

RESEARCH ARTICLE

Childhood Cancer Incidence and Survival 1985-2009, Khon Kaen, Thailand

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Abstract

Background: The Khon Kaen Cancer Registry (KKCR) was established in 1984. Previous population-based incidences and survivals of childhood cancer in Thailand were determined using a short cancer registration period. **Materials and Methods:** Data were retrieved of all children residing in Khon Kaen, between 0–15 years, diagnosed as having cancer and registered in the KKCR (1985-2009). The follow-up censored date was December 31, 2012. The childhood cancers were classified into 12 diagnostic groups, according to the International Classification of Childhood Cancer. The incidence was calculated by the standard method. Survival of childhood cancer was investigated using the KKCR population-based registration data and overall survival calculated using the Kaplan Meier method. **Results:** In the study period, 912 newly diagnosed cases of childhood cancer were registered. The respective mean and median age was 6.4 (SD=4.6) and 6 (0-14) years. The age-peak for incidence was 0–4 years. The age-standardized rate (ASR) was 83 per million. Leukemia was the most common cancer (N=360, ASR 33.8) followed by neoplasms of the central nervous system (CNS, N=150, ASR 12.8) and lymphoma (N=79, ASR 7.0). 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 52% (95% CI: 53-56.9) for all cancers. The respective 5-year overall survival for (1) acute lymphoblastic leukemia (ALL), (2) acute non-lymphoblastic leukemia (ANLL), (3) lymphoma, (4) germ cell tumors, (5) renal tumors, (6) retinoblastoma, (7) soft tissue tumors, (8) CNS tumors, (9) bone tumors, (10) liver tumors, and (11) neuroblastoma was (1) 51%, (2) 37%, (3) 63%, (4) 74%, (5) 67%, (6) 55%, (7) 46%, (8) 44%, (9) 36%, (10) 34%, and (11) 25%. **Conclusions:** 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 that reported in developed countries while survival for CNS tumors, neuroblastoma and germ cell tumors is comparable.

Keywords: Incidence - survival - childhood cancer - khon kaen - Thailand

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Introduction

In Thailand, 21% of the population is under 15 (National Statistics Office, 2003) and although cancers among this age group are rare, ~1,000 were diagnosed with cancer based on the expected incidence (Vattanasapt, 1999; Wiangnon et al., 2003; Thai Pediatric Oncology Group, 2011). Between 2007-8, the respective cancer related mortality rates in Thai children 6-12 and 13-18 was 2.16 and 2.13 per 100,000 (Sutra et al., 2009).

The previous population-based incidences of childhood cancer in Thailand were calculated by extrapolating the incidences from the data, which was limited because of the small number of cancer registries. Recently, the Thai Pediatric Oncology Group (ThaiPOG) reported on the country incidence between 2003 and 2005; but survival was thus limited to children registered during this period.

In addition, the previously reported survival of childhood cancer patients was described with respect to specialized hospitals and/or institutions. The aim of the current investigation was to perform a long-term population-based retrospective study of the incidence of childhood cancer in a homogeneous population in Khon Kaen province.

Registration area and registry procedures: Khon Kaen province is located in northeastern Thailand. The province covers an area of 10,886 km² with a population of 1.7 million (Figure 1). The Khon Kaen Cancer Registry (KKCR) was established in 1984 at the Faculty of Medicine, Khon Kaen University. The KKCR has been conducting both hospital and population-based registration.

The data on cancer patients was collected using both active and passive methods from all hospitals and private clinics in the province. The registrars regularly

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Figure 1. Khon Kaen Map

visit all registered sites. The medical charts of patients diagnosed with cancer were reviewed and the cancer data registered by registry personnel. Any questionable cases were traced to the original resource of information for clarification. Multiple primary cases were checked by physicians using their original records and with any other physicians concerned. Death certificates with a mention of cancer were collected from the population statistics of the office of the Ministry of Interior. The vital status of registered cases has been regularly updated by checking with the population statistics of the office of the Ministry of Interior. To prevent duplication, all data were reviewed and checked with existing registry files before data entry. All the data were verified, checked for duplication coded and entered into the CanReg4 software.

Materials and Methods

Data on all childhood cancers were retrieved from the KKCR data set for the period 1985-2009. Cancer sites, morphology and behavior were coded according to the International Classification of Diseases for Oncology-3rd edition (ICD-O-3) (WHO, 2000). Tumor types were grouped according to the International Childhood Cancer Classification (ICCC) (Kramarova et al., 1996). Both histologically-verified and non-verified patients were included. All patients were observed until the end of December 2012. The 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 persons. ASRs for five-year age groupings (viz., 1985-1989, 1990-1994, 1995-1999, 2000-2004, 2005-2009) were calculated for both boys and girls (Jensen et al., 1991). Five-year cumulative survival rates were calculated using the Kaplan–Meier method. The Generalized Linear Model (GLM) method was applied for analysis based on incidence rates, corresponding p-values.

Population denominators

The population denominators used for calculation of the incidence rate were (a) the numbers of children from the population censuses in 1990 and 2000 and

(b) the estimated projected numbers based on data of 2010 (National Statistic Office, 2003). This provided an annual estimate by age group and sex. Notably, the child population has been continuously decreasing since 1980s. According to the 2000 census, 435,369 children were under 15 (25.1% of the Khon Kaen population) with similar numbers of boys and girls. On average, 30.8% were under 5, 34.8% were under 10, and 34.4% were under 15 (National Statistic Office, 2003) (Table 1).

Results

There were 912 cases with childhood cancer diagnosed between 1985-2009 (boys=526, girls=386, ratio 1.4:1). The respective mean and median age was 6.4 (SD=4.6) and 6 (0-14) years. The age-peak for incidence was between 0 and 4 years. The follow-up duration totaled 101,250 months. The death rate was 1.11 per 100 person-months (95%CI: 1.02-1.2). The 5-year overall survival was 52% (95%CI: 53-56.9) for all cancers (Table 2).

Most of the pediatric cancers were histologically-confirmed (83.7%) but the proportion varied between 52.4% for cancer of the central nervous system (ICCC group III) and 99.7% for leukemia (ICCC group I).

The age-standardized rate (1985-2009) was 83 per million. The incidence varied between 58.1 and 99.3 per million according to the 5-year interval. The time trend analysis revealed that childhood cancers increased in boys and girls (9%, p=0.004 and 7% p=0.05) (Table 3, Figure 2). Leukemia was the most common cancer (N=360, ASR 33.8) followed by neoplasms of the central nervous system (CNS) (N=150, ASR 12.8) and lymphoma (N=79, ASR 7.0). (Table 3) Among the leukemias, acute lymphoblastic leukemia (ALL) was more common than acute non-lymphoblastic leukemia (ANLL) (ratio, 3.9:1). ALL was more common among boys than girls (ASRs 31.1 vs 20.3) while the incidence of ANLL between sexes was not different in both sexes. Non-Hodgkin lymphoma (NHL) is more common than Hodgkin (HD) and Burkitt’s lymphoma (ASRs 3.08, 0.82, 1.34, respectively). All types of lymphomas are more common among boys than girls.

Table 1. Population, Under 15 Years of Age, Khon Kaen, Thailand

Age group	Males			Females		
	1990	2000	2010	1990	2000	2010
0-4	73,394	69,218	51,900	69,746	64,886	48,000
9-May	89,058	78,230	58,000	85,308	73,311	55,300
14-Oct	96,632	76,926	65,000	90,826	72,778	62,500
Total	259,084	224,374	174,900	245,880	210,975	165,800

Table 2. Number of Cases by Sex and Duration, between 1985-2009 in Khon Kaen, Thailand

Year of diagnosis	Males		Females	
	Number	%	Number	%
1985-1989	96	19	68	18
1990-1994	102	20	76	20
1995-1999	110	21	91	24
2000-2004	114	22	86	22
2005-2009	92	18	65	17

Table 3. Childhood Cancer Incidences for Both Sexes between 1985-2009 in Khon Kaen, Thailand

ICCC group	1985-1989	1990-1994	1995-1999	2000-2004	2005-2009	1985-2009
Leukemias, myeloproliferative diseases and others	28	27.8	41.1	41.9	35	33.8
Lymphomas and reticuloendothelial neoplasms	7.2	6.5	7.8	8	5.8	7
CNS and miscellaneous intracranial and intraspinal neoplasms	7.3	15.8	17	13	12.1	12.8
Neuroblastoma and other peripheral nervous cell tumors	1.4	1.6	4.5	4.8	6.4	3.8
Retinoblastoma	3	4.2	1.1	7.6	6.9	4.6
Renal tumor	4.1	5.3	2.1	4.1	4.1	4.1
Hepatic tumors	1.6	3.4	1	2.3	1.4	2.1
Malignant bone tumors	2.4	1.6	2.5	2.3	3.1	2.6
Soft tissue and other extra-osseous sarcomas	1.5	4.8	4.3	7	4.7	4.6
Germ cell tumors, trophoblastic tumors, and others	2	2.2	5.1	4.3	5.3	4
Overall incidence (all cancers)	58.1	72.2	92.7	99.3	88.7	83

Table 4. Survival Rates of Childhood Cancers between 1985-2009 in Khon Kaen, Thailand

ICCC gr	Survival (%)	95%CI
Leukemias, myeloproliferative diseases and others	49	0.43-0.55
Lymphomas and reticulo-endothelial neoplasms	63	0.52-0.76
CNS and miscellaneous intracranial and intra-spinal neoplasms	44	0.36-0.53
Neuroblastoma and other peripheral nervous cell tumors	25	0.12-0.52
Retinoblastoma	55	0.40-0.75
Renal tumor	67	0.51-0.89
Hepatic tumors	34	0.16-0.72
Malignant bone tumors	36	0.20-0.62
Soft tissue and other extra-osseous sarcomas	46	0.32-0.62
Germ cell tumors, trophoblastic tumors, and others	74	0.62-0.88
All groups	52	0.48-0.55

Table 5. Survival Rates of Children with Acute Lymphoblastic and Acute Non-Lymphoblastic Leukemia between 1985-2009 in Khon Kaen, Thailand

ICCC group	Survival (%)	95%CI
Acute lymphoblastic leukemia		
1985-2009	51	0.45-0.59
1985-1995	35	0.26-0.49
1996-2005	56	0.47-0.66
2006-2009	70	0.54-0.92
Acute myeloblastic leukemia		
1985-2009	37	0.26-0.53
1985-1995	21	0.09-0.48
1996-2005	45	0.28-0.71
2006-2009	34	0.11-1

Survival

The probability of 5-year overall survival (OS) was 52% (95%CI: 0.48-0.55). Survival differed by type of cancer. The best outcome with highest overall survival was for germ cell tumors (74%) while the worst outcome was for sympathetic tumors (neuroblastoma) (25%) (Table 4).

The 5-year overall survival for leukemia was 49% (1985-2009) (Table 4, Figure 3). The respective survival for ALL and ANLL (1985-2009) was 51% and 37%. The survival for ALL had increased from 35% between 1985-95 to 56% between 1996-2005 to 70% between 2006-9. By comparison, survival rates of ANLL remained unchanged (Table 5).

The overall 5-year survival for lymphoma was 63% (95%CI: 0.52 - 0.76). The survival for Hodgkin disease is better than for non-Hodgkin lymphoma (albeit non-significantly; p=0.45) (Figure 4).

The respective 5-year overall survival for (1) germ

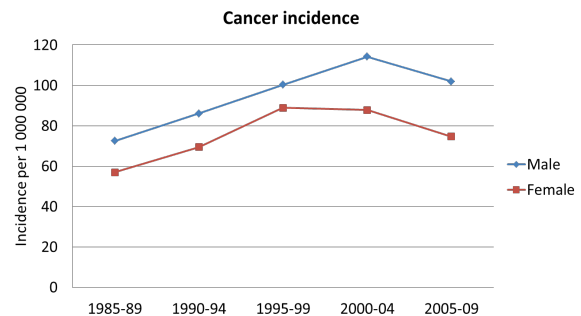


Figure 2. Childhood Cancer Incidences between 1985-2009 in Khon Kaen, Thailand

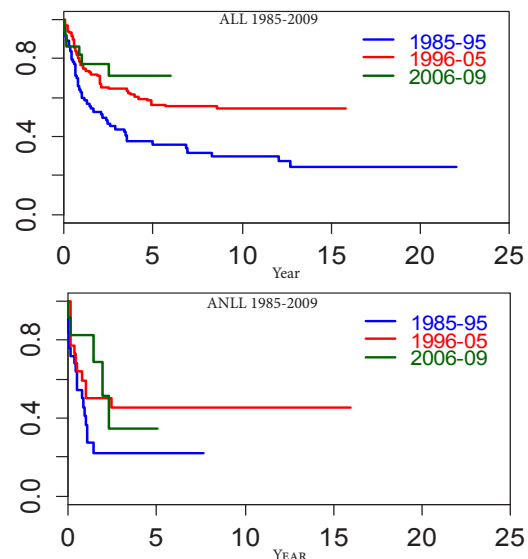


Figure 3. Survival Rates of Children with Acute Lymphoblastic and Myeloblastic Leukemia, by 10-year Interval between 1985-2009 in Khon Kaen, Thailand

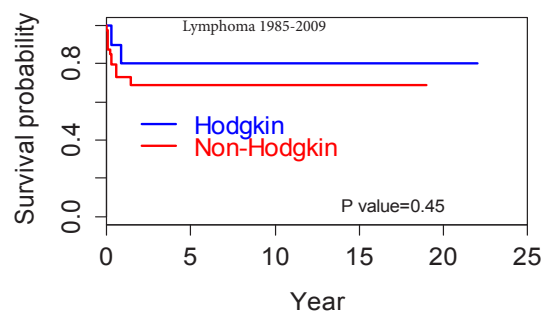


Figure 4. Survival Rates of Children with Hodgkin Disease and Non-Hodgkin Lymphoma between 1985-2009 in Khon Kaen, Thailand

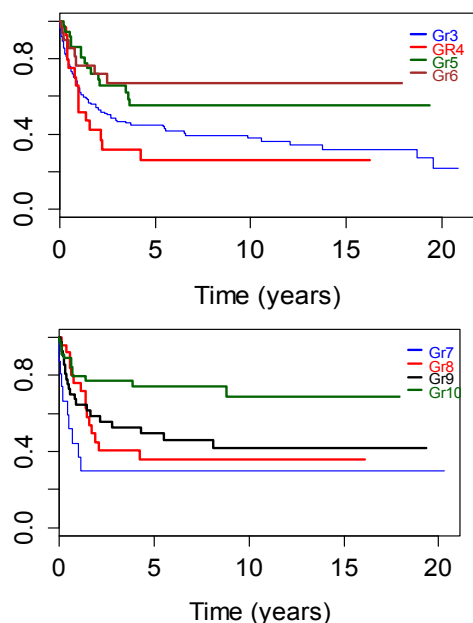


Figure 5. Survival Rates of Children with Solid Tumors between 1985-2009 in Khon Kaen, Thailand. Gr3, CNS tumor; Gr4, neuroblastoma; Gr5, retinoblastoma; Gr6, renal tumors; Gr7, hepatic tumors; Gr8, bone tumors; Gr9, soft tissue sarcoma; Gr10, germ cell tumors

cell tumors, (2) renal tumors, (3) retinoblastoma, (4) soft tissue tumors, (5) CNS tumors, (6) bone tumors, (7) liver tumors, and (8) sympathetic tumor (neuroblastoma) was (1) 74%, (2) 67%, (3) 55%, (4) 46%, (5) 44%, (6) 36%, (7) 34% and (8) 25%.

Discussion

This is the first study in Thailand to survey the incidence of all types of childhood cancer over an extended period from a unique population in Khon Kaen province. The microscopic verification (MV) of all cancers was satisfactorily high (83.7%) even though the MV for CNS tumors was limited (52.4%). The age-standardized rate (ASR, 83 per million) was in the range of those extrapolated from the population-based incidences of 4 registries between 1988-1994 (ASR 70.7) (Vattanasapt, 1999) and 1995-1997 (ASR 93) (Wiangnon et al., 2003). The incidence reported by the ThaiPOG for the whole country survey between 2003-5 was 74.9 (Wiangnon et al., 2011). The respective incidence of childhood cancer in Khon Kaen between 1988-1991 and 1985-2000 was 58.7 and 73 per million (Sriamporn et al., 1996; Wiangnon et al., 2004). These incidences were lower than the incidence in this study, which may reflect under-coverage; especially during the early registration era. Notwithstanding the long-term registration, the incidence was still lower than rates reported for western countries albeit comparable to other Southeast Asian countries (Parkin et al., 1998).

As in childhood cancer elsewhere, leukemia is the most common cancer, for which the incidence in Khon Kaen is similar to those of resource-rich countries (Ries et al., 1999). Notably, the incidence of brain tumor was low even though the neuroimaging equipment in Thailand has not been a limiting factor during the last 20 years. Some

patients, however, may not have been fully investigated using this modality, resulting in under diagnosis of CNS tumors. Microscopic verification was also rather low for this group of tumors.

Bone tumor incidences were low compared to those of western countries and resource-rich countries in Asia. Generally, bone tumors are more common in adolescents and young adults and we limited the age of children up to 15. Lymphoma incidence was also low without a clear explanation.

Childhood cancer is becoming an important cause of death in Thailand as poverty-related causes are declining (Sutra et al., 2009). Over the past two decades, childhood cancer mortality has declined dramatically in resource rich countries (Ries et al., 1999; Gatta et al., 2005). The decrease over this period is partially due to the effects of (a) understanding tumor biology and (b) improvements in diagnosis and therapy (Redner, 2011).

Overall survival (OS) of all childhood cancers in the current analysis was lower than those of developed countries; however, it was comparable to population-based survival in Osaka (Ajiki et al., 2004), Thailand (52 vs 54.9) (Wiangnon et al., 2011) and in Khon Kaen at a university hospital (Kamsa-ard et al., 2004). The study of survival of childhood cancers in a population-based in Thailand was unable to identify any trends because of the short duration of the study (i.e., between 2003-5).

Mortality from childhood cancer between 1975-1995 in the USA decreased by 40% (Ries et al., 1999). Indeed, the outcome has been improving for all types of cancer, especially for leukemia and lymphoma. The five-year survival of lymphoid leukemia has surpassed 80% in the Nordic countries, Western and Southern Europe, the United Kingdom, and West Germany (Gatta et al., 2005). Our outcomes for leukemia remain low, especially for ANLL. The survival of ALL patients has been gradually increasing from 35% (1985-95) to 70% (2006-9). The survival of ANLL patients remains inferior (21-45%).

Abandonment of chemotherapy was the most common cause of treatment failure, which was strongly related to poor socioeconomic status and financial support. In 2003, the National Security Office (NHSO) implemented universal health coverage nationwide and since then adherence to intensive cancer treatment has significantly risen. In 2006, the NHSO provided and supported a disease management program for the treatment of childhood leukemia and lymphoma. Common treatment protocols were used nationwide. In principle, risk stratification and monitoring of leukemia diagnosis and treatment was obligatory using flow cytometry. In addition, the use of chemotherapy also increased over the period together with overall improvement of supportive care, which resulted in the improvement of ALL survival to 73% (Seksarn et al., 2011). Notwithstanding, the survival of ANLL was not satisfactorily improved at the national level (Seksarn et al., 2011). Nowadays and importantly, the quality of life is also evaluated for these cancer survivors (Pakakasama et al., 2010).

The two referral-hospitals in Khon Kaen province have pediatric oncologists treating childhood cancers. According to the Thai national referral system, all cases

residing in Khon Kaen must be referred to one of these 2 centers, in which institutional protocols are initially used. In 2000, many treatment protocols in our institution were revised and developed by modifying the standard international chemotherapy protocol. These were used until the national protocol was implemented in 2006. Survival of ALL was significantly improved during this change.

Among the solid tumors, the highest 5-year OS was observed for germ cell tumor (74%) followed by Wilms' tumor (67%), retinoblastoma (55%), rhabdomyosarcoma (46%), CNS tumor (44%), bone tumor (36%), hepatoblastoma (34%), and neuroblastoma (25%). In general, the OS rates are still not comparable to those reported for resource-rich countries (Ries et al., 1999), except for population-based settings (Ajiki et al., 2004). Survival rates, however, remain below progressive international standards (Gatta et al., 2005).

Recently, the Thai Pediatric Oncology Group proposed common protocols for nationwide use. Improvement of survival and quality of life for children with cancers including survivors are expected (ThaiPOG, 2014).

In conclusion, the incidence and survival rates of childhood cancer in Khon Kaen are lower than those reported for western countries. Survival is, nevertheless, increasing over time after implementation of national protocol and improvement of supportive care facilities. Quality of life of childhood survivors needs to be studied systematically.

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