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Original Article

Implementing *Yogyakarta Pediatric Cancer Registry* for 16 Years: a report of hospital-based childhood cancer registry

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Abstract

Background A hospital-based cancer registry can be used as a guide to decision-making. Considering the limited cancer registry data in the population, the *Yogyakarta Pediatric Cancer Registry* (YPCR) is one of the pioneers of hospital-based pediatric cancer registries in Indonesia. The YPCR was started in 2000 in Dr. Sardjito Hospital.

Objective To describe the characteristics of childhood cancer and the outcomes by analyzing overall survival (OS) and event-free survival (EFS) based on data from Yogyakarta Pediatric Cancer Registry.

Methods Data were collected from the YPCR for the period of 2000 to 2016. Childhood cancers were classified into 12 groups based on the *3rd edition International Classification for Childhood Cancer* (ICCC). Incidence, frequency, and distribution of cases were grouped by sex, age, and patients' place of residence. Incidence was further analyzed using SPSS software. Kaplan-Meier test was used to analyze OS and EFS.

Results Within the study period, 2,441 children aged 0-18 years were diagnosed with cancer. The highest incidence was found in the 1-5-year age group. The most common diagnoses found were leukemia, myeloproliferative disorders, and myelodysplastic disease (58%); lymphoma and reticuloendothelial neoplasm (8%); retinoblastoma (6%); soft tissue and other extra-osseous sarcomas (5%); as well as neuroblastoma and other peripheral nervous cell tumors (5%). The OSs of acute lymphoblastic leukemia (ALL), high risk ALL (HR-ALL), and standard risk (SR-ALL) were 31.8%, 18.5%, and 43.9%, respectively. The EFSs of ALL, HR-ALL, and SR-ALL were 23.9%, 14.7%, and 32.4%, respectively. For solid tumors, the OS was 13.7% and EFS was 6.4%.

Conclusion The number of new cases of childhood cancer has increased in the last few years. The Yogyakarta Pediatric Cancer Registry (YPCR), which serves as a hospital-based pediatric cancer registry, has an important role to evaluate clinical and non-clinical aspects of childhood cancer. **[Paediatr Indones. 2019;59:188-94; doi: http://dx.doi.org/10.14238/pi59.4.2019.188-94]**.

Keywords: *childhood cancer registry; hospital-based cancer registry; childhood cancer incidence*

The trend in childhood cancer incidence has increased in recent years.[1] In Switzerland, there were more than 2,000 new cases of childhood cancer, with more than 80% of Swiss resident aged <15 years. Ninety-two percent of the cases were malignant. Leukemia was the most common cancer found, followed by central nervous system (CNS) malignancy, lymphoma, and neuroblastoma.[2] In Japan, there were more than 1,500 new childhood cancer cases from 2009-2011. Leukemia

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was the leading diagnosis found in the study (38.1%), followed by CNS malignancy, lymphoma, germ cell and other gonadal tumors, and neuroblastoma.[3] In the other hand, survival rates of childhood cancer patients have increased in the past few decades. In 1960, the 5-year survival rate of patients with childhood cancer was less than 30%, but the current 5-year survival of such patients is more than 80%, indicating successful therapy in recent years.[4] Such data can only be obtained from a well-maintained cancer registry, which could be either population-based or hospital-based.

Cancer registry is the key to establish cancer management strategies. It is also a reliable tool to determine the burden of disease as well as to gather the information for causative study.[5] *The International Agency for Research on Cancer* (IARC) stated that only 8% of the population in Asia has been covered by population-based cancer registry, compared to other regions, such as North America which has 90% population coverage, and Europe which has 60%. The limitations in diagnosis and therapy, lack of reliable data of the population, cultural beliefs, unstable economic and political conditions, and massive migration complicate the process of establishing a population-based registry. These limitations result in an underreported incidence rate.[6] As such, establishing a hospital-based registry may be a simpler way to obtain reliable information on childhood cancer and an important step toward population-based registry data collection. The data from a hospital-based cancer registry can be a powerful instrument for clinical epidemiology and evidence-based medicine, as well as a valuable source of information to guide decision-making. However, hospital-based patient registry cannot be used to measure real incidence and mortality in the population, since the data are only obtained from patients with access to the referral hospital.[6]

The Yogyakarta Pediatric Cancer Registry (YPCR) is based on patient data from the Pediatric Wards in Dr. Sardjito Hospital, Yogyakarta, which serves as a referral hospital for many pediatric cancer patients in Indonesia. In 2001, a twinning project between Universitas Gadjah Mada and the *Saskatchewan Cancer Agency*, Canada, was launched to create a computerized cancer registry at Dr. Sardjito Hospital. Before this project began, Indonesia did not have any pediatric cancer registry, so we had little data to measure incidence, mortality, and outcomes, or to evaluate the clinical and non-clinical aspects of pediatric cancer. The objectives of this project were to develop a hospital-based, computerized pediatric cancer registry, and to compare demographics of childhood cancers between the hospital-based YPCR and the population-based *Saskatchewan Cancer Registry*.[7]

This study marks 16 years of YPCR data collection. The aim of this study was to describe the characteristics of childhood cancer in Dr. Sardjito Hospital, and to investigate treatment outcomes of childhood cancer by analyzing overall survival (OS) and event-free survival (EFS). We hope that this study will bring more improvements and innovation in the YPCR and a nationwide, population-based childhood cancer registry in the future.

Methods

Data were collected during 2000-2016 from the YPCR. Trained registrars update the data from patients in Pediatric Wards at Dr. Sardjito Hospital into YPCR. Data such as patients' characteristics, demographic information, diagnoses, cancer treatments, follow-up status, and the use of traditional healing practices were recorded in the registry. Quality control was performed to ensure the completeness of records, consistent data, and no duplications.

Childhood cancer was defined as patients aged 0-18 years who were diagnosed with cancer according to the *International Classification of Disease Oncology* (ICD-O), 3rd edition.[8] Diagnoses were further classified based on the *International Classification of Childhood Cancer* (ICCC), 3rd edition[9] into 12 main groups: I) Leukemias, myeloproliferative diseases (MPD), and myelodysplastic diseases (MDD); II) Lymphomas and reticuloendothelial neoplasms; III) CNS and miscellaneous intra-cranial and intra-spinal neoplasms; IV) Neuroblastoma and other peripheral nervous cell tumors; V) Retinoblastoma; VI) Renal tumors; VII) Hepatic tumors; VIII) Malignant bone tumors; IX) Soft tissue and other extraosseous sarcomas; X) Germ cell tumors, trophoblastic tumors, and neoplasms of gonads; XI) Other malignant epithelial neoplasms and malignant melanomas; and XII) Other and unspecified malignant neoplasms. The diagnosis was made through clinical examination, pathology report, as well as imaging examination and other supporting laboratory test.

New cases, frequency, and distribution of cases were grouped by sex and age (<1 year, 1-5 years, 6-9 years, 10-14 years, and 15-18 years). These groupings were made in order to assess cancer trends based on sex and age. The cases were also grouped by patients' residence, in order to track the regions of referral. The frequency and distribution of the cases was analyzed using *SPSS* software, while 16-year and 6 year OS and EFS were analyzed using Kaplan-Meier test. Survival analyses of ALL and solid tumors were calculated at 16 and 6 years of observation.

Results

Total of new cases of childhood cancer recorded in the YPCR increased from 2000-2016 (**Figure 1**). During that period, there were 2,441 children aged 0-18 years

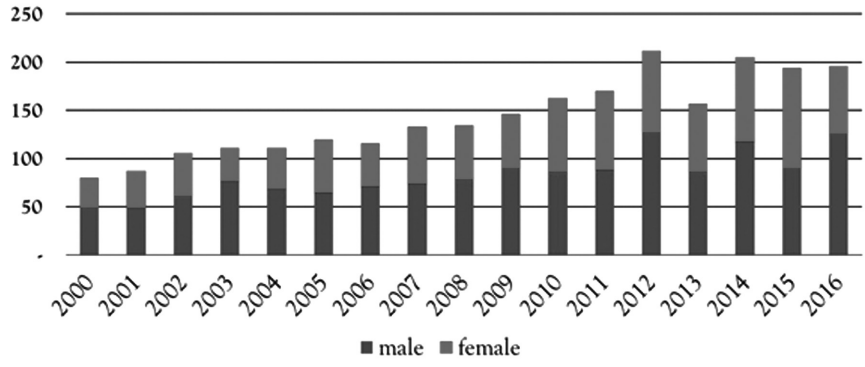

Figure 1. Childhood cancer new cases in Dr. Sardjito Hospital per year

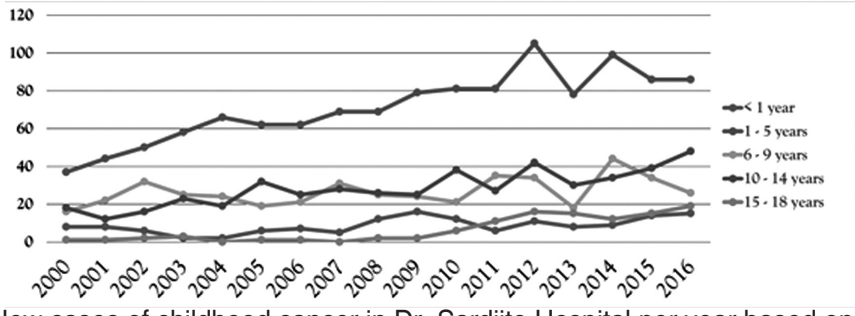

Figure 2. New cases of childhood cancer in Dr. Sardjito Hospital per year based on age group

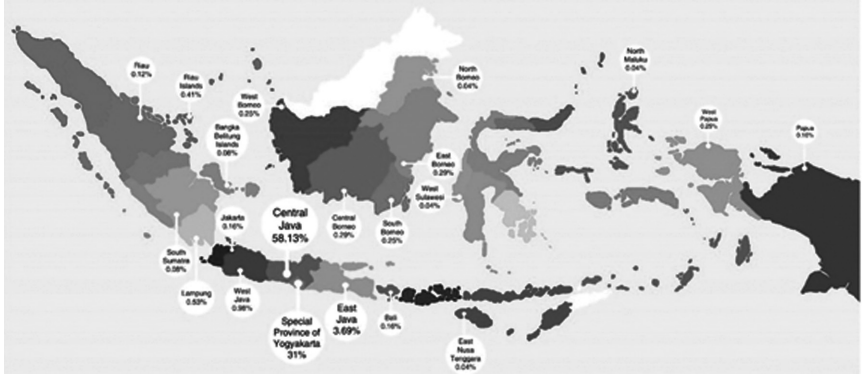

Figure 3. Referral origin of childhood cancer patients in Dr. Sardjito Hospital

were diagnosed with cancer. The largest number of new cases were found in the 1-5-years age group (49,7%), followed by the 10-14-years age group (19,7%), then the 6-9-years age group (18,5%) (**Figure 2**). Overall, the number of new cases in every age group increased in the past few years, especially in the 15-18-year group, which escalated almost 20 times in 16 years of study. The most common diagnoses were leukemia, MPD and MDD (58%); followed by lymphoma and reticuloendothelial neoplasm (8%); retinoblastoma (6%); soft tissue and other extra-osseous sarcomas (5%); and neuroblastoma and other peripheral nervous cell tumors (5%) (**Table 1**). The total number of male patients was 1,398 and female patients was 1,043 (**Table 1**). Each year, males predominated the childhood cancer population (**Figure 1**). The male to female ratio was 1.34 to 1. Most patients referred to Dr. Sardjito Hospital came from Central Java (58.13%), Yogyakarta Special Province (31%), and East Java (3.69%), however, many also came from other regions throughout Indonesia (**Figure 3**).

Trends in diagnoses varied by age group (**Figure 4**). The most common childhood cancers found in < 5 years age group were in the leukemia, MPD, and MDD category, particularly ALL, followed by nephroblastoma, hepatic tumor, and neuroblastoma and other peripheral nervous cell tumors. In 5-9 years age group, the most common childhood cancers were leukemia, MPD and MDD, mostly ALL; then lymphoma and reticuloendothelial neoplasms, out of whom 67% were non-Hodgkins lymphoma (NHL), followed by soft tissue and other extraosseous sarcomas, in which all cases were diagnosed with rhabdomyosarcoma, and neuroblastoma and other peripheral nervous cell tumors. In 10-14 years age group, the most common childhood cancers were leukemia, MPD and MDD, of which ALL accounted

Table 1. Childhood cancer incidence in Dr. Sardjito Hospital

Characteristics		N=2,441
Sex		
Male		1,398 (57.3)
Female		1,043 (42.7)
Age group		
< 1 year		147 (6.02)
1-5 years		1,212 (49.7)
6 -9 years		451 (18.5)
10 - 14 years		482 (19.7)
15 - 18 years		107 (4.4)
No data		42 (1.7)
Diagnosis		
I.	Leukemias, myeloproliferative diseases, and myelodysplastic diseases	1,427 (58.5)
II.	Lymphomas and reticuloendothelial neoplasms	190 (7.8)
III.	CNS and miscellaneous intracranial and intra-spinal neoplasms	81 (3.3)
IV.	Neuroblastoma and other peripheral nervous cell tumors	112 (4.6)
V.	Retinoblastoma	147 (6.0)
VI.	Renal tumors	103 (4.2)
VII.	Hepatic tumors	41 (1.7)
VIII.	Malignant bone tumors	49 (2.0)
IX.	Soft tissue and other extraosseous sarcomas	133 (5.4)
X.	Germ cell tumors, trophoblastic tumors, and neoplasms of gonads	105 (4,3)
XI.	Other malignant epithelial neoplasms and malignant melanomas	41 (1.7)
XII.	Other and unspecified malignant/ neoplasms	12 (0.5)

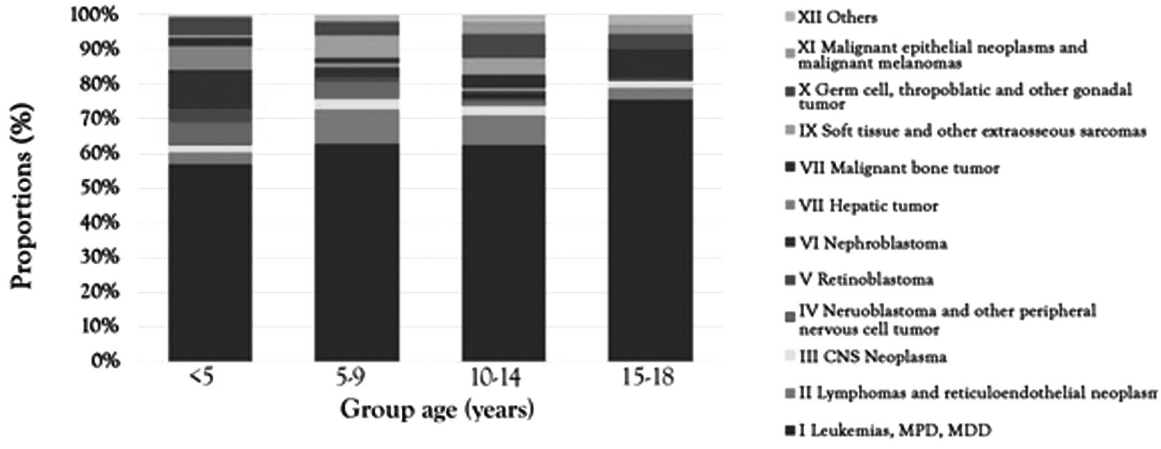

Figure 4. Proportion of childhood cancer cases based on group age

for more than half of the cases; followed by lymphoma and reticuloendothelial neoplasms, with NHL as the most common diagnosis; germ cell, trophoblastic and other gonadal tumors, with most cases diagnosed to have teratoma; and lastly, soft tissue and other extraosseous sarcomas, mostly diagnosed with rhabdomyosarcoma. The most common childhood cancers found in 15-18 years age group were leukemia, MPD, and MDD, with ALL as the most common diagnosis; malignant bone tumors all of whom had osteosarcoma; germ cell tumors, trophoblastic and other gonadal tumors, with 2 cases of teratoma and 1 case of ovarian carcinoma; and lastly lymphoma and reticuloendothelial neoplasms, in which all the cases were NHL. In total, leukemia, more specifically ALL, had the highest incidence of all childhood cancer, in every age group.

In the past 16 years, childhood cancer incidence trends increased year by year. The highest incidence was in 2012 and the lowest was in 2013. The total of the leukemia, MPD and MDD group's new cases had the highest increment, with a 3 times higher new cases in 2016 compared to that in 2000, when the YPCR started. New cases of leukemia were mostly found in the <5 years age group, which accounted for half of the total incidence of leukemia, then decreased with subsequent increase in age groups.

Survival rate analyses of ALL and solid tumor patients who received chemotherapy from 2000-2016 were performed at 16 and 6 years of observation. The OS rate of ALL was 31.8% (**Figure 5**), with OS rate of high risk (HR) ALL of 18.5% and OS rate of standard risk (SR) ALL of 43.9%. Furthermore, EFS of ALL during the study period was 23.9%. The EFS of HR ALL was 14.7% and the EFS of SR ALL was 32.4% (**Figure 5**). The OS rate of solid tumor was 13.7% (**Figure 5**) and the EFS was 6.4% (**Figure 6**).

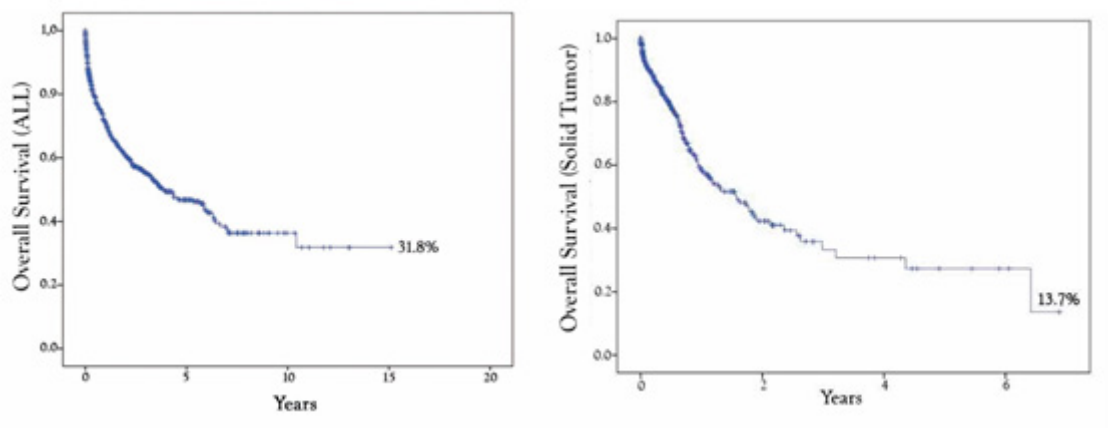

Figure 5. Overall survival of ALL and solid tumor

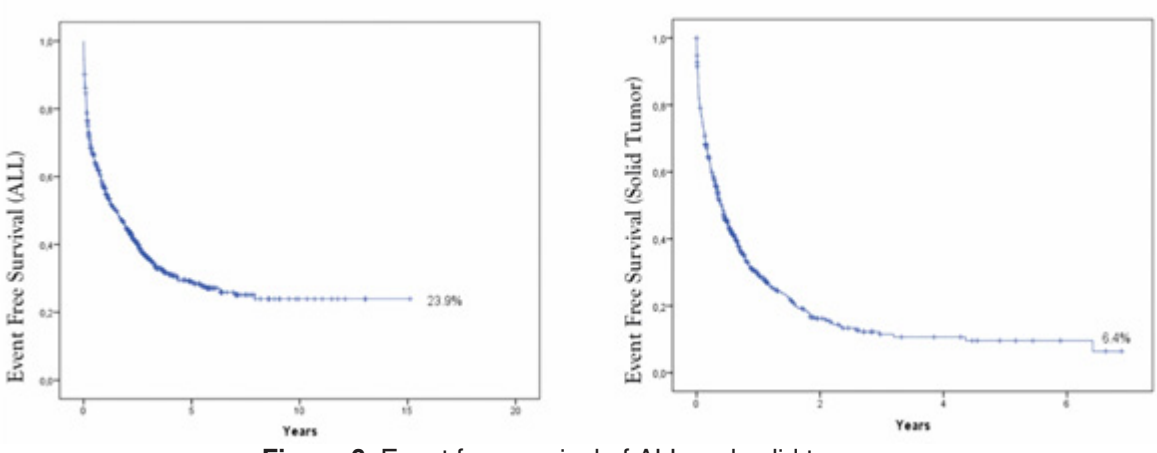

Figure 6. Event free survival of ALL and solid tumor

Discussion

Epidemiologic studies of childhood cancer are useful for revealing periods of tumor initiation by analyzing age distributions of cancer, which then provide deeper understanding about the etiology of cancer. For example, genetic syndromes and higher birth weight are well-established risk factors, but they only account for a small proportion of cases.[10,11] Moreover, survival data are also important to develop surveillance programs for cancer survivors and to determine survival trends which can be used to evaluate progress related to treatment. However, obtaining data for epidemiologic studies of childhood cancer have been difficult to achieve, particularly in Asia, due to the lack of complete, comprehensive, nationwide epidemiological reports on childhood cancer.[12]

The Yogyakarta Pediatric Cancer Registry (YPCR) was initiated in 2000 as a pioneer of computerized, hospital-based childhood cancer registry in Indonesia. It was expected to close the gap of childhood cancer epidemiological information before a nationwide, population-based childhood cancer registry could be developed. The registry has been running for 16 years to date, and has recorded data on 2,441 childhood cancer cases, including 1,398 male and 1,043 female patients. The number of childhood cancer new cases has increased yearly, for both males and females. Male patients predominated over females almost every year, with an overall 1.34:1 ratio. This finding was similar to male to female ratios in previous studies, such as in Canada which had 1.12:1, and in Australia which had 1.14:1.[13,14] In Australia, the highest incidence was found in the 0-4-year age group, while in Indonesia it was found in the 1-5-year age group.[13]

The increasing trends in childhood cancer incidence in Indonesia may be due to changes in diagnostic, coding, or registration practices,[15,16] which may have been propagated by Indonesia's recently-launched universal health coverage in 2014. National health insurance allows all residents in Indonesia to have free access to health services. Those with financial problems have access to their nearest primary health care facility, as well as to tertiary health care, if needed. The health insurance system also enables children with signs and symptoms of cancer to be referred to a tertiary hospital such as Dr. Sardjito Hospital where the YPCR is located, for further investigation and free treatment. The improvement in economic and educational status of the population may also be other factors encouraging more people to seek medical help.

We found that the leukemia, MPD, and MDD category was the most common diagnosis in childhood cancer, accounting for 58.5% of all the cases. In other countries, the leukemia percentages were 35% in Shanghai, China and Chennai, India, 33% in Germany, 30% in Ireland and France, and 27% of pediatric cancers in the United States.[17,18] Our findings were relatively similar, hence, we can conclude that leukemia is the most common cancer in childhood.

The strength of this study was the fact that YPCR is the pioneer of computerized, hospital-based childhood cancer registry in Indonesia, as Indonesia does not have a nationwide, population-based, childhood cancer registry. The weakness of this study was that the data were from one hospital, thus, not representive of epidemiological data for the region or nation. Since not everyone has access to the Dr Sardjito hospital, it was not possible to calculate childhood cancer incidence in the population. Even when health services are free, some people cannot afford transportation fees or other expenses needed during hospitalization.

In conclusion, the number of new cases of childhood cancer has increased in the last few years. A cancer registry is necessary to conduct epidemiological studies and evaluate the clinical and non-clinical aspects of childhood cancer, especially since childhood cancer new cases have increased in the last few years.

Conflict of Interest

None declared.

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