy of GLOBOCAN data for estimating the incidence of childhood cancer.<sup>[3]</sup> The local incidence of childhood cancer varies substantially in the published data including that from India.<sup>[4,5]</sup> It has been hypothesized that underdiagnosis and consequently under-registration, which is disproportionately high in low and middle income countries (LMIC), leads to an “incidence gap” and underestimates the cancer burden, and are hence not reflected in the GLOBOCAN 2018 data.<sup>[6]</sup> This theory has been further substantiated by independent simulation-based studies that have estimated the annual global childhood cancer burden is nearly 45% greater than that historically reported, between 360,000 to 400,000, when children who develop cancer but are never registered are counted.<sup>[7,8]</sup>

Due to perceived incomplete case-finding, misdiagnosis within the fragmented Indian health system and significantly lower incidence-rates of childhood cancer in India, the currently reported childhood cancer from GLOBOCAN 2018 likely represent an underestimate.<sup>[5,9]</sup> In this study, we aim to use observed data rather than simulation to estimate the number of children (0-14 years), as well as number of children and adolescents (0-19 years), in India who develop cancer every year. Additionally, we report these data at the national and state/union territory (UT) level for the purposes of supporting cancer control planning.

## **MATERIALS & METHODS**

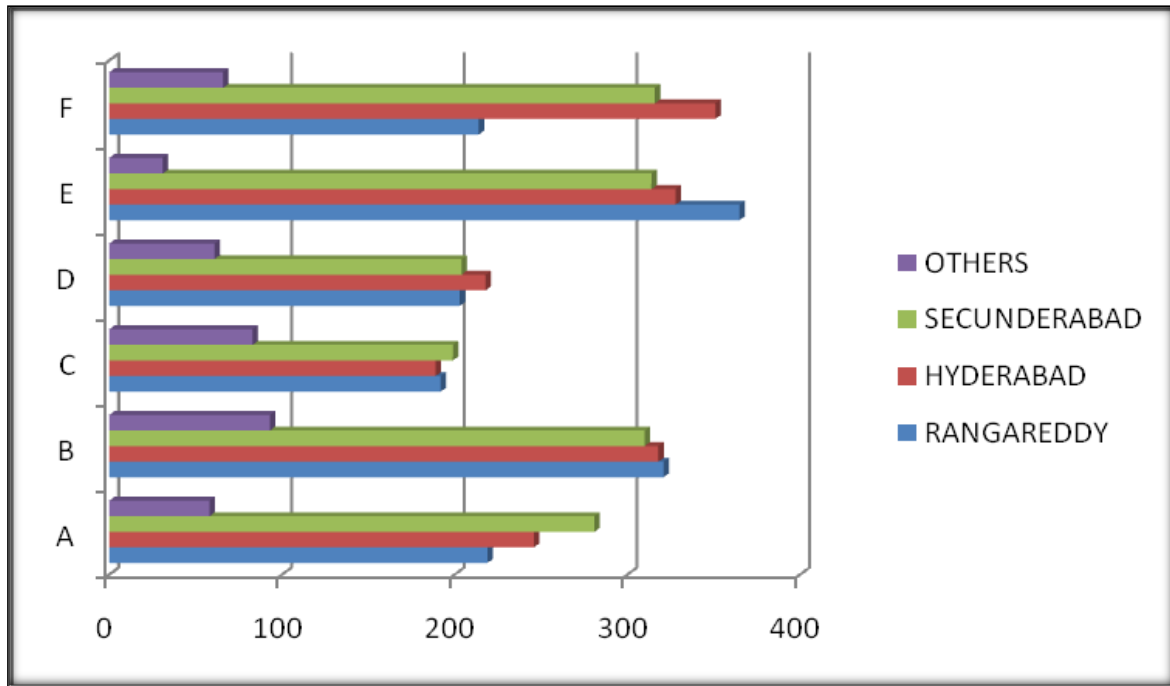
Age-specific (five year groups), sex-specific, and state/UT-specific population data from India Census 2011 was used. These data pre-date the division of Andhra Pradesh in 2014. Conducted every 10 years since 1872, phase one of the 2011 census began on 1<sup>st</sup> April 2010 and included house-listing and collecting information for the National Population Register. The second phase was the population enumeration phase done from 9 to 28 February, 2011. Global average incidence rates from the International Incidence of Childhood Cancer 3 (IICC3) report were used. Conducted by the International Agency for Research on Cancer with the specific purpose of collecting and disseminating childhood cancer data, IICC-3 is the

third monograph following from IICC-1 published in 1988 and IICC-2 published in 1998. Only population based cancer registries were invited. The target period covered the years starting with 1990, and targeted the age range of 0-19 years. IICC-3 uses observed data on cancer incidence from countries or regions covered by population-based cancer registries and unlike GLOBOCAN does not extrapolate to produce selected national, regional or global cancer burden estimates. Incidence rates per million person-years for the 0-14years (children) and 0-19 years (children and adolescents) age groups were age-adjusted using the world standard population to provide age-standardised incidence rates, using the age-specific incidence rates for individual age groups (0-4 years, 5-9 years, 10-14 years, and 15-19 years). Statistical analyses: Number of incident cases for 0-14years, 0-19 years and individual age groups (0-4 years, 5-9 years, 10-14 years, and 15-19 years) was calculated by multiplying incidence rates with the denominator population for the country and each state/UT. To get cancer-specific incident cases according to the International Childhood Cancer Classification third edition in 0-14 years age group, cancer-specific incidence rates were multiplied with the denominator population for the country and each state/UT. As cancer specific incidence rates were not available for 0-19 year age group, cancer-specific incident cases for this age group were obtained by adding incident cases in the 0-14year age group derived above and cancer-specific incident cases in the 15-19 year age group. To derive the cancer-specific incident cases in 15-19 year age group, cancer-specific incidence rates for this age group were multiplied with the denominator population for the country and each state/UT.

## RESULTS

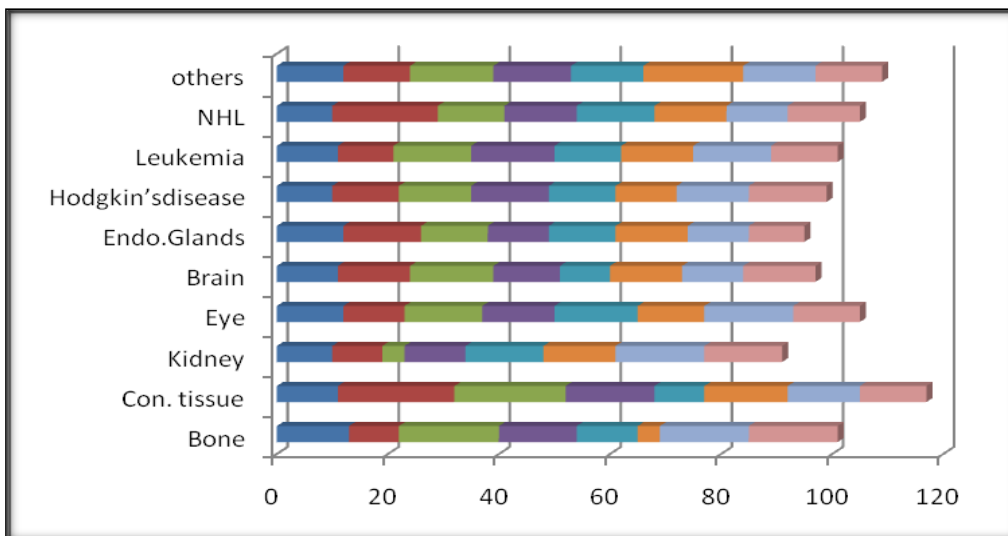
**Table 1: Average I Age- and Gender-Specific Incident Cases of Cancer in Children and Adolescent in Telangana**

Population Based on Registry	Male (Years)			Female (Years)		
	0-9	10-14	14-19	0-9	10-14	14-19
Rangareddy	219	321	192	203	365	214
Hyderabad	246	318	189	218	328	351
Secunderabad	281	310	199	204	314	316
Others	58	93	83	61	31	66



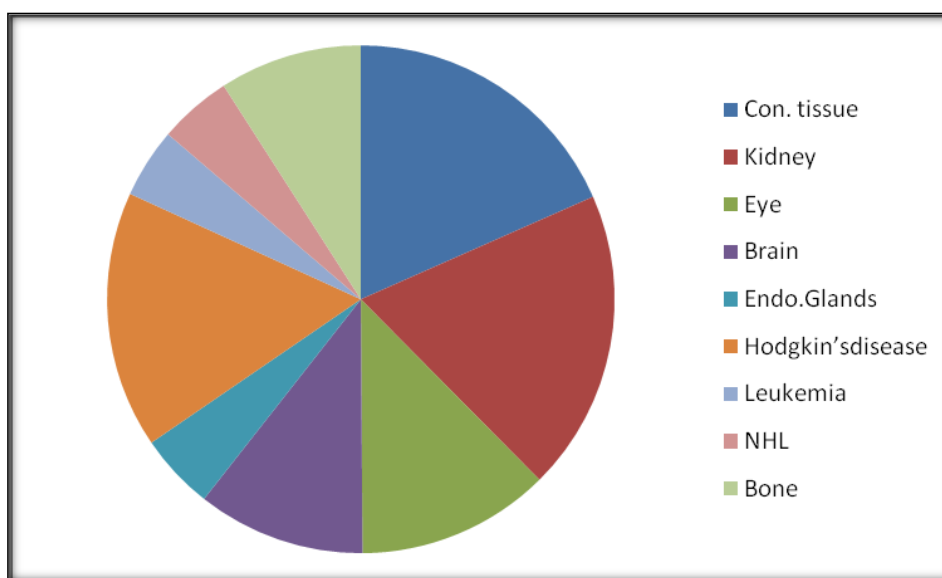
**Table 2: International Childhood Cancer Classification Type-Specific Incident Cases of Cancer in Children 0-14 Years of Age in Telangana**

Site	Male				Female			
	RGD	HYD	SCB	OTH	RGD	HYD	SCB	OTH
Bone	13	9	18	14	11	04	16	16
Con. tissue	11	21	20	16	09	15	13	12
Kidney	10	9	4	11	14	13	16	14
Eye	12	11	14	13	15	12	16	12
Brain	11	13	15	12	09	13	11	13
Endo.Glands	12	14	12	11	12	13	11	10
Hodgkin's disease	10	12	13	14	12	11	13	14
Leukemia	11	10	14	15	12	13	14	12
NHL	10	19	12	13	14	13	11	13
Others	12	12	15	14	13	18	13	12



**Table 3: International Childhood Cancer Classification Type-Specific Incident Cases\* of Cancer in Children 0-19 Years of Age in Telangana**

Site	Male (0-19)				Female (0-19)			
	RGD	HYD	SCB	OTH	RGD	HYD	SCB	OTH
Con. tissue	91	66	81	71	64	72	49	56
Kidney	95	62	88	51	35	24	28	37
Eye	61	38	26	39	41	26	73	19
Brain	53	28	25	36	46	38	45	29
Endo.Glands	24	28	34	51	26	58	34	28
Hodgkin'sdisease	81	25	36	35	67	28	93	23
Leukemia	22	19	23	45	24	28	39	30
NHL	23	45	19	32	28	14	26	58
Bone	45	61	28	36	29	32	51	60



Using globally observed data and local population estimates, the national number of children (0-14 years) and, children and adolescents (0-19 years) that may develop cancer every year are based on 2011 census as 52,366 and 76,805 persons, respectively [Table 1]. The national incidence for boys and girls of 0-14 years of age are 29,425 and 23,045 persons, respectively, and 42,160 boys and 33,694 girls for those 0-19 years of age. Uttar Pradesh, Bihar, Maharashtra, West Bengal and Madhya Pradesh are the five states with the largest absolute burden of disease [Table 1]. Leukemias, central nervous system (CNS) tumors and lymphomas are the three most common cancers in the 0-14 years age group contributing to 33.0%, 20.1% and 10.8% of the total burden [Table 2], and account for 27.0%, 16.8% and 13.9%, respectively of the total burden in the 0-19 years age group [Table 3].

## DISCUSSION

The National Cancer Registry Program (NCRP) in India provides data for the observed individual population based cancer registries which include all patients with cancer diagnosed and registered, and cover less than 10% of the Indian population. The NCRP report, however, does not extrapolate to provide an estimate of the national incidence of childhood cancer. National estimates used for cancer control planning in India are provided by the GLOBOCAN 2018 models that are built using individual cancer registry data from the NCRP report, national vital statistic data sets and economic development covariates.<sup>[2]</sup> In this analysis, using internationally standardized incidence rates and population estimates from India, we found that the incidence of childhood cancer is 54.8% larger in 0 to 14 years age range (52366 vs 28712) and 50.3% larger in 0 to 19 years age range (76805 vs 38640) compared to GLOBOCAN 2018. We hypothesize the large observed difference between the two estimates is due to the substantial number of cases that are not diagnosed and/or registered in India. For health systems planning, calculating both the number of patients who will develop cancer and the number of patients who are diagnosed and registered is critical information. Knowing the current healthcare utilization needs presently is critical for states to make allocation decisions today. However, as cancer control plans typically are written as multi-year plans, identifying the gap between the observed and expected cases is important. In particular, as strategies to improve access and referral are often built into national cancer control plans, these calculations can inform prioritization, decision-making, monitoring procedures and budgeting. Not only is the incidence of diagnosed and registered (GLOBOCAN 2018) approximately half of those who develop cancer (our estimates),

The estimated proportion of girls diagnosed and registered with cancer is 10% less than boys. This aligns with the narrative of female children with cancer experiencing relatively greater barriers to accessing healthcare. Similarly the differential of the GLOBOCAN 2018 estimates and those from our analysis is greatest in CNS tumors and lowest in leukemias. This may reflect the relatively sick nature of leukemia patients, and easy availability of automated blood counts and bone marrow examination as compared to more sophisticated and technology dependent interventions like neuroimaging and neurosurgery. There is also a component of underascertainment in diagnosed CNS tumors as currently NCRP datasets exclude tumors with 'benign' or 'uncertain' behavior and such tumors constitute 40-50% of CNS tumors in children and adolescents. Limitations of our analysis are that we are using the

2011 census data and hence have likely slightly overestimated the incidence of new cases. Although the population of India is projected to peak around 2050, that for children ages 0-19 years is expected to peak between 2010 to 2020. And hence one can argue that the burden in 2011 will be higher by a few percentage points than the burden in 2020 and beyond. The census 2011 however remains the most reliable estimates of population at the state and union territory level and hence was used. It is also difficult to be more precise to the relative contributions of under-diagnosis versus under registration although there is some evidence to support that under-diagnosis is the main component of 'incidence gap' in the burden. The contribution of underdiagnosis and under-registration may vary across states depending on the healthcare accessibility but in our analysis we have assumed that it is same across states. Perhaps the most important question in regard to our estimates is its reliability and accuracy. While there is a degree of uncertainty around the burden, its reliability can be inferred from two arguments. Firstly, is the central tenet that environment plays a minor role in the etiology of childhood cancer hence the variation in the incidence of childhood cancer across the world is limited.<sup>[4]</sup> Secondly, under-diagnosis and other aspects of impaired healthcare access like delayed diagnosis, abandonment of treatment, etc. are well-recognized issues in LMIC. Our estimates of 45-50% underdiagnosed children mirrors other recently published data which reached similar conclusions using differing methodologies.<sup>[7,8]</sup>

## CONCLUSION

In conclusion, our analysis proposes new estimates of incident childhood cancer cases in India. We also provide estimates at state and union territory level. This has enormous implications for all childhood cancer stakeholders who aim to provide access, treatment and chance of long-term cure to every child with cancer. It also suggests that access to diagnosis is as big, if not a bigger problem, than access to complete treatment and needs to be tackled early and urgently. Future regional, national and international research on childhood cancer epidemiology and healthcare accessibility would help further refine these estimates.

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