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# Nationwide Study of Cancer in HIV-Infected Taiwanese Children in 1998–2009

## To the Editors:

We previously reported an increased incidence of cancers in a nation-

wide registry of 15,269 HIV/AIDS patients in Taiwan in 1998–2009.<sup>1</sup> Excluded from that cohort were HIV-infected patients younger than 15 years. In this study, we determined the cancer incidence in this group of HIV-infected children and compared their incidence to that of noninfected children in the general population.

With approval from the National Health Research Institutes, Taiwan, the National Health Insurance Research Database (NHIRD) was searched for children younger than 15 years with HIV/AIDS in the 1998–2009 databases as previously described.<sup>1</sup> Patients subsequently diagnosed with cancer were identified based on the ICD-9-CM diagnosis codes. To calculate expected rates of cancer, data were obtained from a database linked by the Office of Statistics of the Department of Health using the NHIRD and death certificate database. This data set consisted of 1.8 million individuals randomly sampled from the Registry for Beneficiaries of the NHIRD, which contains registration and original claim data of every person who was a beneficiary of the National Health Insurance program during the period 1998–2009 (approximately 23.72 million individuals). All individuals under the age of 15, totaling 297,387 individuals, were then selected as the control group.

The incidence density (ID) and standardized incidence rate (SIR) for each cancer type were calculated. Person-years analysis was performed in strata of age, calendar period, and cancer type to estimate the ID and SIR. The start date for the calculation of person-years was the date of first HIV/AIDS clinic visit and the end date was December 31, 2009, as no deaths occurred during the follow-up period. The ID of each type of cancer after HIV infection was calculated by dividing the number of observed cancer cases by the total person-years at risk for that cancer. The SIR for each cancer type was calculated by dividing the observed number of cases by the number that would be expected if age-, sex-, and calendar period-specific rates of the comparison population applied.<sup>2</sup> The 95% confidence interval (CI) was calculated by Poisson distribution. All analyses were conducted using SAS version 9.2 (SAS Institute Inc., Cary, NC). A 2-tailed *P* value of <0.05 was considered statistically significant.

A total of 230 HIV-infected children were identified. There were 131 males and 99 females. Seven of these children were diagnosed with cancer (Table 1). When compared with non-HIV-infected children, increased SIRs were seen in HIV-infected children with Kaposi sarcoma (SIR = 30,513.7, 95% CI: 3426.89 to 110,169.44), cancer of the lung and bronchus (SIR = 108.32, 95% CI: 1.42 to 602.67), and cancer of the testis (SIR = 106.86, 95% CI: 1.4 to 594.53).

Most of the reported cases of cancer in children with HIV are AIDS-defining cancers such as Kaposi sarcoma and Non-Hodgkin lymphoma or non-AIDS-defining cancers such as leukemia. Our study showed cancers of the lung and testis, which are very uncommon in children. A case of primary lung cancer in a child with AIDS was previously reported by Biggar et al.<sup>3</sup> This study identified the first case of testicular cancer in a child with HIV. Unfortunately, the histopathology of the testicular tumor in this child is unknown.

The only previous study in Asia was performed in Thailand, which reported a 10-time higher incidence of cancers in HIV-infected children compared with non-HIV-infected children, but this study was performed in children born before perinatal antiretroviral therapy.<sup>4</sup> In the advent of antiretroviral therapy, the incidence of AIDS-defining cancers in children has decreased dramatically<sup>5</sup> but that of non-AIDS-defining cancers has continued to rise. Epidemiologic data suggest that antiretroviral therapy may reduce the incidence of AIDS-defining cancers in children because of improved immunosurveillance induced by antiretroviral therapy.<sup>6,7</sup> However, immune dysregulation has been reported to persist in some children on antiretroviral therapy.<sup>8,9</sup> A limitation of this study was that there were no perinatal antiretroviral therapy exposure data, as these data would help confirm whether the cancer incidence was related to antiretroviral exposure. Many of the cancers have been associated with an infectious etiology in HIV-infected adults<sup>1</sup> and children.<sup>10</sup> Although a causal role has not yet been established for some cancers, human papilloma virus (HPV) infection has been associated with lung cancer<sup>11</sup> and testicular cancer<sup>12</sup> in adults.

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**TABLE 1.** Incidence Density (ID) and Standardized Incidence Ratio (SIR) of Cancers Among HIV-Infected Children in Taiwan Between 1998–2009

Cancer	Male			Female			Total		
	ID	SIR	95% CI	ID	SIR	95% CI	ID	SIR	95% CI
Kaposi sarcoma	130.11	Inf*	(Inf to Inf)	177.69	22730.65	(297.09 to 126470.1)	150.23	30513.7	(3426.89 to 110169.44)
Non-Hodgkin lymphoma				177.69	61.93	(0.81 to 344.56)	75.11	2.09	(0.03 to 11.62)
Liver and biliary system				177.69	1.25	(0.02 to 6.94)	75.11	0.74	(0.01 to 4.13)
Bronchus and lung				177.69	606.15	(7.92 to 3372.54)	75.11	108.32	(1.42 to 602.67)
Testis	130.11	106.86	(1.4 to 594.53)						
Leukemia				177.69	0.49	(0.01 to 2.71)	75.11	0.2	(0 to 1.11)

\*SIR for Kaposi sarcoma in males could not be calculated as there were no cases in the general population.

Although this was a nationwide study encompassing 12 years, the number of HIV-infected children in Taiwan is low. This is because of Taiwan Centers for Disease Control's implementation of nationwide antenatal HIV-1 screening and chemoprevention programs in 2005. As a consequence, the number of HIV-infected children with cancer is also low. Although regular screening for the whole spectrum of cancers is not recommended in children with HIV because of the small number of cases, the possibility of rare cancers in children younger than 15 years, such as lung cancer and testicular cancer, has to be kept in mind.

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