10-Year-Childhood Malignancy Profile Province-Wide in Indonesia (2009-2018): Yogyakarta Pediatric Cancer Registry

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Abstract

Background: In 2001, Dr. Sardjito Hospital initiated a systematic hospital-based registry, Yogyakarta Pediatric Cancer Registry (YPCR). This study aims to present an epidemiological profile of childhood malignancies diagnosed in Dr. Sardjito General Hospital and compare it with the previous study [1] **Methods:** Childhood cancer was diagnosed in children aged 0-18 years, from January 2009 to December 2018, and analyzed. Childhood malignancies were categorized based on age, sex, and disease group according to the International Classification of Childhood Cancer (ICCC-3). An estimated annual average incidence rate (AAIR) of childhood cancer was calculated. We visualized the number of patients and their regions of origin by geographic mapping. **Result:** There were 1,788 new cases registered in YPCR during the study period. Of these, 58% were male, with a male-to-female.4:1.0. The mean age at diagnosis was 6.3 years old, the median age was 5 years and 56% of cancers were diagnosed in the age group of 0-5 years old. The most common diagnosis category was leukemia (ICCC-3 Category I), which accounted for 60% of all childhood malignancies. The three most common diagnoses included: ALL (44%), AML (13%), and retinoblastoma (6%). Of the 1,077 patients diagnosed with leukemia, 58% were males, most often diagnosed at 0-5 years old (53%). There were 679 patients registered with solid tumors mostly diagnosed at 0-5 years old (57%). The AAIR of leukemia and solid tumors was 26.8 and 17.5 per million, respectively. **Conclusion:** There was an increase in the number of childhood malignancies in 2009-2018 compared to the 2000-2009 study. The number of patients referred to our hospital increased, indicating a better referral system to the pediatric cancer center. This study is expected to provide data on the hospital-based pediatric cancer registry in Indonesia and promote systematic pediatric cancer registries in other centers.

Introduction

The magnitude of the global burden of childhood and adolescent cancer is poorly quantified, estimating that 80% of all children with cancer live in low-income and middle-income countries (LMIC), where the cure rates of childhood cancer are far below the high-income countries[2]. This indicates a need for improved registration and documentation of cancer cases[2,3].

Dr. Sardjito General Hospital (SGH) is a tertiary care academic hospital associated with Universitas Gadjah Mada, located in the Yogyakarta Special Region (YSR), Indonesia. Indonesia is an archipelago with more than 16,000 islands, although 56% of the population lives on the main island of Java. YSR, in south-central Java, is the 4th most populated province in Indonesia with a total population of 3,762,200 and a population density of 1,201 per km^2 as of 2017[4]. SGH is the only tertiary referral hospital for pediatric cancer patients from the YSR province and the surrounding area. The referral area comprises most of the southern region of Central Java.

The earliest cancer registry in Indonesia started in Semarang, Central Java, in 1970. Subsequently, many hospital-based, pathology-based, and population-based cancer registries developed until 2004. Nevertheless,

these efforts had varying success due to a lack of human resources, no institutional unit responsible for developing the registry, and a lack of clear policies. In 2006, the Indonesian Ministry of Health established the Sub Directorate of Cancer Control within the Directorate of Non-Communicable Diseases. This directorate initiated the establishment of a sustainable national cancer registry[5]. Indonesia's national cancer registry is primarily hospital-based, compiling data across centers, and focuses on adult cancer rather than pediatric, likely underreporting the pediatric cancer incidence.

In 2001, SGH did a collaborative project with Saskatchewan Cancer Agency, Canada, to establish the Yogyakarta Pediatric Cancer Registry (YPCR), an electronic hospital-based pediatric cancer registry in SGH, Yogyakarta City. Given the relatively large number of children with cancer in LMICs, the opportunity for epidemiologic research makes hospital-based registries potentially cost-effective[6]. A prior ten-year study[1] using data from YPCR was done to describe basic pediatric cancer profiles treated in SGH during 2000-2009. Since this study, YPCR continues to register pediatric cancer cases and has undergone continuous development. This study aims to describe the recent pediatric cancer profile from the last ten years and compare this profile with the previous study[7].

Methods

Children aged 0 - 18 years of age diagnosed with cancer and registered in YPCR between January 2009 and December 2018 were included. Primary demographic data (age, sex, diagnosis, patients' origin) were collected and diagnoses were categorized according to the International Classification of Childhood Cancer (ICCC-3)[8]. The average annual incidence rate (AAIR) was calculated as the annual average of ten-year incidence divided by the pediatric population in the respective area during a single year, then multiplied by a million[7]. Anticipating the fluctuation of population size over a decade, the pediatric population estimates in 2014 were used, as it is the middle year between 2009 to 2018[9].

Data collection and analysis

Since 2001, pediatric cancer patient data have been captured via hospital hardcopy and electronic medical records and entered into a Statistical Package for the Social Sciences (SPSS) database. Intensive training on the registry methodology was provided on-site at the Saskatchewan Cancer Registry office from July to August 2002[1]. Quality control checks were performed with due diligence paid to the completeness of records, standard consistency of data generated, and checks to avoid duplication of records. During the data collection process, verification of information for accuracy and completeness is performed manually by registry staff.

Data were analyzed to generate descriptive statistics using SPSS software program version 21. Continuous data are presented as mean and standard deviation (SD) or median and interquartile range (IQR) for normally distributed and skewed data, respectively. Categorical variables are presented as percentages and counts. The numbers were classified by the diagnosis and the family residential origin. We performed geographic mapping of the number of patients by location of family residence using Tableau 10.2.

Results

There were 1,788 newly diagnosed children registered in YPCR from January 2009 to December 2018. All diagnoses were pathologically confirmed. Of those 58% (n = 1,032) were male and 42% (n = 756) were female with a ratio of 1.4:1.0. The cancers were mostly diagnosed between 0-5 years of age (56%; n = 997) (Table 1).

Data mapping

From 34 provinces all around Indonesia, SGH received referrals from 26 provinces. Most patients were from Central Java province (60%; n=1,078), followed by YSR (29%; n=519). There were 80 patients (4%) who came from outside Java Island. The furthest referral was from Papua province, more than 3,000 kilometers away from YSR (0.4%; n=7).

As the majority of patients came from YSR and Central Java, a focused mapping into these two regions is depicted in figure 1. YSR comprises four regencies and one city. Central Java consists of 29 regencies and six cities. Patients came from the whole area of YSR, while from Central Java, patients mostly came from the Southern area. Most of the patients from the northern part of Central Java are being treated in DR Kariadi, Semarang (the capital city of Central Java). Mapping of the number of patients per location was shown based on disease categories, including leukemia (Supplemental Figure S1), solid tumors (Supplemental Figure S2), retinoblastoma (Supplemental Figure S3), and lymphomas and reticuloendothelial neoplasms (Supplemental Figure S4).

The number of patients per year

The number of patients fluctuated each year (Fig. 2). Between 2009 and 2018, 2012 had the highest number of newly diagnosed patients (212), followed by 2014 (209). The number of newly diagnosed children steadily increased from 2009 to 2012, then it suddenly plummeted in 2013 with only 158 patients, then rose again in 2014. After 2016, the direction became a downtrend, with 2018 as the lowest number of patients (140). We presented data on a number of patients over the year for each disease category, such as leukemia and solid tumors, in Supplemental Figures S5 and S6. The decrease in the number of patients in 2013 and 2018 was mainly in part due to solid tumor cases diagnosed being much lower.

Disease category based on ICCC-3

The most common diagnosis category in YPCR was leukemia (ICCC-3 Category I), which accounted for 60% (n=1077) of all childhood malignancies. The most frequent specific diagnoses were acute lymphoblastic leukemia (44%, n=791), acute myeloblastic leukemia (13%, n=235), and retinoblastoma (6%, n=109) (Supplemental Table S1). Based on these findings, ICCC-3 Group I (leukemia), II (lymphomas and reticuloendothelial neoplasms), and V (retinoblastoma) were the majority of cases diagnosed in SGH.

Leukemia

The most frequently diagnosed was acute leukemia (57%, n=1026) consisting of acute lymphoblastic leukemia 44%, n= 791.

Solid Tumors

All cancers in ICCC-3 group II-XII and unclassified (benign tumors) were further categorized as solid tumors. There were 679 patients with solid tumors recorded in YPCR during 2009-2018, 57% (389) males and 43% (290) females. The most frequent diagnosis was retinoblastoma (ICCC-3 group V), which accounted for 16% (109 cases) of all pediatric solid tumors in SGH diagnosed from 2009 to 2018. This number was followed by lymphomas and reticuloendothelial neoplasms (ICCC-3 group II) with 97 cases (14%). Solid tumor diagnoses were evaluated by the age of diagnosis (0-5 years, 6-12 years, 13-15 years, and 16-18 years) to examine differences in diagnosis by age.

Retinoblastoma

In the last ten years, there were 109 patients with retinoblastoma registered in YPCR. There were 57 males (52%) and 52 females (48%). As expected, most were diagnosed between 0-5 years of age (95%, n=104), with only five children (5%) diagnosed at six years of age or older (Table 2). The mean age at diagnosis of retinoblastoma was 2.3 years (median 2).

Lymphomas and reticuloendothelial neoplasms

There were 129 patients within this category. Of these, there were 92 males (71%) and 37 females (29%). The majority were diagnosed at 0-5 years old (50%, n=64). Non-Hodgkin Lymphoma was the most frequently diagnosed in this category (52%, n=67).

The average annual incidence rate (AAIR) of pediatric malignancy

The AAIR of all cases of pediatric malignancy in YSR was 48.8 per million populations (Table 3). The AAIR of leukemia and solid tumors was 26.8 and 17.5 per million, respectively.

Comparison of Childhood Cancer Incidence Rate between YSR and other regions

Table 4, shows the comparison between the average annual incidence rate of childhood cancer between YSR, globally[10] in Southeast Asia[10], and in Thailand[11]. Our center's incidence rates are generally lower than the numbers documented in other countries.

Discussion

This study explored an epidemiological profile of malignancies diagnosed in 1788 children in Indonesia. This study indicates there was a 60% increase in the number of childhood malignancies in the 2009-2018 study compared to the 2000-2009 study, with leukemia being the most common malignancy.

As this study was a comparative study, data in this study will be compared with the previous study in SGH done by Ali et al[1]. The number of patients registered during the 2009-2018 study increased by almost 60% compared to the 2000-2009 study (1,788:1,124). The increase did not directly mean an increase in childhood cancer incidence. An apparent increase can result from fewer undiagnosed cancer, a better referral system, or better awareness in society about childhood cancer. We also estimated that an increasing number were caused by implementing national health insurance called Universal Health Coverage (UHC). The other cause can be explained by the increase of population in YSR, having an increase in the annual population growth rate from 1.04% during 2000-2010 to 1.17% during 2010-2017[4].

The male to female ratio did not change much, with the male to female ratio of 1.3:1 (compared to 1.7:1 in the previous study). Male sex was positively associated with most cancer[10]. The socio-cultural aspect could explain the male predominance, which includes prioritizing male referral to better health access, while female children tended to be neglected. While the ratio is still unbalanced, there might be improvements in equity for women compared to the prior study.

Most patients were from Central Java and the YSR area. The proportion from these two regions (89%) decreased compared to the previous study (94%), showing that there was an increasing number of patients who came from outside the referral area of SGH, especially from outside of Java Island. This finding could signify a better referral system and may indicate a need for a tertiary pediatric cancer center outside Java Island.

Childhood cancers were most often diagnosed in the age group of 0-5 years old (56%; n=997). This corresponds well to a study[2], stating that the 0–4-year age group had the most significant contribution to the global burden of childhood cancer. A notable change was shown in the proportion of age at diagnosis. There was an increase in the proportion of children diagnosed in the 13-15 years and 16-18 years of age groups. The percentage of patients diagnosed with cancer at 16-18 years rose from 0.4% in the 2000-2009 period to 4% in the 2009-2018 period. The increased proportion of adolescents and young adults seen in this study could be due to UHC in 2014. Prior to the universal coverage, older children and adolescents did not have routine health prevention programs; however, now, with UHC, people in all age groups can get free medical access, with coverage for 78% of the total Indonesian population[13]. The number of patients in the 16-18 years of age group might still be underreported in this study because of the possibility that patients in these age groups were referred to adult oncology specialists.

Leukemia was still the leading disease among pediatric cancer in SGH, accounting for 60% of all childhood malignancies in the 2009-2018 study and 57% in the 2000-2009 study. The number of patients with leukemia and lymphoma peaked in 2014, following the establishment of UHC.

The incidence rate of leukemia in YSR was 26.8 per million population, which is lower than the global incidence rate of 46.4 per million population, and lower compared to that of Southeast Asia of 52.7[10]. This could signify underdiagnosis rather than an actual lower incidence.

The incidence rate of retinoblastoma in YSR was 2.2 per million population, which is lower compared to the 6.0 per million population in Southeast Asia[10]. Most of our retinoblastoma patients came in the late stages. Some of them seek traditional medicine before finding a healthcare provider. Lack of awareness about retinoblastoma in developing countries causes a delay in seeking medical attention[14]. For example, children with familial retinoblastoma do not present early and have significant mortality[15]. Some of the reasons are inadequate healthcare facilities, delays in the referral system, and lack of genetic counseling and testing. Leander et al[16] showed the impact of retinoblastoma awareness programs on an early presentation of the disease in healthcare facilities.

Non-Hodgkin Lymphoma in our center (2.6 per million) also had a lower incidence compared to South-Eastern Asia (5-9 per million). The incidence rate of rhabdomyosarcoma in YSR was 2.5, corresponding to the South-Eastern incidence rate in 0-14 years old (1-4 per million)[17]. In the previous study by Ali et al[1], rhabdomyosarcoma was not one of the six most common diagnoses. However, in the past ten years, it was the fourth most diagnosed pediatric cancer in SGH. This finding can be explained by a better referral system and implementation of UHC

We found an unexpectedly low proportion of patients with central nervous system (CNS) tumors in our center, where CNS tumors ranked sixth most comment (3.5%; n=64), although CNS tumors are the second most common childhood cancer globally following leukemia[3]. Some CNS tumors may not have been diagnosed, and some may have been referred to neurologists or neurosurgeons and so were not included in our registry. CNS tumors tend to present with non-specific symptoms, such as vomiting and weight loss, that require access to advanced technologies to make a precise diagnosis[10]. Missing access to facilities in LMIC may cause under-diagnosis of CNS tumors due to the rarity of childhood cancer, disease awareness, and financial circumstances[18,19]. In SGH, there are barriers to operating on CNS tumors and pathologically confirming the diagnosis due to limitations in performing microsurgery.

The calculated incidence rate for the most common childhood cancer diagnoses in our center tended to decrease for unknown reasons, even with a growing population, better referral system, and increased access to health care due to the implementation of UHC. The most probable cause was the referral of patients to other clinics in the region. During the study period, a pediatric oncology unit was established in Solo, which is 70 km away and about 2 hours driving with the support of our center in SGH. Also, some patients in the northern part of Central Java may have elected to go to the academic clinic in Semarang. Furthermore, it is not clear how many patients were referred to four private hospitals in the area. This shows that patients might be referred to other pediatric centers besides SGH, emphasizing the importance of collaboration in registration across hospitals in a region or even on a nationwide registry. Undiagnosed cases may also contribute to our low incidence of childhood cancer. Ward et al[17] stated that in South Asia, including Southeastern Asia, the rate of undiagnosed pediatric cancer could reach 49%. These underdiagnoses might be due to poor access to primary care, which leads to late diagnosis and eventual death from the disease at home, or misdiagnosis due to inadequate diagnostics (such as lymphoma misdiagnosed as tuberculosis, or leukemia diagnosed as Dengue).

International Incidence of Childhood Cancer stated that the number of registered cases needs to be at an absolute minimum number to provide a stable estimated incidence rate, resulting in at least 200 cases in the age range 0-14 years or at least 300 cases in the age range 0-19 years[10]. Our incidence rate data for the number of leukemia cases in YSR complied with the condition. However, the incidence rate of other diseases besides leukemia does not properly estimate the incidence rate in YSR. It is challenging to estimate incidence from one hospital-based registry. In addition, the challenge of collecting epidemiological data in LMIC is also unreliable census data, under-reporting cases, the non-accuracy of diagnoses, and dubious certified documentation of mortality[20,21]. The proposed solution to this problem is a national collaboration between pediatric oncology centers and essentially all clinics treating children, be it government or private, in Indonesia to achieve a nationwide registry. Accurate childhood cancer burden data are crucial for prioritizing resource planning and health policy. Raising awareness of childhood cancer by educating the public and health care workers will help reduce the survival gap between the developed and developing countries[14,16].

For the last 10 years, YPCR underwent much-improved data quality and data collection process to become the primary data in which various coordinated teams are processing each diagnosis. YPCR is not only sustainable but also continues to grow. However, as YPCR was only a single hospital-based registry, there were many limitations of YPCR in presenting childhood cancer data. A national population-based registry should be created. It would be helpful to build an integrated registry between pediatric oncology centers, at least in Central Java and the Yogyakarta area, to provide a better epidemiological study of childhood cancer.

We have some limitations of the study; not all patients have the complete data in their medical records. For example, data on the social-economic status and educational background.

There was an increase in the number of childhood patients diagnosed with cancer in the 2009-2018 study period by almost 60% compared to the 2000-2009 profile, also with an improvement in the number of patients coming from outside of the referral area of SGH, especially outside of Java Island. Mapping the number of patients per location in ten years and the incidence rate in our region could be achieved. Leukemia was reported as the most frequent malignancy, with an increased proportion of malignancies diagnosed in teenagers. This finding could be a sign of a better referral system from remote areas to the pediatric cancer center and better access to a health care facility with UHC in Indonesia. Further collaboration between the pediatric cancer center and the national registry is warranted to facilitate more studies on childhood malignancy. We do hope that this study could advocate the policymaker to give a better service to those who suffered.

Conflict of Interest

The authors have no financial conflicts of interest to disclose.

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References

1. Ali K, Sutaryo S, Purwanto I, Mulatsih S, Supriyadi E, Widjajanto PH, Sumadiono S, Nurse J. Yogyakarta pediatric cancer registry: an international collaborative project of university gadjah mada, university of saskatchewan, and the saskatchewan cancer agency. Asian Pac J Cancer Prev. 2010 Jan 1;11(1):131-6.
2. Bhakta N, Force LM, Allemani C, Atun R, Bray F, Coleman MP, Steliarova-Foucher E, Frazier AL, Robison LL, Rodriguez-Galindo C, Fitzmaurice C. Childhood cancer burden: a review of global estimates. The lancet oncology. 2019 Jan 1;20(1):e42-53.
3. Johnston WT, Erdmann F, Newton R, Steliarova-Foucher E, Schüz J, Roman E. Childhood cancer: estimating regional and global incidence. Cancer Epidemiology. 2021 Apr 1;71:101662.
4. Statistik BP. Statistical Yearbook of Indonesia. Population and employment. BPS-Statistics Indonesia, Jakarta; 2018. pp 85.
5. Wahidin M, Noviani R, Hermawan S, Andriani V, Ardian A, Djarir H. Population-based cancer registration in Indonesia. Asian Pacific Journal of Cancer Prevention. 2012;13(4):1709-10.
6. Howard SC, Metzger ML, Wilimas JA, Quintana Y, Pui CH, Robison LL, Ribeiro RC. Childhood cancer epidemiology in low-income countries. Cancer: Interdisciplinary International Journal of the American Cancer Society. 2008 Feb 1;112(3):461-72.
7. Supriyadi E, Widjajanto PH, Purwanto I, Cloos J, Veerman AJ, Sutaryo S. Incidence of childhood leukemia in Yogyakarta, Indonesia, 1998–2009. Pediatric blood & cancer. 2011 Oct;57(4):588-93.
8. Steliarova-Foucher E, Stiller C, Lacour B, Kaatsch P. International classification of childhood cancer. Cancer. 2005 Apr 1;103(7):1457-67.

9. Statistik BP. Statistics of D.I. Yogyakarta Province, Population and employment. BPS-Statistics of D.I. Yoyakarta Province, Yogyakarta; 2014. pp 63.
10. Steliarova-Foucher E, Colombet M, Ries LA, Moreno F, Dolya A, Bray F, Hesseling P, Shin HY, Stiller CA, Bouzbid S, Hamdi-Cherif M. International incidence of childhood cancer, 2001–10: a population-based registry study. The Lancet Oncology. 2017 Jun 1;18(6):719-31.
11. Bidwell SS, Peterson CC, Demanelis K, Zarins KR, Meza R, Sriplung H, Wiangnon S, Chotsampancharoen T, Chitapanarux I, Pongnikorn D, Daoprasert K. Childhood cancer incidence and survival in Thailand: A comprehensive population-based registry analysis, 1990–2011. Pediatric blood & cancer. 2019 Jan;66(1):e27428.
12. Williams LA, Richardson M, Marcotte EL, Poynter JN, Spector LG. Sex ratio among childhood cancers by single year of age. Pediatric blood & cancer. 2019 Jun;66(6):e27620.
13. Idris F, Anggraini M, Humaidi I, Ma'ruf MI, Rahmitasari R. BPJS Information: Towards Universal Health Coverage 2019. BPJS Kesehatan, Jakarta, Indonesia; 2019. pp 6
14. Jain M, Rojanaporn D, Chawla B, Sundar G, Gopal L, Khetan V. Retinoblastoma in Asia. Eye. 2019 Jan;33(1):87-96.
15. Chawla B, Hasan F, Azad R, Seth R, Upadhyay AD, Pathy S, Pandey RM. Clinical presentation and survival of retinoblastoma in Indian children. British Journal of Ophthalmology. 2016 Feb 1;100(2):172-8.
16. Leander C, Fu LC, Pena A, Howard SC, Rodriguez-Galindo C, Wilimas JA, Ribeiro RC, Haik B. Impact of an education program on late diagnosis of retinoblastoma in Honduras. Pediatric blood & cancer. 2007 Nov;49(6):817-9.
17. Ward ZJ, Yeh JM, Bhakta N, Frazier AL, Atun R. Estimating the total incidence of global childhood cancer: a simulation-based analysis. The Lancet Oncology. 2019 Apr 1;20(4):483-93.
18. Rutherford ME, Mulholland K, Hill PC. How access to health care relates to under-five mortality in sub-Saharan Africa: systematic review. Tropical medicine & international health. 2010 May;15(5):508-19.
19. Erdmann F, Feychting M, Mogensen H, Schmiegelow K, Zeeb H. Social inequalities along the childhood cancer continuum: an overview of evidence and a conceptual framework to identify underlying mechanisms and pathways. Frontiers in public health. 2019 Apr 18;7:84.
20. Kellie SJ, Howard SC. Global child health priorities: what role for paediatric oncologists?. European Journal of Cancer. 2008 Nov 1;44(16):2388-96.
21. Steliarova-Foucher E, Stiller C, Kaatsch P, Berrino F, Coebergh JW, Lacour B, Perkin M. Geographical patterns and time trends of cancer incidence and survival among children and adolescents in Europe since the 1970s (the ACCIS project): an epidemiological study. The Lancet. 2004 Dec 11;364(9451):2097-105.

Legends

FIGURES

FIGURE 1. Geographic distribution of family residential origin for children with cancer diagnosed at SGH from 2009-2018 and originating from Central Java or YSR provinces (N = 1,597).

FIGURE 2. Number of children diagnosed with cancer per year at SGH from 2009 – 2018 (N = 1,788)

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SUPPORTING INFORMATION

1. SUPPLEMENTAL FIGURE S1. Geographic distribution and the number of leukemia patients diagnosed at SGH from 2009-2018 and originating from Central Java or YSR provinces (N = 950).
2. SUPPLEMENTAL FIGURE S2. Geographic distribution and the number of solid tumor patients diagnosed at SGH from 2009-2018 and originating from Central Java or YSR provinces (N = 391).
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7. SUPPLEMENTAL TABLE S1. Top-10 Diagnoses of children diagnosed with cancer at SGH from 2009-2018 and specifically for patients from YSR (N = 1,510)

FIGURES

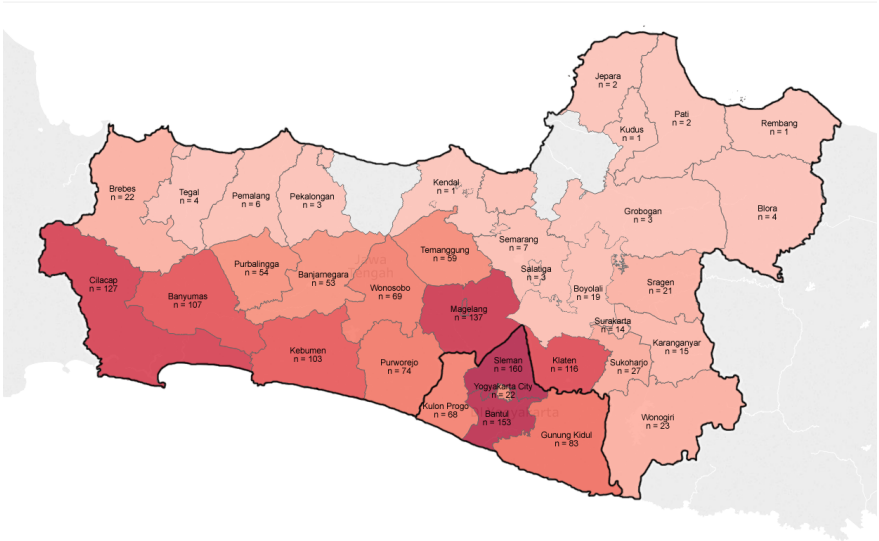

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FIGURE 1. Geographic distribution of family residential origin for children with cancer diagnosed at SGH from 2009-2018 and originating from Central Java or YSR provinces (N = 1,597). A darker shade indicates a greater number of patients. A region without shade indicates that there were no patients who came from these areas. Bold lines are provincial borders.

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FIGURE 2. Number of children diagnosed with cancer per year at SGH from 2009 – 2018 (N = 1,788)

TABLE 1. Basic demography of childhood malignancy in Dr. Sardjito General Hospital, Yogyakarta, Indonesia from 2009-2018 (N=1,788)

All childhood malignancy cases		
Gender	N	%
Male	1,032	58
Female	756	42
Age Group	N	%
0-5 years old	997	56
6-12 years old	514	29
13-15 years old	211	11
16-18 years old	66	4
Leukemia		
Gender	N	%
Male	624	58
Female	453	42
Age Group	N	%
0-5 years old	567	53
6-12 years old	330	31
13-15 years old	133	12
16-18 years old	37	4
Diagnosis	N	%
Acute lymphoblastic leukemia	791	73
Acute myeloid leukemia	232	21.5
Chronic myeloid leukemia	38	3.5
Myelodysplastic syndromes	12	1
Juvenile Myelomonocytic Leukemia	2	<1
Multiple Myeloma	1	<1
Congenital Myelomonocytic Leukemia	1	<1
Retinoblastoma		
Gender	N	%
Male	57	52
Female	52	48
Age Group	N	%
0-5 years old	104	95
6-12 years old	5	5
13-15 years old	0	0
16-18 years old	0	0
Lymphomas and reticuloendothelial neoplasms	*Lymphomas and reticuloendothelial neoplasms*	*Lymphomas and reticuloendothelial neoplasms*
Gender	N	%
Male	92	71
Female	37	29
Age Group	N	%
0-5 years old	64	50
6-12 years old	43	33
13-15 years old	17	13
16-18 years old	5	4

All childhood malignancy cases		
Diagnosis	N	%
Non-Hodgkin Lymphoma	67	52
Histiocytosis	31	24
Burkitt Lymphoma	13	10
Hodgkin Lymphoma	12	9
Anaplastic Large Cell Lymphoma	2	2
Follicular Lymphoma	1	<1
Histiocytoma	1	<1
Lymphoma Maligna	1	<1
NK Cell Lymphoma	1	<1

TABLE 2. Total cases and age of diagnosis of solid tumors based on the ICCC-3 disease category at SGH from 2009-2018 (N = 679)

Solid Tumors	**Total cases**	**Age Group**	**Age Group**	**Age Group**	**Age Group**
		0-5 years old	6-12 years old	13-15 years old	16-18 years old
V. Retinoblastoma	109	104	5	0	0
II. Lymphomas and reticuloendothelial neoplasms	97	34	43	16	4
IX. Soft tissue sarcomas	83	39	33	10	1
X. Germ cell tumors	83	45	24	10	4
IV. Neuroblastoma	64	52	11	1	0
VI. Renal tumors	59	53	5	1	0
III. CNS neoplasms	42	15	21	5	1
Benign tumors	42	33	7	2	0
VIII. Malignant bone tumors	36	5	11	16	4
XI. Carcinoma and melanomas	36	1	18	14	3
VII. Hepatic tumors	24	19	4	0	1
XII. Other and unspecified malignant neoplasms	4	0	2	2	0

CNS: central nervous system

TABLE 3. Number of cases and the average annual incidence rate (AAIR) in Yogyakarta Special Region (YSR) based on the ICCC-3 disease category (N = 1,788)

ICCC-3 Disease Category	**N**	**%**	**YSR AAIR**
Leukemia	1,077	60	26.8
II. Lymphomas and reticuloendothelial neoplasms	129	7	4.5
V. Retinoblastoma	109	6	2.2
IX. Soft tissue sarcomas	83	5	2.6
X. Germ cell tumors	83	5	2.2
IV. Neuroblastoma	64	4	2.2
VI. Renal tumors	59	3	2.0
III. CNS neoplasms	42	2	2.3
Benign Tumor	42	2	1.7
VIII. Malignant bone tumors	36	2	1.3
XI. Carcinoma and melanomas	36	2	0.6
VII. Hepatic tumors	24	1	0.5
XII. Other and unspecified malignant neoplasms	4	<1	0.1
All cases	1,788	100	48.8

ICCC: International Classification of Childhood Cancer; YSR: Yogyakarta Special Region; AAIR: average annual incidence rate; CNS: central nervous system

TABLE 4. Comparison of the average annual incidence rate of childhood cancer between Yogyakarta Special Region, Global, Southeast Asia and Thailand

	Yogyakarta	Global[a]	Southeast Asia[a]	Thailand[b]
All Childhood Cancer	48.8	152.8	-	98.5
Leukemia	26.8	46.4	52.7	36.1
Lymphomas	4.5	15.2	9.5	10.3
CNS neoplasms	2.3	28.2	12.9	12
Neuroblastoma	2.2	10.4	4.4	3.2
Retinoblastoma	2.2	4.5	6.0	2.7
Renal tumors	2.0	8.2	5.4	3.2
Hepatic tumors	0.5	2.3	3.2	2.2
Malignant bone tumors	1.3	5.7	5.6	4.5
Soft tissue sarcomas	2.6	8.9	5.2	4.8
Germ cell tumors	2.2	4.9	5.7	6.2
Carcinoma and melanoma	0.6	4.6	5.0	7.2
Other and unspecified	0.1	1.2	4.1	6

CNS: central nervous system

[a]2017 publication, age range from 0-19 years old. Calculated from weighted average from 4 age specific rates using the weights of the world standard population[10].

[b]2018 publication, age range from 0-19 years old. Rates were Age-standardized incidence rates calculated per million person-years[11].