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Cancer in adolescents: Incidences and trends during 1995–2009 in Taiwan

Giun-Yi Hung [a,b,c], Chao-Chun Chen [c,d], Jiun-Lin Horng [e,1], Li-Yih Lin [a,1,*]

[a] Department of Life Science, National Taiwan Normal University, Taipei, Taiwan
[b] Division of Pediatric Hematology and Oncology, Department of Pediatrics, Taipei Veterans General Hospital, Taipei, Taiwan
[c] Department of Pediatrics, National Yang-Ming University School of Medicine, Taipei, Taiwan
[d] Department of Pediatrics, Taipei Veterans General Hospital Hsinchu Branch, Hsinchu, Taiwan
[e] Department of Anatomy and Cell Biology, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan

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ABSTRACT

This study aimed to describe cancer incidence rates and trends specifically for adolescents aged 15–19 years during 1995–2009 in Taiwan. The incidence counts and census data were obtained from the population-based Taiwan Cancer Registry. During the 15-year study period, 4122 adolescents were diagnosed with cancer. The overall incidence rate was 155.2 per million person-years. Other epithelial tumors were the most frequently diagnosed cancer group (23.7%), followed by leukemias (18.0%) and lymphomas (13.9%). When compared to rates in Western countries, a significantly low rate of lymphomas was found. Moreover, rates of the subtypes of melanomas and nasopharyngeal carcinomas being 1/10- and 4-times rates in Western countries were the most striking variations. During 1995–2009, the overall rate of adolescent cancer did not significantly change. However, the most significant upward and declining trends in incidence rates were found for male germ cell neoplasms (annual percent change, APC, 6.4%) and hepatic tumors (APC, -11.1%), respectively. Further investigation and enhancement of the public discourse of possible lifestyle and environmental risk factors associated with increasing trends of certain adolescent cancers should be carried out in Taiwan.

Introduction

Cancer in adolescents aged 15–19 years old is rare, comprising <1% of all cancers in the United States, Europe, and England [1–3]. Because of the rarity, incidence patterns of adolescent cancers are understudied, and little information is available in the literature. Most of the descriptive cancer surveillance reports are from Western countries [2–6]. In Taiwan, only 1 previous study reported adolescent cancer incidences and relative frequencies using data from a single institution [7]. As a transformation stage from childhood to adulthood, the distribution of cancer types among adolescents is unique, with a portion of the types being identical to those that occur during childhood and the others being categorized as adult cancers. However, it is critical to realize that adolescent cancers have distinct biological behaviors, and the response to treatments may differ from their counterparts in children or adults [8–11]. This fact is reflected by observations of remarkably increased survival rates in childhood cancer in the past few decades as a result of improvements in treatment protocols and coordinated international research, contrasted with limited improvements in cancer survival rate in adolescents.

This study aimed to describe the cancer incidence rates and trends specifically for adolescents aged 15–19 years. Moreover, to compare cancer incidence rates in children and data from other countries, type of cancers in this analysis were categorized according to the International Childhood Cancer Classification, Third Edition (ICCC-3) [12].

Materials and methods

Data collection

Cancer incidence counts and census data were obtained from the population-based Taiwan Cancer Registry (TCR) [13], which is organized and funded by the Health Promotion Administration, Ministry of Health and Welfare, Taiwan and which began cancer registration in 1979. Since enactment of the *Cancer Control Act* in 2003, hospitals with a capacity of ≥50 beds that provide outpatient and hospitalized cancer care are mandated to submit cancer data to a central cancer registry, which substantially improved the completeness and case ascertainment of cancer registration [14,15]. In addition, Taiwan launched a single-payer National Health Insurance program in 1995 [16]. This compulsory universal social insurance program has a coverage rate of up to 99% and enables all individuals to easily access medical services and prompt treatment. Regarding the quality indicators defined by the International Agency for Research on Cancer (IARC) for patients aged < 20 years, the percentage

* Corresponding author. Tel.: +886 2 77346316; fax: +886 2 29312904.
E-mail address: linly@ntnu.edu.tw (L.-Y. Lin).
[1] These authors contributed equally to this work.

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of microscopically verified cases (MV%) was 93.7% for all cancers combined in 1995–2009. The percentage of death certification only cases (DCO%) is another indicator of data validity, which fell from 10.3% in 1995 to 0.6% in 2009, as described elsewhere [17]. These indicators not only reflect the high quality of the TCR data but also a steady improvement over time.

Incidence rates for all cancers in adolescents (aged 15–19 years) and children (aged 0–14 years) diagnosed in 1995–2009 were analyzed and compared. Diagnoses were categorized into 12 main groups and 47 subgroups according to the ICCC-3 [12]. Only malignant tumors were included in this analysis. Tumors not classified in the ICCC-3 and *in situ* cancers were excluded. We abbreviated 7 of the 12 major ICCC-3 groups as follows: leukemias (leukemias and myeloproliferative and myelodysplastic diseases), lymphomas (lymphomas and reticuloendothelial neoplasms), central nervous system (CNS) neoplasms (CNS and miscellaneous intracranial and intraspinal neoplasms), neuroblastomas (neuroblastoma and other peripheral nervous cell tumors), soft-tissue sarcomas (soft-tissue and other extraosseous sarcomas), germ cell neoplasms (germ cell tumors, trophoblastic tumors, and neoplasms of the gonads), and other epithelial neoplasms (other malignant epithelial neoplasms and malignant melanomas). The dataset used in this study included case numbers grouped according to the year of diagnosis, sex, age in years, and ICCC-3 groups and subgroups, which contained no personal information. This study was approved by the Data Release Review Board of the Health Promotion Administration, Ministry of Health and Welfare, Taiwan, which waived the requirement for informed consent.

Analyses

Incidence rates for each cancer type among adolescents were calculated and expressed per million person-years in accordance with the ICCC-3 into the main groups and subgroups by sex. To avoid presenting unstable data, rates in this study were not shown if the annual case number was <10. Rates of the 12 main ICCC groups were further compared to those in children. For the analysis of time trends, the annual percent change (APC) and corresponding 95% confidence intervals (CI) were calculated. A Joinpoint regression model and permutation test (Joinpoint Regression Program, vers. 4.0.4; Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute, Bethesda, MD) were employed to identify significant changes that allowed up to three joinpoints [18,19]. Statistical significance was determined if the 95% CI of the APC did not include zero ($p < 0.05$). To compare our data with those of other countries, we searched databases and published papers available on the internet (Medline, National Center for Biotechnology Information, and PubMed) and compiled world rates from Western countries and East Asia for comparison.

Results

In total, 4122 patients aged 15–19 years were diagnosed with cancers during the 15-year study period. The overall incidence rate was 155.2 per million person-years. Incidence rates according to the ICCC-3 groups, subgroups, and sex are illustrated in Table 1. The population at risk, case numbers, and incidence rates by the year 1995–1999, 2000–2004, and 2005–2009 are demonstrated in Table 2. Other epithelial tumors (group XI of the ICCC) were the most frequently diagnosed cancer, accounting for nearly a quarter of all cancers (23.7%), followed by leukemias (18.0%) and lymphomas (13.9%). The most common ICCC subgroups were thyroid carcinomas, other and unspecified carcinomas, and lymphoid leukemias. Cancer incidence rates between adolescents and children were compared by ICCC-3 groups and are depicted in Fig. 1. Embryonal tumors, including neuroblastomas and retinoblastoma, were mainly found in children. Also, leukemias and CNS neoplasms were more common in children than in adolescents. In contrast, incidence rates of lymphomas, malignant bone tumors, soft-tissue sarcomas, germ cell neoplasms, and other epithelial neoplasms were higher in adolescents than in children.

In terms of data-quality indicators defined by the IARC, the DCO% for overall cancers among ages 15–19 years was about 10% (average, 5.4% during 1995–1999, 1.1% during 2000–2004 and 0.3% during 2005–2009). As shown in Table 2, the MV% was 94.3% for all cancers combined during the 15-year study period. The MV% results for most ICCC-3 main groups were >93% with the exceptions of hepatic tumors (group VII, 50.0%) and other and unspecified malignant neoplasms (group XII, 70.6%). Moreover, the mortality versus incidence ratio decreased from 43% in 1995 to 27.8% in 2009.

Incidence rates by gender

The male-to-female (M/F) incidence rate ratio (IRR) was 1.1 for all cancers combined (Table 1). The cancer incidence rates were 161.1 and 148.9 per million person-years for males and females, respectively. Sex-based differences in incidence rates were observed. Males had higher incidence rates than females in the majority of ICCC-3 groups, except for germ cell neoplasms (M/F IRR = 0.9) and other epithelial neoplasms (M/F IRR = 0.7). The male predominance was most pronounced for hepatic tumors (M/F IRR = 1.8), malignant bone tumors (M/F IRR = 1.7), and lymphomas (M/F IRR = 1.7). When comparing incidence rates according to ICCC-3 subgroups, the highest M/F IRRs (>2) were observed for myelodysplastic syndrome and other myeloproliferative diseases, Burkitt's lymphomas, unspecified malignant hepatic tumors, Ewing tumors and related sarcomas of the bone, intracranial and intraspinal GCTs, malignant extracranial and extragonadal GCTs, and nasopharyngeal carcinomas (NPCs) with M/F IRRs ranging 2.5–4.9. Gonadal carcinomas occurred almost exclusively in females. A female predominance (M/F IRR < 1) was also observed in astrocytomas, other specified malignant bone tumors, other specified soft-tissue sarcomas, malignant gonadal GCTs, other and unspecified malignant gonadal tumors, thyroid carcinomas, malignant melanomas, and other specified malignant tumors, with M/F IRRs ranging 0.2–0.9.

Temporal trends

Cancer incidence trends according to ICCC-3 groups are summarized in Table 3 and Fig. 2. During 1995–2009, the overall incidence of adolescent cancer did not significantly change (APC, 0.8%; 95% CI, –0.2%–1.7%) (Fig. 2A). Specifically, incidence rates significantly rose in 3 main groups: lymphomas (Fig. 2D), soft-tissue sarcomas (Fig. 2E) and germ cell neoplasms (Fig. 2F), with APCs ranging 2.2%–2.6%. Hepatic tumors (ICCC VII) were the only cancer group that had a significant declining trend in incidence rates (APC, –7.8%, Fig. 2G). Incidence rates did not significantly change during the 15 years for the others, including leukemias (Fig. 2C), CNS neoplasms, malignant bone tumors, and other epithelial neoplasms (Fig. 2B).

For males, significant upward trends in rates were observed for leukemias (APC, 2.8%) and germ cell neoplasms (APC, 6.4%); whereas, among females, rates significantly rose for lymphomas (APC, 3.4%) and soft-tissue sarcomas (APC, 2.9%). For hepatic tumors and other epithelial neoplasms, significantly decreased incidence rates were observed in males (APC, –11.1% and –2.9%, respectively), but not in females.

Incidence rates by country

Results from countries of the Western world (the United States, Europe, England, and the Netherlands) and East Asia (Japan and Korea) are compiled in Table 4 [3,4,20–23]. The overall incidence rate in Taiwan was lower than those of the US, Europe, and the Netherlands; was similar to those in England and Korea; and was higher than that in Japan. When compared to results from other countries by cancer type, the most prominent variation was found for hepatic tumors, in which the rate was >3-times higher compared with the US, Europe, and Japan. In contrast, the incidence rate of lymphomas was significantly lower in Taiwan, at approximately half the rates of Western countries. The rate of leukemias was only second to the US, but was higher than all the others. Rates of malignant bone tumors, soft-tissue sarcomas, and other epithelial neoplasms were either consistent or slightly lower than those of other countries. The rate of germ cell neoplasms was significantly lower than those for the US and Europe; however, this rate could not be compared with rates from England, the Netherlands, and Korea,