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Original Article

Hepatoblastoma incidence in Taiwan: A population-based study

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Abstract

Background: The incidence of hepatoblastoma is not well known in Taiwan. The goal of this study was to investigate the incidence rates of hepatoblastoma by age and sex.
Methods: The data of patients with hepatoblastoma diagnosed from 1995 to 2012 were obtained from the population-based Taiwan Cancer Registry. Incidence rates of hepatoblastoma according to sex and age were analyzed. This study employed the published methods of International Agency for Research on Cancer to calculate the age-standardized incidence rates (ASIRs), standard errors, 95% confidence intervals (CIs), and standardized incidence rate ratios (SIRRs).
Results: In total, 211 patients were diagnosed with hepatoblastoma during the 18-year study period. The ASIR was 0.76 per million person-years. Hepatoblastoma was predominantly diagnosed in children (n = 184, 87.2%). By contrast, adolescents/adults (n = 10, 4.7%) and elderly people (n = 17, 8.1%) were rarely affected. The incidence peaked at ages 0−4 years with corresponding ASIR of 7.3 per million person-years. A significant male predilection was only found in children and elderly people, with male-to-female SIRRs of 1.23 and 1.89, respectively. During 1995−2012, the overall incidence of hepatoblastoma significantly increased only in children (annual percent change: 7.4%, 95% CI 3.9%−11.1%, $p < 0.05$) and specifically in boys (annual percent change: 6.5%, 95% CI 1.9%−11.2%, $p < 0.05$).
Conclusion: Only 27 patients aged ≥ 15 years with hepatoblastoma were identified in this study, the existence of adult hepatoblastoma still requires novel molecular tools to elucidate. The association between the upward trend of hepatoblastoma incidence in boys and increased survival of prematurity in Taiwan warrants further investigations.

Keywords: Hepatoblastoma; Incidence; Taiwan

1. Introduction

Hepatoblastoma is most commonly found in infants and young children aged <5 years.[1] Historically, the existence of hepatoblastoma in adults has been reported but remains controversial.[2-3] A review article demonstrated that only 45 adult cases of hepatoblastoma had been reported through March 2011.[4] Some of these cases were hepatitis B virus (HBV)- and hepatitis C virus (HCV)-negative and had no underlying liver disease, in contrast to classical hepatocellular carcinoma

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(HCC) cases that have cirrhosis or fibrosis of the remaining liver tissue and HBV or HCV seropositivity. Moreover, previous case reports and review articles revealed that prognoses of hepatoblastoma in adults were uniformly poor,[2−11] which contrasted with those in children. Population-based surveillance can help to survey the existence of adult hepatoblastoma and further characterize these rare tumors. Hence, using the data from the population-based Taiwan Cancer Registry (TCR), this study surveyed hepatoblastoma incidences among children and adults; moreover, secular trends of HB incidence among age groups during 1995−2012 were also analyzed.

2. Methods

2.1. Data collection

The data of patients with hepatoblastoma diagnosed from 1995 to 2012 were obtained from the TCR. Specifically, for children, the incidence data of HCC was also extracted to explore the trend of distribution in liver cancer subtypes during the study period. The TCR is organized and funded by the Health Promotion Administration, Ministry of Health and Welfare, Taiwan. A Cancer Registry Advisory Board was organized and responsible for standardizing the procedures, definitions of terminology, and coding of the reporting system for the registry. The TCR was launched in 1979, since the enactment of the *Cancer Control Act* in 2003, hospitals with a capacity of 50 or more beds that provide outpatient and hospitalized cancer care are mandated to submit cancer data to a central cancer registry office, and a trace-back procedure was also implemented, which substantially improved the completeness and case ascertainment of cancer registration.[12,13] In addition, Taiwan launched the single-payer National Health Insurance (NHI) program in 1995.[14] This compulsory universal social insurance system now covers 99.6% of Taiwan's population, and 93% of the hospitals and clinics are NHI-contracted, making it extremely convenient for all residents to get care. Beginning with 2002 incidence data, the *International Classification of Diseases for Oncology, Third Edition* (ICD-O-3) was used by TCR for coding instead of the ICD-O, Field Trial Edition. In the ICD-O-3, primary liver cancer is classified in "C22, cancer of the liver and intrahepatic bile ducts," and the histology code for hepatoblastoma is 89703 (and 81703, 81713, 81723, 81733, 81743, and 81753 for HCC). The Census data by 5-year age group and sex were obtained from the Department of Statistics, Ministry of the Interior, Taiwan. Regarding the main measures of data quality defined by the International Agency for Research on Cancer (IARC), the proportion of microscopically verified cases (MV%) was 91.54% for all cancers combined in 2012. The percentage of cancer cases identified with death certification-only (DCO%) is another indicator of data validity, which decreased from 19.63% in 1995 to 0.72% in 2012. Specifically, for primary liver cancers, the mortality to incidence rate ratio was 1.05 in 1995 and decreased to 0.70 in 2012. MV% ranged from 38.9% in 1995 to 47.61% in 2012, and DCO% was 1.41% in 2012.[15] These measures reflect the high quality of the TCR data, with steady improvement over time, and its achievement of a standard comparable to other cancer registries in Western countries.[16,17] The data source of this study is the TCR public-access database (http://www.hpa.gov.tw/BHPNet/Web/Stat/Statistics.aspx) that consists of case numbers grouped according to the year of diagnosis, sex, and age (in 5-y age intervals). In addition, the MV% of hepatoblastoma and HCC were obtained via the Health and Welfare Data Science Center (HWDC), Taiwan. The HWDC guards the privacy of all enrollees, and provided the data to researchers who have obtained ethical approval. Before the release, all information that could potentially identify an individual person was encrypted. This observational study was approved by the Institutional Review Board of Taipei Veterans General Hospital, Taiwan (IRB-TPEVGH No.: 2016-10-001C). Because these data contain no identifiable personal information, the review board requirement for written informed consent was waived.

2.2. Analyses

Incidence rates were calculated and are expressed per million person-years by the age group and sex. Age-specific incidence rates were stratified into 18 subgroups by 5-year age intervals (from 0 to 4 to ≥85 y). The age-standardized incidence rate (ASIR) is the weighted average of the age-specific rate, where the weight is the proportion of individuals in the corresponding age group of a standard population. Calculating the ASIRs of subgroups by using the same standard population can correct for potential confounding effects derived from differences in the age composition of the population over time. In this study, the World Health Organization World Standard Population was used to calculate the ASIRs and to examine variations among age groups (http://www.who.int/healthinfo/paper31.pdf). Three age groups were compared, as follows: children (aged 0−14 y), adolescents/adults (aged 15−59 y), and elderly people (aged ≥60 y). By using Microsoft Office Excel 2007, this study employed the published methods of IARC to calculate the incidence rates, standard errors, 95% confidence intervals (CIs), and standardized incidence rate ratios (SIRRs).[18] The relative risks of cancer, ratio of ASIRs (ie, SIRRs), and 95% CIs were calculated to compare the cancer incidence by sex. The SIRRs were considered to significantly differ if the estimated 95% CI did not contain 1. Time trends in incidence rates were examined by fitting joinpoint models (Joinpoint Regression Program, version 4.0.4; Statistical Methodology and Applications Branch, Surveillance Research Program, National Cancer Institute, Bethesda, MD) to the ASIRs, which were restricted to a maximum of 3 joinpoints (4 line segments).[19,20] The annual percent change (APC) and corresponding 95% CI were calculated to express the trends in incidence rates among age groups. APC was considered statistically significant if the 95% CI did not include 0 ($p < 0.05$).

3. Results

In total, 211 patients were diagnosed with hepatoblastoma during the 18-year study period, yielding an annual average of

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