RESEARCH COMMUNICATION

Childhood Cancer Incidence and Survival 2003-2005, Thailand: Study from the Thai Pediatric Oncology Group

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Abstract

Background: Previous population-based incidences of childhood cancer in Thailand were achieved by extrapolating from data limited to a small number of cancer registries, not from the whole country. In addition, survival of childhood cancer patients is often described in specialized hospitals and/or institutions, but not in the general population. Methods: All children aged 0–15 years who were newly diagnosed as having cancer were registered from 18 treatment centers during 2003-5 and classified into 12 diagnostic groups according to the International Classification of Childhood Cancer. Incidences were calculated by a standard method and survival was investigated using the ThaiPOG (Thai Pediatric Oncology Group) population-based registration data. Overall survival was calculated by the Kaplan Meier method. Results: In the study period (2003-5) 2,792 newly diagnosed cases of childhood cancer were registered, with mean and median ages of 6.5 (SD=0.13) and 5.0 (0-14) years, respectively. The age-peak was between 1 and 4 years and the age-standardized rate (ASR) was 74.9 per million. Leukemia was the most common cancer (N=1421, ASR 38.1) followed by lymphoma (N=266, ASR 6.4) and neoplasms of the central nervous system (CNS, N=246, ASR 6.3). The follow-up duration totaled 101,250 months. The death rate was 1.11 per 100 person-months (95%CI: 1.02 -1.20). The 5-year overall survival was 54.9% (95%CI: 53.0%-56.9%) for all cancers. The respective, 5-year overall survival for (1) acute lymphoblastic leukemia (ALL), (2) acute non-lymphoblastic leukemia (ANLL), (3) lymphoma, (4) retinoblastoma, (5) renal tumors, (6) liver tumors, (7) germ cell tumors, (8) CNS tumors, (9) neuroblastoma, (10) soft tissue tumors and (11) bone tumors were (1) 64.5%, (2) 35.1%, (3) 59.5%, (4) 73.1%, (5) 70.4%, (6) 44.5%, (7) 70.6%, (8) 41.7%, (9) 33.6%, (10) 50.1%, and (11) 33.7%. Conclusions: The incidence of childhood cancer is lower than in western countries. Respective overall survival for ALL, lymphoma, renal tumors, liver tumors, retinoblastoma, soft tissue tumors is lower than those reported in developed countries while for CNS tumors, neuroblastoma and germ cell tumors the figures are comparable.

Keywords: Childhood cancer - incidence - survival - ThaiPOG

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Introduction

In Thailand, 21 percent of the population is constituted by children <15 years of age (National Statistics Office, 2003) and, although cancer among this age group is rare, approximately 1,000/year were expectedly diagnosed with cancer calculating based on the incidence in previous studies (Vattanasapt et al., 1999; Wiangnon et al., 2003). During 2007-8 the cancer related mortality rates in Thai children aged 6-12 and 13-18 were 2.16 and 2.13 per 100,000, respectively (Sutra et al., 2009).

The previous population-based incidences of childhood cancer in Thailand were achieved by extrapolating the incidences from the data limited to small number of cancer registries, not from the data of the whole country. In addition, the previously reported survivals of childhood cancer patients were described in specialized hospitals and/or institutions. The aim of this investigation is to perform a population-base prospective study of the incidence rate of childhood cancer in Thailand and to analyze 5-year survival in Thai children with cancer.

Materials and Methods

Since 2003, the ThaiPOG (Thai Pediatric Oncology Group) has recorded diagnoses of malignant tumors in children (0-15 years). The population-based data of childhood cancer were provided by 18 centers in the country, comprising 7 medical school hospitals, 10 regional hospitals and 1 medical institution (Figure 1). To assess

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Figure 1. Collaborating Centers across Thailand

the coverage of childhood cancer diagnosis, questionnaires were sent to all hospital in the whole country. The result revealed that all cases of childhood cancer were referred to 18 centers included in the study. Cancer sites, morphology and behavior, were coded according to the ICD-0-3. The tumor types were grouped according to the International Childhood Cancer Classification (ICCC) (Kramarova, 1996). Both histologically verified and nonverified patients were included. The data were collected through a web-based registration under a standardized format, using double entry method under internal and external audit processes. All patients were observed until the end of December 2010. Aged-standardization rate (ASR) was performed using a direct method with groups 0-14 years (0-4, 5-9 and 10-14 years) (Parkin et al., 1998). ASRs were calculated by the direct method, using the world standard population and expressed per million person-years. Five-year cumulative survival rates were calculated using the Kaplan–Meier method.

Population denominators

The population denominators used for calculation of the incidence rate were estimated from the population censuses (National Statistic Office, 2003). This provides an annual estimate by age group and sex. In 2004 census, approximately 13.4 million children were aged less than 15 (21.6 % of the whole Thai population), 51.3% of whom were boys. On average, 5.16% were <1 year, 23.9% were aged 1-4 years, 35.4% were aged 5-9 years and 35.5% were 10 years or older.

Results

There were 2,792 cases with childhood cancer diagnosed during 2003-2005 (boys =1,602, girls =1,190, ratio 1.3:1). The mean and median ages were 6.5 (SD=0.13) and 5.0 (0-14) years, respectively. The age-peak for incidence was between 1 and 4 years. Most of the

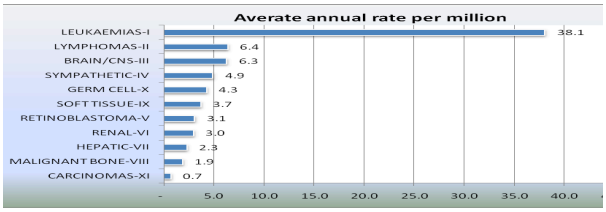

Figure 2. Age-adjusted Incidence Rates for childhood Cancer by ICCC Group, Age<15, Both Sexes, 2003-2005

pediatric cancers were histologically confirmed (98.4%) but the proportion varied between 71.1% for cancer of the central nervous system (ICCC group III) and 100% for leukemia (ICCC group I). The age-standardized rate was 74.9 per million. Leukemia was the most common cancer (N=1,421, ASR 38.1) followed by lymphoma (N=266, ASR 6.4) and neoplasms of the central nervous system (CNS) (N=246, ASR 6.3). (Figure 2, Table 1).

Among leukemias, acute lymphoblastic leukemia (ALL) is more common than acute non-lymphoblastic leukemia (ANLL) with the ratio of 3.1:1. ALL is more common in boy than in girl (ASRs 31.4 vs 24.2) while ANLL incidence is not different in both sexes. Non-Hodgkin lymphoma (NHL) is more common than Hodgkin's disease (HD) and Burkitt's lymphoma (ASRs 3.3, 1.6, 1, respectively). Lymphoma is more common in boys than in girls in all types. In CNS tumors, primitive neuroectodermal tumor is more common than astrocytoma, especially in young age group (Table 1).

Survival

There were 2,792 new cases of childhood cancer registered during January 2003 to December 2005. The censor dated on 31 December 2010. Median follow-up period was 40.7 months (0.1-60 months). There were 1,242 deaths, 66 (5.31%), 477 (38.4%), 337(27.1 %) and 362 (29.2%) for age group of <1, 1-4, 5-9 and 10-14 years, respectively.

Regarding to the follow up of 101,250 person-months and 1,242 (44.1%) deaths, the mortality rate was 1.11 per 100 person-months (95% CI: 1.02-1.2). The probability at 5-year overall survival (OS) is 54.9 % (95% CI: 53.0-56.9) (Table 2). Survival differed by type of cancer. The best outcome with highest overall survival is for retinoblastoma (73.1%) while the worst outcome is evidenced in bone tumor and sympathetic tumor (neuroblastoma) (33.6% and 33.7%). The survival of ALL is better than the one of ANLL significantly (log rank test 126.40, p-value <0.001). The durations of follow up in patient with ALL and ANLL are 42,495 and 8,631 person-month, respectively. Mortality rates of patient with ALL and ANLL are 0.82 and 2.45 per 100 person-months, respectively. The 5 years survival for ALL is 64.9% (95%CI: 61.7-67.9) while ANLL is 35.5 (95%CI: 30.2-40.8) and CML survival is 50.6% (95%CI: 35.7-63.8) (Figure 3).

Lymphoma

The overall survival for lymphoma is 59.5% (95%CI: 53.0% - 65.4%). The respective, 5-year overall survival rates for (1) HD, (2) NHL and (3) Burkitt were (1) 69.3%,

Table 1. Incidences of Cancers in Childhood, Both Sexes Combined, Thailand 2003-2005

Type of Cancer	Number of cases					Rel. freq.(%)			Rate per million						
	< 1	1-4	5-9	10-14	All	M/F	Overall	Group	0-4	5-9	10-14	Crude	ASR	Cum.	%MV
I. Leukemias	82	576	418	345	1421	1.3	50.9	100	55.5	30	24	35.4	38	547	100
Lymphoid	42	451	330	206	1029	1.4	36.9	72.4	41.6	24	14.3	25.6	28	397.5	100
Acute non-lymphocytic	35	109	73	111	328	0.9	11.7	23.1	12.1	5.2	7.7	8.2	8.6	125	100
Chronic myeloid	4	11	12	24	51	1.6	1.8	3.6	1.3	0.9	1.7	1.3	1.3	19.5	100
Other specified	1	5	3	4	13	0.9	0.5	0.9	0.5	0.2	0.3	0.3	0.3	5	100
II. Lymphomas	5	57	102	102	266	2.4	9.5	100	5.2	7.3	7.1	6.6	6.4	98	94.4
Hodgkin's disease	1	10	32	24	67	3.2	2.4	25.2	0.9	2.3	1.7	1.7	1.6	24.5	97.0
Non-Hodgkin lymphomas	3	24	46	64	137	2.3	4.9	51.5	2.3	3.3	4.5	3.4	3.3	50.5	95.6
Burkitt's lymphoma	1	16	16	4	37	2.4	1.3	13.9	1.4	1.1	0.3	0.9	1	14	97.3
Miscellaneous	0	1	2	4	7	0.8	0.3	2.6	0.1	0.1	0.3	0.2	0.2	2.5	100
Unspecified	0	6	6	6	18	2.6	0.6	6.8	0.5	0.4	0.4	0.4	0.4	6.5	66.7
III. Brain and spinal neoplasms	14	73	102	57	246	1.3	8.8	100	7.3	7.3	4	6.1	6.3	93	71.1
Ependymoma	3	9	8	6	26	2.7	0.9	10.6	1	0.6	0.4	0.6	0.7	10	92.3
Astrocytoma	0	16	22	16	54	1.2	1.9	22	1.3	1.6	1.1	1.3	1.3	20	85.2
Primitive neuroectodermal	5	25	37	17	84	1.1	3	34.1	2.5	2.6	1.2	2.1	2.2	31.5	94.0
Other gliomas	5	17	29	9	60	0.9	2.1	24.4	1.9	2.1	0.6	1.5	1.6	23	36.7
Unspecified	1	6	6	9	22	2.7	0.8	8.9	0.6	0.4	0.6	0.5	0.5	8	18.2
IV. Sympathetic nervous system	32	92	30	9	163	1.2	5.8	100	10.5	2.1	0.6	4.1	4.9	66	92.0
Neuroblastoma	32	92	30	9	163	1.2	5.8	100	10.5	2.1	0.6	4.1	4.9	66	92.0
V. Retinoblastoma	19	71	7	0	97	1.3	3.5	100	7.6	0.5	0	2.4	3.1	40.5	86.6
VI. Renal tumors	19	61	14	3	97	0.9	3.5	100	6.7	1	0.2	2.4	3	39.5	89.7
Wilms' tumor	16	58	11	2	87	1.1	3.1	89.7	6.2	0.8	0.1	2.2	2.7	35.5	89.7
Renal carcinoma	1	1	3	1	6	0.5	0.2	6.2	0.2	0.2	0.1	0.1	0.2	2.5	83.3
Other specified	2	2	0	0	4	-	0.1	4.1	0.3	0	0	0.1	0.1	1.5	100
VII. Hepatic tumors	26	30	8	13	77	1.9	2.8	100	4.7	0.6	0.9	1.9	2.3	31	61.0
Hepatoblastoma	25	28	4	4	61	1.5	2.2	79.2	4.5	0.3	0.3	1.5	1.9	25.5	57.4
Hepatic carcinoma	1	0	4	9	14	3.7	0.5	18.2	0.1	0.3	0.6	0.3	0.3	5	71.4
Other specified	0	1	0	0	1	-	0	1.3	0.1	0	0	0	0	0.5	100
Unspecified	0	1	0	0	1	-	0	1.3	0.1	0	0	0	0	0.5	100
VIII. Malignant bone tumors	0	6	25	57	88	1.4	3.2	100	0.5	1.8	4	2.2	1.9	31.5	100
Osteosarcoma	0	4	19	53	76	1.4	2.7	86.4	0.3	1.4	3.7	1.9	1.6	27	100
Ewing's sarcoma	0	2	6	4	12	1.4	0.4	13.6	0.2	0.4	0.3	0.3	0.3	4.5	100
IX. Soft tissue sarcoma	20	44	33	40	137	1.3	4.9	100	5.4	2.4	2.8	3.4	3.7	53	100
Rhabdomyosarcoma	9	29	16	18	72	1.9	2.6	52.6	3.2	1.1	1.3	1.8	2	28	100
Fibrosarcoma	2	3	4	5	14	0.8	0.5	10.2	0.4	0.3	0.3	0.3	0.3	5	100
Other specified	9	12	13	17	51	0.9	1.8	37.2	1.8	0.9	1.2	1.3	1.3	19.5	100
X. Germ cell and gonadal	28	40	31	69	168	1.4	6	100	5.7	2.2	4.8	4.2	4.3	63.5	89.3
Intracranial intraspinal GC	1	4	13	32	50	4.0	1.8	29.8	0.4	0.9	2.2	1.2	1.1	17.5	92
Other non-gonadal germ cell	9	5	2	8	24	0.7	0.9	14.3	1.2	0.1	0.6	0.6	0.7	9.5	75
Gonadal germ cell	8	17	11	11	47	0.9	1.7	28	2.1	0.8	0.8	1.2	1.3	18.5	97.9
Gonadal carcinoma	10	14	4	17	45	1.4	1.6	26.8	2	0.3	1.2	1.1	1.2	17.5	84.4
Other malignant gonadal	0	0	1	1	2	-	0.1	1.2	0	0.1	0.1	0	0.1	1	100
XI. Epithelial neoplasms	2	4	10	16	32	1.3	1.1	100	0.5	0.7	1.1	0.8	0.7	11.5	100
Thyroid	0	0	4	7	11	0.2	0.4	34.4	0	0.3	0.5	0.3	0.2	4	100
Nasopharyngeal	0	0	2	7	9	8.0	0.3	28.1	0	0.1	0.5	0.2	0.2	3	100
Skin	1	0	2	0	3	2.0	0.1	9.4	0.1	0.1	0	0.1	0.1	1	100
Adrenocortical carcinoma	1	3	1	1	6	5.0	0.2	18.8	0.3	0.1	0.1	0.1	0.2	2.5	100
Other and unspecified	0	1	1	1	3	0.5	0.1	9.4	0.1	0.1	0.1	0.1	0.1	1.5	100
TOTAL	247	1054	711	704	2792	1.3	100.0	100.0	109.7	55.9	49.5	71.7	74.9	1,075	98.4

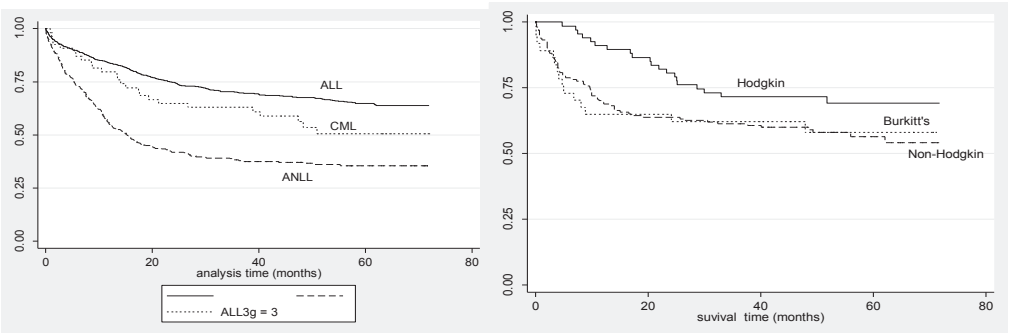

Figure 3. Survival of Leukemia and Lymphoma Patients by Type

Table 2. Survival by Group and Type of Childhood Cancer

Diagnosis	No. of patients	Deaths/100 PM (95%CI)	% Survival Probability (95%CI) at 1 year	at 3 years	at 5 years
Leukemia	1,421	1.12 (1.02-1.2)	76.9 (74.6-79.0)	62.0 (59.4-64.5)	57.4 (54.6-60.1)
ALL	1,029	0.82 (0.74-0.91)	83.9 (81.5-86.0)	70.1 (67.2-72.8)	64.9 (61.7-67.9)
ANLL	328	2.45 (2.14-2.81)	54.7 (49.2-59.9)	32.9 (32.9-43.4)	35.5 (30.2-40.8)
Chronic	51	1.23 (0.83-1.82)	79.6 (66.2-88.2)	62.9 (48.7-74.3)	50.6 (35.7-63.8)
Other	13	1.59 (0.66-3.83)	64.8 (30.9-85.2)	55.6 (23.7-78.7)	55.6 (23.7-78.7)
Lymphoma	266	1.05 (0.80-1.27)	74.1 (68.4-78.9)	63.9(57.9-69.4)	59.5 (53.0-65.4)
CNS tumor	246	1.9 (1.61-2.24)	63.2 (56.8-69.0)	45.9 (39.5-52.0)	41.7 (35.2-48.0)
Sympathetic tumor	163	2.4 (1.98-2.91)	64.8 (56.8-71.7)	39.5 (31.9-47.0)	33.6 (26.0-41.2)
Retinoblastoma	97	0.66 (0.45-0.96)	84.5 (75.7-90.4)	73.1 (63.0-80.8)	73.1 (63.0-80.8)
Renal tumor	97	0.71 (0.48-1.02)	80.0 (70.5-86.7)	71.6 (61.4-79.5)	70.4 (60.1-78.5)
Hepatic tumor	77	1.95 (1.44-2.63)	63.2 (51.3-72.9)	45.9 (34.5-56.7)	44.5 (33.1-55.2)
Malignant bone	88	2.01 (1.55-2.61)	72.7 (62.1-80.8)	43.2 (32.7-53.2)	33.7 (23.3-44.3)
Soft tissue tumor	137	1.29 (1.01-1.65)	77.4 (69.4-83.5)	58.4 (49.7-66.1)	50.1 (40.4-59.0)
Germ cell	168	0.68 (0.51-0.90)	82.7 (76.1-87.7)	73.8 (66.5-79.8)	70.6 (62.9-77.1)
Carcinoma	32	0.9 (0.51-1.58)	81.3 (63.0-91.1)	68.8 (49.7-81.8)	60.8 (40.9-75.8)
Over all	2,792	1.2 (1.14-1.27)	75.1 (73.4-76.6)	59.8 (57.9-61.7)	54.9 (53.0-56.9)

PM, person-month

(2) 56.5%, (3) 70.4% and (4) 58%. The survival for HD is better than NHL (log rank test = 4.70, p = 0.030) and Burkitt's lymphoma.

Solid tumors (Table 2 and Figure 4)

The respective, 5-year overall survival rates for (1) retinoblastoma, (2) germ cell tumors, (3) renal tumors, (4) soft tissue tumors, (5) liver tumors, (6) CNS tumors, (7) bone tumors, and (8) sympathetic tumor (neuroblastoma), were (1) 73.1%, (2) 70.6%, (3) 70.4% , (4) 50.1%, (5) 44.5%, (6) 41.7% , (7) 33.7%, and (8) 33.6%.

Discussion

This is the first study in Thailand that surveyed the incidence of childhood cancer by collecting all childhood cancers from all treating institutions in the whole country. All childhood cancer cases were covered as result from the survey of the referral practice according to national referral system. The microscopic verification of all cancer was satisfactorily high (94%) even though the MV for CNS was unacceptably limited (71%). The age-standardized rate (ASR, 74.9 per million) is in between among those extrapolated from population-based incidence from 4 registries during 1988-1994 (ASR 70.7) (Vattanasapt, 1999) and 1995-1995 (ASR 93) (Wiangnon, 2003). However, the incidence is lower than those of western countries but comparable to Southeast Asian countries (Parkin, 1998). Like in the childhood cancer elsewhere, leukemia is the most common cancer which the incidence in Thailand is similar to those of resource-rich countries. Notably, the incidence of brain tumor is low even though the neuroimaging equipment is not limited in Thailand. However, some patients may not be fully investigated by this method which resulting under diagnosis of CNS tumors. In addition, the microscopic verification is rather low in this group of tumor. Lymphoma and bone tumor incidences are obviously low compare to those of western countries and resource-rich countries in Asia without any clear explanation.

Currently, in Thailand childhood cancer is becoming an important cause of death since the poverty related causes are declining (Sutra et al., 2009). Over the past two decades, childhood cancer mortality in the United States and Europe has declined dramatically (Ries et al., 1999; Gatta et al., 2005). At present, approximately three out of four children in USA who are diagnosed with cancer can be cured (Ries et al., 1999). The decrease in the death rate of childhood cancer patients in these periods has been suggested to be due to the effects of improvements in diagnosis and therapy (Lanzkowsky, 2011).

Overall survival (OS) of all childhood cancers in this analysis is lower than the ones of developed countries. However, it is comparable to survival of population-based

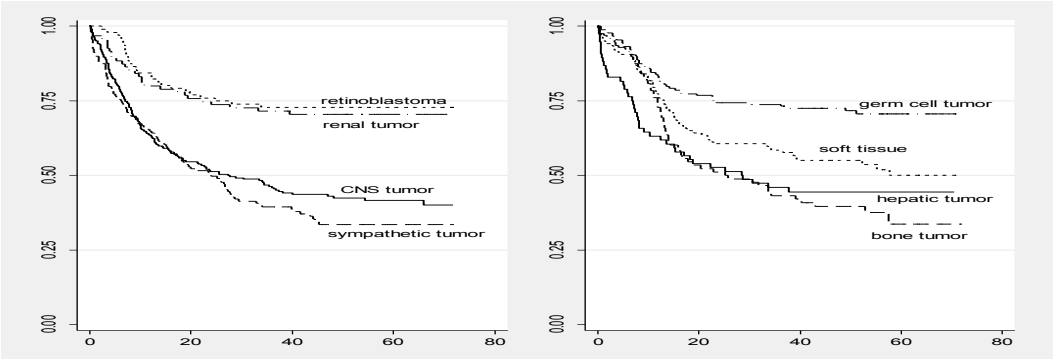

Figure 4. Survival of Solid Tumour Patients by Type. Including (CNS, Retinoblastoma, renal tumor, connective tissue tumor, hepatic, germ cell, sympathetic and bone tumours)

from Osaka (Ajiki et al., 2004). In the past, survival of childhood cancer patients in Thailand was often described in specialized hospitals and/or institutions, but not in the general population (Kamsa-ard et al., 2004; Hongeng, 2007). Results of clinical trials or reports from certain institutions have shown that the survival rates of childhood cancer patients were markedly enhanced with improvements in therapeutic methods. However, it is possible that results obtained from patients subjected to clinical trials or those hospitalized in specific institutions may not represent a trend in the general population. This is the first nationwide study to analyze 5-year survival in Thai children with population-based cancers diagnosed between 2003 and 2005. All the childhood cancer cases in the whole country were evidently included in the study.

Mortality of childhood cancer during 1975-1995 in USA has been decreasing by 40% (Ries et al, 1999). The outcome has been improving for all type of cancer especially leukemia and lymphoma. Five-year survival for lymphoid leukemia was less than 80% in 1983 to 1985 but had surpassed 80% in the Nordic countries, Western and Southern Europe, the United Kingdom, and West Germany in 1992 to 1994 (Gatta et al., 2005). Our outcomes of leukemia were still low. The 5-year overall survival (OS) rates for ALL and ANLL were 64.9% and 35.5%, respectively. However, during the study period there was no common protocol for risk classification and treatment. The immunophenotype subgroup of leukemia and lymphoma was not universally evaluated but limited to only some university hospitals. In addition, abandonment of chemotherapy was the most common cause of treatment failure, which was strongly related to poor socioeconomic status and financial support. After 2006, national protocol in disease management program by National Health Security Organization was implemented. Risk stratification and monitoring of leukemia diagnosis and treatment was obligatory by using flow cytometry. This resulted in improvement of ALL survival to 73% (Seksarn, 2010). Still, the survival of ANLL was not satisfactorily improved. The 5-year survival of non-Hodgkin lymphoma (56.5%) is comparable to those of western countries but the one of Hodgkin disease (69.3%) is unsatisfactorily inferior.

Among the solid tumor, the highest 5-year OS was observed in retinoblastoma (73.1%) followed by germ cell tumor (70.6%), Wilms' tumor (70.4%), rhabdomyosarcoma (50.1%), hepatoblastoma (44.5%), CNS tumor (41.7%), bone tumor (33.7%) and neuroblastoma (33.6%). In general, the OS rates are comparable to those reported of the resource-rich countries in population-based setting (Ries et al., 1999; Ajiki et al., 2004). However, these survivals are still below those of the international progress (Gatta, 2005).

During last 10 years, the National Health Security Organization has been providing the free medical service with full coverage to the entire population. Hence, patients have more adherence to intensive cancer treatment. In addition, the use of chemotherapy also increased over the period together with the overall improvement of supportive care in the intensive-care setting for acute infections and toxicity related to intensive chemotherapy and also for metabolic complications, life-threatening hemorrhage, and other effects of the disease on organ function. The survival is expectedly increased in the near future. Quality of life of the survivor is another concern. Lately, the quality of life has been evaluated in these cancer survivors in the study period (Pakakasama et al., 2010). To improve the survival for treatable childhood cancers, the national protocols for leukemia and lymphoma must be evaluated and the other national treatment protocols should be developed.

In conclusion the incidence of childhood cancer is lower than those of western countries. Respective overall survival for ALL, lymphoma, renal tumors, liver tumors, retinoblastoma, soft tissue tumors is lower than reported in developed countries while for CNS tumors, neuroblastoma and germ cell tumors is comparable. The updating of follow-up in our patient sample will hopefully provide indications of long-term survival, cure rates, and incidence rates of second tumors.

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