RESEARCH COMMUNICATION

Trends in Incidence of Childhood Lymphoma in Khon Kaen, Thailand, 1985-2008

Aunjai Srina[1], Arunee Jetsrisuparb[1], Patcharee Komvilaisak[1], Supot Kamsa-ard[2], Surapon Wiangnon[1*]

Abstract

Background: Lymphoma is the second most common of childhood cancer in Thailand, but data on trends over time are limited. Objective: To perform a statistic assessment of the incidence trend of childhood lymphoma in Khon Kaen, Thailand, between 1985 and 2008. Method: All children aged < 15 years newly diagnosed with lymphoma according to International Childhood Cancer Classification (ICCC) during January 1, 1985- December 31, 2008 were collected from data base of Khon Kaen Provincial Registry. Aged-adjusted incidence rates (ASRs) were calculated by standard method and trends were calculated using the generalized linear model method <GLM>, which utilizes incidence-rate-base logarithms. Results: During 1985-2008 there were 72 children (47 boys and 25 girls) who were diagnosed with lymphoma in Khon Kaen province. The peak age-group of disease was in the 5-9 year olds for both sexes. All cases were pathologically proven. Non-Hodgkin lymphoma (NHL) was more common than Hodgkin disease (ratio 7:1). The overall ASR was 6.04 per million (95%CI: 4.64 to 7.45) and the ASR was 7.64 per million (95%CI: 5.44 to 9.84) in boys and 4.37 per million (95%CI: 2.64 to 6.10) in girls. Significant increases were observed for boys, since the 2006 to 2008 ASR was 15.3 per million (95%CI: 5.73 to 25.0). Trend analyses during 1985 - 2008 showed that incidence among boys for lymphoma increased by 1.38 percent per year (95%CI:- 4.6-8.3) while the incidence among girl decreased by 2.6 percent per year (95%CI:- 12-6.8). Conclusions: Our data showed that the incidence of childhood lymphoma in Khon Kaen province was similar to the one of Thailand but lower than those of western countries. During the past 24 years, the incidence trend seems to be increasing in boys but decreasing in girls. Interpretation is difficult without a better understanding of what underlies the reported changes.

Keywords: Childhood - lymphoma - incidence - trends - cancer registry - Khon Kaen

Asian Pacific J Cancer Prev, **11**, 1-6

Introduction

In general lymphoma is the third most common of childhood cancer. In Thailand, the age-standardized rate (ASR) of childhood lymphoma in during 1988-1994 was 7.4 per million (Sriamporn, 1996) and during 1995-97 was 8.9 (Wiangnon, 2004). During 2003-5 Thai Pediatric Oncology Group (ThaiPOG) registered all childhood cancer and demonstrated the ASR of childhood lymphoma of 6.4 per million (ThaiPOG, 2010). It was second to leukemia which ASR of 42.6.The etiology of lymphoma is unknown. However, radiation, viral infection, immune deficiency, socioeconomic status and genetic abnormality may predispose to development of lymphoma (Lanzkowsky, 2005).

Khon Kaen is a province located in the Northeast of Thailand with the current population of 1.89 million (Human Resources Planning Division, National Economic and Social Development Board, 1995). Khon Kaen Cancer Registry (KKCR) was established in 1984 at the Faculty of Medicine and Srinagarind Hospital, Khon Kaen University. During the economic development, the life style has been changed in Khon Kaen from agriculture community to semi-industrial society. In Khon Kaen province during 1985-2002, Kamsa-ard has reported that the incidence of childhood leukemia has been increasing by 2.4% per year in boys and 4.1% per year in girls (Kamsa-ard, 2006). At present there is no trend in incidence of childhood lymphoma reported in Thailand. This study aims to assess the trend in the incidence of childhood lymphoma in Khon Kaen between 1985 and 2008.

Materials and Methods

We analyzed incidences and trends of incidence of lymphoma in children under 15 years in Khon Kaen Province, Thailand during 1985-2008. The diagnosis of lymphoma as defined by third edition International Classification of Diseases for Oncology behavior code 3 or higher was included. The diagnosis of childhood

*[1]Department of Pediatrics, Faculty of Medicine, Khon Kaen University, [2]Cancer Unit, Srinagarind Hospital. *For correspondence : suraponwiangnon@gmail.com*

lymphoma included in the study was coded according to the International Childhood Cancer Classification (ICCC) (Kramarova, 1996). Both histologically and non-histologically verified patients were included. HIV infected case as underlying disease was recorded, if positive.

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 express per million person-years.

Sources of data

We retrieved the population-based cases of childhood lymphoma from the Khon Kaen Cancer Regsitry (KKCR) which has been operating the population-based cancer registration since 2008 under standard procedure (Esteban, 1995). Cancer sites, morphology and behavior, are coded according to the International Classification of Diseases for Oncology (ICD-0-3). Death certificates were collected from the Provincial Chief Medical Officer's office and/or the Civil Registration Section at each district. All the data were verified, checked for duplication, coded and entered into the CANREG software. (Available from: http://www.iacr.com.fr/). To assess the coverage of cases with childhood lymphoma diagnosis in Khon Kaen Province, the data were checked in data set of Udonthani Provincial Cancer Registry and Bangkok Metropolitan Cancer Registry at National Cancer Institute, in case some cases were referred.

Population denominators

The population denominators used for calculation of the incidence rate were estimated from the population censuses, conducted by the Human Resources Planning Division, National Economic and Social Development Board, Prime minister's office (1995).

Statistical methods

ASRs were calculated by the direct method, using the world standard population and express per million person-years. ASR and 95 % confidence interval of the incidence rates were used for analysis (Jensen et al., 1991). Generalized Linear Model (GLM) method was used for analysis based on annual incidence rates and 95 % confidence interval of the rates (http://www.statsoft.com/textbook/stglm.html).

Results

During the study period from 1985-2008, 72 (47 boys and 25girls) newly diagnosed cases of childhood lymphoma residing in Khon Kaen Province were included. There was no case from Khon Kaen Province registered in another registry. There is no case with HIV as underlying disease. Boys were affected more frequently than girls (ratio 1.9:1). The common age group was 5-9 years (44%) followed by 10-14 year (34.7%) and 0-4 years (20.8%). All cases were histologically verified. The mean and median ages were 7.8 year (SD 3.9) and 7 years (0.5-14), respectively. Non-Hodgkin lymphoma (NHL) was more

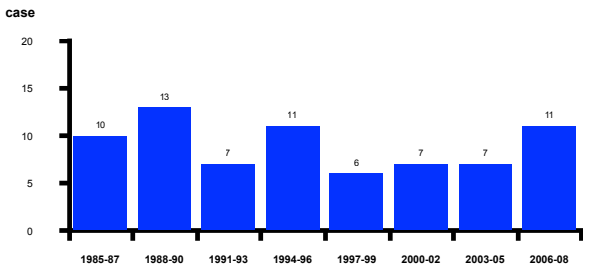

Figure 1. Number of Cases in Childhood Lymphoma in Khon Kaen, 1985-2008

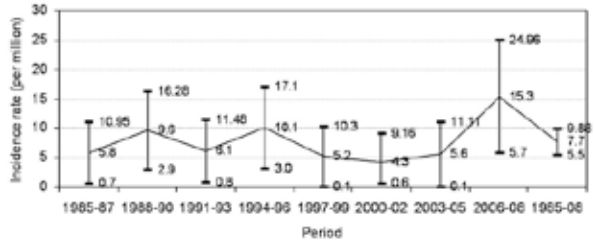

Figure 2. Incidence Rate (per Million per Year) of Childhood Lymphoma in Khon Kaen 1985-2008, Boys

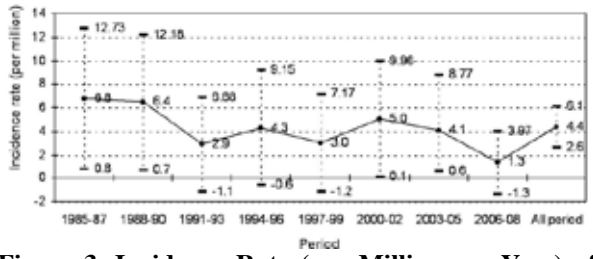

Figure 3. Incidence Rate (per Million per Year) of Childhood Lymphoma in Khon Kaen, 1985-2008, Girls

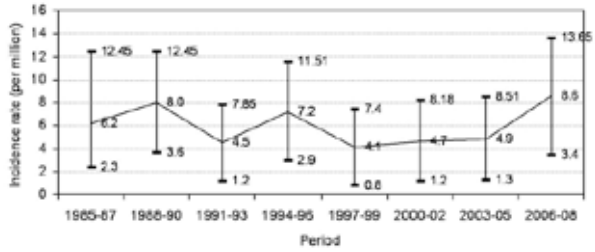

Figure 4. Incidence Rate (per Million per Year) of Childhood Lymphoma in Khon Kaen, 1985-2008, Both Sexes

common than Hodgkin Disease (HD) (ratio 7:1) (Table 1). The average number of cases at the 3 year interval was shown in Figure 1.

Between 1985 and 2008, the ASR of corresponding of 72 cases was 6.04 per million children (95%CI: 4.64 to 7.45). The ASRs for boys and girls were 7.64 per million (95%CI: 5.44 to 9.84) and 4.37 per million (95%CI: 2.64 to 6.10), respectively. Pattern of ASRs in boys were slightly fluctuated between 4.3-10.1 per million and the rate was sharply increasing in 2007 (15.3 per million) (Figure 2). The ASRs in girl are generally lower than in boys at each time point and notably reducing during the study period (Figure 3). The ASRs of both sexes were shown in Figure 4.

Using GLM modeling for the annual percent change (APC), the incidence has been increased by 1.8 percent

Table 1. Baseline Demographic and Clinical Characteristics of Childhood Lymphoma in Khon Kaen, 1985-2008

Characteristics	Number of cases (N=72)	Percentage
1. Gender		
Boys	47	65.28
Girls	25	34.72
2.Age group (year)		
0-4	15	20.84
5-9	32	44.44
10-14	25	34.72
3.Basis of diagnosis		
Pathological proved	72	100.0
4.Type of disease		
Non-Hodgkin disease	63	70.0
Hodgkin disease	9	12.0

Table 2. Trends of Childhood Lymphoma in Khon Kaen, 1985-2008

Sex	Annual percent change	95%:CI
Female	-2.6	-12.0-6.8
Male	+1.8	- 4.6-8.3
Both sexes	-0.28	- 6.3-5.8

per year in boy (95%CI:- 4.6 to 8.3) while the incidence has been decreased by 2.6 % per year in girls (95% CI: -12 to 6.8). The APC for both sexes has been decreased by 0.28 percent per year (95%CI: -6.3 to 5.8) (Table 2).

Discussion

Lymphoma is the second most common of childhood cancer in Thailand after leukemia (ASR 6.4) (ThaiPOG, 2010) while it is generally the third most common in other countries (IARC, 1998). The etiology is unknown. The possible risk factors are genetics, socioeconomic status, viral infection especially HIV and Epstein Barr virus, radiation and organic substances. (Lanzkowsky, 2005) Even though, Thailand has been endemic area of HIV infection, in our study there is no HIV infected case as underlying disease.

The incidence of childhood lymphoma in Khon Kaen is similar to that of Thailand's incidence (ThaiPOG, 2007; 2010) but lower than those of the neighbors in Asia and developed countries in the West (IARC, 1998). However, the registration coverage conceivably was complete since the number of case remained stable for the whole period except for at the end of the study. In general childhood lymphoma in Thailand was shown lower than the West incidence in previous studies (IARC, 1998; Wiangnon, 2003). According to the gender, boys are generally more affected than girls, (7.64 vs. 4.37 per million) (Parkin, et al., 1998). In the United States, Surveillance Epidemiology, and End Results (SEER) program reported that the ASRs were 19.9 per million in boys, and 10.2 per million in girls (Ries et al., 1998). In previous study in Thailand during 1995-1997, the ASRs were 10.6 per million in boys and 7.2 per million in girls. (Wiangnon et al., 2003).

During past 24 years in our study, the incidence trend seems increase in boys but decrease in girls with the estimated annual change was 1.8% per year increase in boy and 2.6% per year decrease in girl. Interpretation is difficult without a better understanding of what underlies the change reported. However, the number of case included in our study may be not big enough. The trends in incidence of childhood lymphoma have been reported internationally both increasing and decreasing. The decreasing trends were reported in USA during 1975-1995 (Linet, 1999). The trends were reported creasing insignificantly (1.4% per year) during 1967-2001 in Piedmon, Italy (Dalmasso, 2005). In Australia, the Australian Pediatric Cancer Registry reported the significant increase in trend incidences of both sexes, 0.5% and 1.2% per year in boy and girl respectively (Baade, et al, 2010). In Germany, all childhood malignancies combined (excluding central nervous system-tumors and neuroblastoma) show a significant trend, +0.7% in western and +1.1% per year in eastern Germany which could be due to life style changes since the reunification in eastern Germany influencing early immune system training. In addition, the trends in incidence of childhood lymphoma was significantly increased in West Germany (0.9% per year) while it was insignificantly decreasing in East Germany (0.9% per year) during 1987-2004 (Spix, 2008). However, the interpretation of the changes for all reports was not fully clear.

In summary, our data showed that the incidence of childhood lymphoma in Khon Kaen province was similar to the one of Thailand but lower than those of western countries. During past 24 years, the incidence trend seems increase in boys but decrease in girls. However, the number of case was rather small. Therefore, we would suggest further study by adding the data of other registries in Thailand.

References

Baade PD, Youlden DR, Valery PC, et al (2010). Trends in incidence of childhood cancer in Australia, 1983-2006. *Br J Cancer*, **102**, 620-6.

Dalmasso P, Pastore G, Zuccolo L, et al (2010). Temporal trend in the incidence of childhood leukemia, lymphoma and solid tumors in north-west Italy, 1967-2001. A report of the childhood cancer registration of Piedmont. *Haematologica*, **90**, 1197-204.

Esteban D, Whelan S, Laudica A, et al (1995). Manual for cancer registry personel. *IARC technical report*, No10. Lyon

General Linear Models (GLM) [online] 1984-2003 [cited 2004 Dec 7]. Available from: http://www.statsoft.com/textbook/stglm.html

Human resources planning division national economic and social development board, Prime Minister's Office (1995). Population projections for Thailand 1990-2020.

IARC (1998). International incidence of childhood cancer, vol. II. Scientific publication no.144. Lyon: international agency for research on cancer.

Jensen OM, Parkin DM, Maclennan R, et al (1991). Cancer registration: principles and methods. IARC scientific publications No.95, Lyon: international agency for research on cancer, 159-76.

Kamsa-ard S, Wiangnon S, Kamsa-ard S, et al (2006). Trends in incidence of childhood leukemia, Khon Kaen, Thailand, 1985-2002. *Asian Pac J Cancer Prev*, **7**, 75-8.

Kramarova E, Stiller CA, Ferlay J, et al (1996). International

classification of childhood cancer. IARC scientific publications, No.29, Lyon: international agency for Research on cancer.

Lanzkowsky P (2005). Hodgkin disease and non-Hodgkin lymphoma. In: Manual of pediatric hematology and oncology, 4th ed. Academic press, Tokyo, 453-511.

Linet MS, Ries GL, Smith AM, et al (1999). Cancer surveillance series: Recent trends in childhood cancer incidence and mortality in the United States. *J Natl Cancer Inst*, **91**, 1051-8.

Parkin DM, Kramarova E, Draper GJ, et al (1998). International incidence of childhood cancer, vol. II, IARC Scientific Publication No. 144.

Ries AGL, Percy C, Bunin G (1999). Cancer incidence and survival among children and adolescents: United States SEER program 1975-1995. National Cancer Institute: SEER Pediatric monograph.

Spix C, Eletr D, Blettner M, et al (2008). Temporal trend in the incidence rate of childhood cancer in Germany 1987-2004. *Int J Cancer*, **122**, 1859-67.

Sriamporn S, Vatanasap V, Martin N, et al (1996). Incidence of childhood cancer in Thailand 1988-1991. *Pediatr Perinat Epidemiol*, **10**,73-85.

Thai Pediatric Oncology Group (2007). Childhood cancer. In: Cancer in Thailand. Vol. IV, Khuhaprema T, Srivatanakul P, Sriplung H, Wiangnon S, Sumitsawan Y, Attasara P. eds, Bangkok. 1998-2000, 71-8.

Thai Pediatric Oncology Group (ThaiPOG) (2010). Childhood cancer incidence and survival in Thailand during 2003-2005. (in press)

Wiangnon S, Kamsa-ard S, Jetsrisuparb A, et al (2003). Childhood cancer in Thailand: 1995-1997. *Asian Pac J Cancer Prev*, **4**, 337-43.

Wiangnon S, Kamsa-ard S, Jetsrisuparb A, et al (2004). Childhood malignancies at Khon Kaen, Thailand: Population-based cancer registry. *Thai J Pediatr*, **43**, 38-43.