Subtype-specific epidemiology of lymphoid malignancies in Taiwan compared to Japan and the United States, 2002-2012

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Abstract

Background: There are many unrevealed parts regarding lymphoma etiology. Previous studies suggested differences in lymphoma epidemiology among countries existed; however, some were one-center studies that were not enough to represent the whole population.

Objective: To provide epidemiological information on lymphoma within Taiwanese and to compare the data with that in Japan and the United States.

Methods: We used Taiwan Cancer Registry Database as our data source. Patients with lymphoma were identified through the ICD-O-3 codes and those with non-Hodgkin lymphoma (NHL) were categorized into three major types and 13 subtypes according to 2008 WHO classification. Incidence of lymphoma was adjusted according to the 2000 world standard population.

Results: During 2002-2012, 21,929 cases were diagnosed with four major types of lymphoma in Taiwan. Aggressive B-cell lymphoma (52.21%, N = 11,450) was the most common type of NHL. Median age at diagnosis of aggressive B-cell lymphoma was the eldest (63.0-65.0 years). Male excess in T/NK-cell lymphoma was the most obvious (sex ratio: 1.39-2.07). The incidence of NK/T-cell lymphoma, nasal type, was higher (male: 0.16-0.34 per 100,000, female: 0.06-0.16 per 100,000) in Taiwan than that in the United States and Japan.

Conclusion: This is the first population-based study in Taiwan to investigate subtype-specific epidemiology of lymphoma. The incidence rates of lymphoma in Taiwan are mostly lower than those in the United States and higher or comparable to those in Japan except for NK/T-cell lymphoma, nasal type, whose age-adjusted incidence in Taiwan is the highest.

Keywords
age-standardized rate, epidemiology, lymphoma, Taiwan Cancer Registry Database

Ko and Chen contributed equally to this study.

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1 | INTRODUCTION

Large-scale and population-based disease epidemiology is critical to inform resource allocation and research prioritization. However, current evidence is scarce, particularly for lymphoid malignancies. Lymphoid malignancies encompass a group of cancers varying enormously from the morphology, histology, immuno-phenotypes, genotypes, as well as the clinical features, treatment, and outcomes.

Recently, more attention has been paid to evaluate the distribution of lymphoma subtypes and to compare their incidences and prevalences between East and West countries, which might help to shed some light on the intricate etiology and associated genetic or environmental risk factors of lymphoid malignancies. As stated in a previous research, the incidences and prevalences between East and West countries, distribution of lymphoma subtypes and to compare their incidences and prevalences between East and West countries.1,2 In contrast, the incidences of follicular lymphoma (FL) were higher in Asian populations than those in North America and Europe.2,3 In contrast, the incidences of follicular lymphoma and chronic lymphocytic leukemia (CLL) were relatively lower in Asians.2,3 The epidemiology of Epstein-Barr virus (EBV) and human T-lymphoblastic virus-1 (HTLV-1) around the world as well as several genetic factors might be the explanation of discrepancy in incidence between Asia and West.4,5

Although several studies have assessed the subtype-specific incidence rates of lymphoid malignancies between Western and Asian countries,6-9 many of them were limited to one-center studies and did not represent the whole population. In addition, because Taiwan is a multiethnic society with Austronesian heritage, the genetic composition of a Taiwanese population might be different from that of a Japanese or a South Korean population to some extent. Therefore, our study aims to conduct an epidemiological study on lymphoid malignancies within the Taiwanese population using Taiwan Cancer Registry Database (TCRD) and to compare the data acquired from Taiwan with that from Japan and the United States7 in order to reveal complicated etiology of lymphoma.

2 | MATERIALS AND METHODS

2.1 | Data source

We collected information of the newly diagnosed lymphoma cases between 2002 and 2012 from the TCRD. The TCRD is a population-based cancer registry established and funded by the Ministry of Health and Welfare (MOHW) in 1979. 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 TCRD covers cancer patients with all ages who have been admitted to or have gone to hospitals with more than 50 beds. With 98.4% completeness and 91.5% diagnoses confirmed with histological and/or cytological verification, the TCRD has been used as a tremendous tool to enhance the quality of cancer care.10,11 All cancer types were coded in the TCRD based on the International Classification of Diseases for Oncology, the Third Edition (ICD-O-3)12 since 2002.

2.2 | Ethical statement

The protocol of our study was approved by the Research Ethics Committee of National Taiwan University Hospital (registration number, 201604051W).

2.3 | Study population

Patients with Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL) were identified using the ICD-O-3 codes reported by registries. Those with NHL were further categorized into three major types (aggressive B-cell lymphoid neoplasm, indolent B-cell lymphoid neoplasms, and T/NK-cell lymphoid neoplasm) and 13 frequently seen subtypes according to the 2008 WHO classification system,1,2 including diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL), chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), Burkitt lymphoma (BL), mantle cell lymphoma (MCL), marginal zone B-cell lymphoma (MZBCL, including MALT), peripheral T-cell lymphoma-NOS (PTCL-NOS), mycosis fungoides (MF), cutaneous T-cell lymphoma (CTCL), anaplastic large T/null-cell lymphoma (ALCL), angioimmunoblastic T-cell lymphoma (AITL), NK/T-cell lymphoma, nasal type (NK/TCL), and adult T-cell leukemia/lymphoma (ATLL). The disease codes used in this study are presented in Table 1. Patients without pathologically confirmed or aged younger than 20 years at the diagnosis were excluded.

2.4 | Statistical analysis

Number of incidence, median age of diagnosis, and sex ratio were calculated and reported annually for patients with HL as well as three major types and 13 subtypes of NHL during the 11 years of study period (from 2002 to 2012). Crude rates and age-standardized rates (ASRs) adjusted by the 2000 world standard population as defined by the World Health Organization13 were both presented as cases per 100 000 persons. We further investigated the distribution (proportion) of both sexes among all subtypes and compared the age-standardized rates with those reported in Japan and the United States. All data in this study were analyzed using SAS® software, version 9.4 (SAS Institute, Cary, NC, USA).
RESULTS

3.1 | Overall incidence

From 2002 to 2012, a total of 21,929 cases were diagnosed with four major types of lymphoma in Taiwan. The crude incidence rates and age-standardized rates of four major types and most of the subtypes of lymphomas increased during the 11-year study period (Figures 1, 2 and S1, S2). Among the four major types, aggressive B-cell lymphoma (52.21%, N = 11,450) was consistently the most common lymphoma followed by indolent B-cell lymphoma (25.24%, N = 5,535) and T/NK-cell lymphoid neoplasm (15.12%, N = 3,315). It was noteworthy that the crude incidence rate of indolent B-cell lymphoma had a more than twofold increase in 11 years (from 1.12 per 100,000 persons in 2002 to 2.39 per 100,000 persons in 2012). The detailed percentages of four major types of lymphoma are demonstrated annually in Figure S3. Hodgkin lymphoma remained the least occurred lymphoma (7.43%, N = 1,629) throughout the study period although we observed a slight increase in crude incidence rates from 0.57 in 2002 to 0.75 in 2012 (Figure 1).

As for the 13 subtypes of NHL, DLBCL accounted for almost half of the lymphoma cases (44.18%, N = 9,688) and occurred far more frequently than the following four frequently diagnosed subtypes, including FL (9.47%, N = 2,076), MZBCL (9.14%, N = 2004), CLL/SLL (5.66%, N = 1,241), and PTCL-NOS (4.73%, N = 1,038). The lowest incidence was seen in ATLL (0.17%, N = 38), and some of the figures regarding this category were unavailable due to insufficient number of patients diagnosed in the calendar year (Table 2).

3.2 | Distribution of age and sex

NHL tended to occur at older ages than HL. Among NHL patients, the median age at diagnosis of aggressive B-cell lymphoid neoplasm was the eldest (63.0-65.0 years) followed by that of indolent B-cell lymphoma (25.24%, N = 5,535) and T/NK-cell lymphoid neoplasm (15.12%, N = 3,315). It was noteworthy that the crude incidence rate of indolent B-cell lymphoma had a more than twofold increase in 11 years (from 1.12 per 100,000 persons in 2002 to 2.39 per 100,000 persons in 2012). The detailed percentages of four major types of lymphoma are demonstrated annually in Figure S3. Hodgkin lymphoma remained the least occurred lymphoma (7.43%, N = 1,629) throughout the study period although we observed a slight increase in crude incidence rates from 0.57 in 2002 to 0.75 in 2012 (Figure 1).

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2002 to 2012 increased gradually and were similar between men and women (Figure 4). Furthermore, the incidences of most lymphoma were higher in males than those in females, especially for aggressive B-cell lymphoma (male: 3.46-4.76 per 100,000; female: 2.95-3.80 per 100,000) and T/NK-cell lymphoma (male: 1.14-1.72 per 100,000; female: 0.67-1.03 per 100,000) in the four major types, and DLBCL (male: 2.95-3.84 per 100,000; female: 2.57-3.18 per 100,000) in the 13 subtypes (Table 2, Figures 4 and S7).

### 3.3 International comparison

Comparisons of subtype-specific incidence rates of lymphoid malignancies among the United States, Japan, and Taiwan are depicted in Figures 5 and S8, and detailed data are presented in Table S1. Notably, during 2002 to 2008, the ASRs of Hodgkin lymphoma in Taiwan (male: 0.57-0.74 per 100,000; female: 0.40-0.56 per 100,000) were obviously lower than that in the United States (male: 2.72-3.17 per 100,000; female: 2.17-2.60 per 100,000) and comparable to that in Japan (male: 0.38-0.59 per 100,000; female: 0.24-0.47 per 100,000) in both sex. The ASRs of aggressive and indolent B-cell lymphoid neoplasms were distinctly different among the United States, Taiwan, and Japan. In patients with DLBCL (Table 2, Figure 5A,B) and MZBCL (Table 2, Figure 5E,F), and in male patients with BL (Table 2 and Figure 5C), the incidences were highest in the US population, lowest in the Japanese population, and intermediate in the Taiwanese population. In contrast, the ASRs were divergent in NK/TCL, nasal type (Table 2, Figure 5G,H). The ASRs of NK/TCL were highest in the Taiwanese population and lowest in the US population.

### 4 DISCUSSION

To the best of our knowledge, this population-based study is the largest and the most comprehensive epidemiologic study to provide information on subtype-specific epidemiology of lymphoid malignancies in the Taiwanese population, and it shows the differences in incidences among Taiwan, Japan, and the United States. Our study has the merits of using the population-based data, which fills the knowledge gap that many of the existing studies are limited to single-center studies and thought to be unrepresentative. In addition, using the year 2000 world standard population for
## Table 2
Number of incident cases and age-standardized rates (ASRs) of patients with HL, three major types and 13 subtypes of NHL in Taiwan between 2002 and 2012

| Disease                              | Number of Incidence/ASR | 2002 |          |          | 2003 |          |          | 2004 |          |          | 2005 |          |          | 2006 |          |          |
|--------------------------------------|-------------------------|------|----------|----------|------|----------|----------|------|----------|----------|------|----------|----------|------|----------|----------|
|                                      |                         | M    | F    | Total   | M    | F    | Total   | M    | F    | Total   | M    | F    | Total   | M    | F    | Total   |
| HL                                   | Number of Incidence     | 81   | 47   | 128    | 76   | 53   | 129    | 84   | 46   | 130    | 69   | 47   | 116    | 88   | 52   | 140    |
|                                       | ASR                     | 0.68 | 0.42 | 0.55   | 0.66 | 0.45 | 0.56   | 0.72 | 0.41 | 0.57   | 0.57 | 0.40 | 0.49   | 0.74 | 0.44 | 0.59   |
| NHL                                   |                         |      |      |        |      |      |        |      |      |        |      |      |        |      |      |        |
| Aggressive B-cell lymphoid neoplasm  | Number of Incidence     | 427  | 360  | 787    | 471  | 359 | 830    | 496  | 385 | 881    | 547  | 387 | 934    | 539  | 421 | 960    |
|                                       | ASR                     | 3.46 | 3.04 | 3.25   | 3.80 | 2.98 | 3.40   | 3.85 | 3.08 | 3.47   | 4.22 | 2.99 | 3.60   | 3.97 | 3.16 | 3.57   |
| DLBCL                                | Number of Incidence     | 364  | 305  | 669    | 395  | 322 | 717    | 407  | 326 | 733    | 443  | 338 | 781    | 450  | 364 | 814    |
|                                       | ASR                     | 2.95 | 2.58 | 2.76   | 3.14 | 2.66 | 2.91   | 3.11 | 2.58 | 2.85   | 3.37 | 2.59 | 2.98   | 3.26 | 2.71 | 3.00   |
| BL                                   | Number of Incidence     | 20   | 22   | 42     | 26   | 13  | 39     | 30   | 19  | 49     | 32   | 18  | 50     | 33   | 25  | 58     |
|                                       | ASR                     | 0.17 | 0.20 | 0.18   | 0.23 | 0.12 | 0.18   | 0.28 | 0.18 | 0.23   | 0.29 | 0.16 | 0.22   | 0.29 | 0.22 | 0.26   |
| MCL                                  | Number of Incidence     | 18   | 5    | 23     | 19   | 3   | 22     | 22   | 6   | 28     | 30   | 6   | 36     | 26   | 6   | 32     |
|                                       | ASR                     | 0.14 | 0.04 | 0.09   | 0.17 | 0.02 | 0.09   | 0.16 | 0.05 | 0.11   | 0.24 | 0.05 | 0.14   | 0.19 | 0.04 | 0.12   |
| Indolent B-cell lymphoid neoplasm    | Number of Incidence     | 139  | 114  | 253    | 155  | 125 | 280    | 139  | 145 | 284    | 195  | 134 | 329    | 188  | 169 | 357    |
|                                       | ASR                     | 1.15 | 0.95 | 1.05   | 1.21 | 1.00 | 1.11   | 1.07 | 1.15 | 1.11   | 1.48 | 0.99 | 1.23   | 1.39 | 1.23 | 1.31   |
| FL                                   | Number of Incidence     | 68   | 50   | 118    | 90   | 68  | 158    | 80   | 64  | 144    | 104  | 70  | 174    | 102  | 81  | 183    |
|                                       | ASR                     | 0.56 | 0.41 | 0.48   | 0.70 | 0.54 | 0.62   | 0.62 | 0.51 | 0.57   | 0.77 | 0.51 | 0.64   | 0.74 | 0.59 | 0.66   |
| CLL/SLL                              | Number of Incidence     | 55   | 27   | 82     | 57   | 28  | 85     | 64   | 40  | 104    | 66   | 37  | 103    | 63   | 36  | 99     |
|                                       | ASR                     | 0.45 | 0.23 | 0.34   | 0.45 | 0.22 | 0.34   | 0.49 | 0.31 | 0.40   | 0.52 | 0.28 | 0.40   | 0.46 | 0.26 | 0.36   |
| MZBCL                                | Number of Incidence     | 67   | 63   | 130    | 58   | 53  | 111    | 52   | 79  | 131    | 79   | 60  | 139    | 70   | 83  | 153    |
|                                       | ASR                     | 0.55 | 0.53 | 0.54   | 0.46 | 0.43 | 0.45   | 0.40 | 0.63 | 0.51   | 0.61 | 0.45 | 0.53   | 0.53 | 0.61 | 0.57   |
| T/NK-cell lymphoid neoplasm          | Number of Incidence     | 140  | 97   | 237    | 171  | 80  | 251    | 151  | 95  | 246    | 177  | 83  | 260    | 201  | 101 | 302    |
|                                       | ASR                     | 1.14 | 0.82 | 0.99   | 1.39 | 0.68 | 1.04   | 1.20 | 0.77 | 0.99   | 1.37 | 0.67 | 1.02   | 1.56 | 0.77 | 1.16   |
| PTCL-NOS                             | Number of Incidence     | 60   | 36   | 96     | 58   | 31  | 99     | 49   | 37  | 86     | 59   | 22  | 81     | 60   | 36  | 96     |
|                                       | ASR                     | 0.49 | 0.31 | 0.40   | 0.46 | 0.26 | 0.36   | 0.38 | 0.29 | 0.34   | 0.45 | 0.18 | 0.32   | 0.46 | 0.27 | 0.37   |
| MF                                   | Number of Incidence     | 9    | 6    | 15     | *    | *   | *      | 13   | 11  | 24     | 10   | 5   | 15     | 19   | 4   | 23     |
|                                       | ASR                     | 0.07 | 0.05 | 0.06   | *    | *   | *      | 0.05 | 0.08 | 0.03   | 0.07 | 0.04 | 0.06   | 0.15 | 0.03 | 0.09   |
| CTCL                                 | Number of Incidence     | 4    | 8    | 12     | 15   | 3   | 18     | *    | *   | *      | 6    | 14  | 3      | 17   | 12  | 5      |
|                                       | ASR                     | 0.03 | 0.06 | 0.05   | 0.13 | 0.02 | 0.08   | *    | *   | *      | 0.03 | 0.10 | 0.02   | 0.06 | 0.09 | 0.04   |
| ALCL                                 | Number of Incidence     | 21   | 9    | 30     | 31   | 14  | 45     | 22   | 20  | 42     | 23   | 16  | 39     | 28   | 13  | 41     |
|                                       | ASR                     | 0.18 | 0.08 | 0.13   | 0.25 | 0.13 | 0.19   | 0.19 | 0.17 | 0.18   | 0.20 | 0.14 | 0.17   | 0.23 | 0.11 | 0.17   |
TABLE 2

| Year | M    | F    | Total | M    | F    | Total | M    | F    | Total | M    | F    | Total | M    | F    | Total |
|------|------|------|-------|------|------|-------|------|------|-------|------|------|-------|------|------|-------|
| 2007 | 84   | 63   | 147   | 86   | 62   | 148   | 92   | 84   | 176   | 104  | 69   | 173   | 105  | 63   | 168   |
| 2008 | 0.69 | 0.56 | 0.62  | 0.71 | 0.54 | 0.63  | 0.72 | 0.71 | 0.71  | 0.86 | 0.57 | 0.72  | 0.83 | 0.56 | 0.69  |
| 2009 | 0.80 | 0.64 | 0.71  | 0.69 | 0.54 | 0.63  | 0.72 | 0.71 | 0.71  | 0.86 | 0.57 | 0.72  | 0.83 | 0.56 | 0.69  |
| 2010 | 0.30 | 0.21 | 0.22  | 0.20 | 0.15 | 0.15  | 0.25 | 0.16 | 0.21  | 0.33 | 0.09 | 0.21  | 0.22 | 0.11 | 0.16  |
| 2011 | 0.30 | 0.21 | 0.22  | 0.20 | 0.15 | 0.15  | 0.25 | 0.16 | 0.21  | 0.33 | 0.09 | 0.21  | 0.22 | 0.11 | 0.16  |
| 2012 | 0.30 | 0.21 | 0.22  | 0.20 | 0.15 | 0.15  | 0.25 | 0.16 | 0.21  | 0.33 | 0.09 | 0.21  | 0.22 | 0.11 | 0.16  |

(Continues)
incidence, adjustment made us able to compare our findings to those in Japan and the United States from the previous studies.7

In our study, the ratio of HL and NHL is consistent with the previous smaller-scale study conducted in Taiwan.8 HL and NHL accounted for 6.09% and 93.32% of all lymphoid malignancies in the previous study,8 and our study obtained the similar results (HL, 7.9%; and NHL, 92.1%). Compared with studies from other countries, NHL tended to occur more frequently in both Eastern and Western countries although the percentages of HL are higher in Western countries.7,8,14-17 In the United States and the United Kingdom (UK), HL constituted 9.96% and 14.41% of patients with lymphoid neoplasms.16,17 In Eastern countries, by contrast, HL accounted for 4.12%, 5.9%, 8.60%, and 7.43% of patients with lymphoid neoplasms in South Korea, Japan, China, and Taiwan (our study), respectively.7,14,15

Because NHL is composed of different types of lymphoma, we further make the comparisons between our results and the previously published one from other countries. B-cell lymphoma (BCL) accounts for the majority of NHL in both Western and Eastern countries.7,8,14-17 In the United States and UK, BCL composes of 93.37% and 93.79% of NHL cases, respectively.16,17 However, the percentages of BCL are slightly lower and are 81.60%, 77.05%, 71.05%, and 83.67% of NHL patients in South Korea, Japan, China, and Taiwan (our study).7,14,15 In detail, the majority of BCL cases was DLBCL in both Eastern and Western countries, and the percentages were variable (38.92% in the United States,18 43.24% in the UK,17 45.8% in the Central and South America, 19 47.75% in South Korea, 15 62.48% in Japan, 7 55.78% in Mainland China,14 and 57.04% in Taiwan, our study). The second and third frequent types of BCL are FL and MZBCL in Japan and Taiwan (our study). FL and MZBCL accounted for 18.60% and 9.93% of BCL patients in Japan,7 and 12.22% and 11.80% in Taiwan. However, the percentage of FL is lower in Mainland China (4.48%)14 and South Korea (2.68%).15 Why the frequencies of FL differ among Asian countries remains uncertain. The previous study suggests several potential risk factors, such as diet modernization, inoculation rate

| Disease                  | Number of Incidence | ASR | 2002 | 2003 | 2004 | 2005 | 2006 |
|--------------------------|---------------------|-----|------|------|------|------|------|
| AITL                     | Number of Incidence |     |      |      |      |      |      |
| ASR                      | 0.08                | 0.09| 0.08 | 0.12 | 0.09 | 0.11 | 0.15 |
| Number of Incidence      |                     |     |      |      |      |      |      |
| ASR                      | 0.15                | 0.12| 0.11 | 0.07 | 0.11 | 0.15 | 0.07 |
| Number of Incidence      |                     |     |      |      |      |      |      |
| ASR                      | 0.11                | 0.15| 0.07 | 0.11 | 0.11 | 0.14 | 0.03 |
| Number of Incidence      |                     |     |      |      |      |      |      |
| ASR                      | 0.14                | 0.03| 0.09 | 0.13 | 0.08 | 0.10 | 0.03 |
| Number of Incidence      |                     |     |      |      |      |      |      |
| ATLL                     | Number of Incidence |     |      |      |      |      |      |
| ASR                      | *                   | *   | *    | *    | *    | *    | *    |
| Number of Incidence      |                     |     |      |      |      |      |      |
| ASR                      | *                   | *   | *    | *    | *    | *    | *    |
| Number of Incidence      |                     |     |      |      |      |      |      |
| ASR                      | *                   | *   | *    | *    | *    | *    | *    |
| Number of Incidence      |                     |     |      |      |      |      |      |
| ASR                      | *                   | *   | *    | *    | *    | *    | *    |
| Number of Incidence      |                     |     |      |      |      |      |      |
| ASR                      | *                   | *   | *    | *    | *    | *    | *    |
| Number of Incidence      |                     |     |      |      |      |      |      |
| ASR                      | *                   | *   | *    | *    | *    | *    | *    |
| Number of Incidence      |                     |     |      |      |      |      |      |
| ASR                      | *                   | *   | *    | *    | *    | *    | *    |
| Number of Incidence      |                     |     |      |      |      |      |      |
| ASR                      | *                   | *   | *    | *    | *    | *    | *    |
| Number of Incidence      |                     |     |      |      |      |      |      |
| ASR                      | *                   | *   | *    | *    | *    | *    | *    |

* Not available due to insufficient case numbers.
of influenza vaccination, single nucleotide polymorphisms (SNPs) within the major histocompatibility complex (MHC) region, and environmental factors. Compared to our study, MZBCL (MALT included) in South Korea is the second majority of BCL, and it composed 19.45% of patients diagnosed with BCL. Helicobacter pylori infection is related to MALT, and H. pylori irradiation is the frontline treatment for the patients with limited stage MALT. Therefore, higher proportion of MZBCL in South Korea may be related to the high prevalence of H. pylori and endoscopy screening policy for gastric cancer.

About T-cell lymphoma (TCL), the incidence rates are higher in Eastern countries than those in Western countries. In the United States and the UK, TCL accounts for 6.63% and 6.21% of NHL, respectively, whereas the incidences of TCL in South Korea, Japan, Mainland China, and Taiwan (our study) are threefold to fourfold higher (17.16%, 19.98%, 28.95%, and 16.33% of NHL patients, respectively).
respectively). Nevertheless, the frequencies of TCL subtypes vary among Asian countries. The most frequent type in Japan is ATLL (45.86% of TCL), but PTCL-NOS in South Korea (31.6%) and Taiwan (31.31%), and NK/TCL in Mainland China (47.04%). In South Korea, NK/TCL is the second common TCL and constitutes 30.9% of TCL.
patients. The disparity in the distribution of TCL subtypes among countries may be attributable to different lifestyles, environmental factors, and genetic polymorphisms. In addition, viral infections also play a pivotal role in TCL, such as EBV infections in NK/TCL, nasal type, and HTLV-1 infections in ATLL. High prevalence of EBV infection in Asian countries and high HTLV-1 carrier rate in southern Japan contribute to the relatively high incidence of NK/TCL and ATLL in these areas. Unlike southern Japan, in which the HTLV-1 prevalence was reported to be the highest in the world (more than 10%), the HTLV-1 prevalence was reported to be between 0.1 and 1% in Taiwan. Another study worldwide (more than 10%), the HTLV-1 prevalence was reported to be the highest in the

adjustments are made according to the 2000 world standard

times but also among Asians living in diverse countries. This

observation strengthens the assumption that the etiology of
lymphoid malignancies consists of genetics, environmental
factors, and lifestyles.

As for subtype-specific sex ratio of lymphoid malignan-
cies in Taiwan, male predominance is most obvious in MCL
patients (sex ratio, 2.18-6.09), which is consistent with the re-
esults found in Hong Kong and in the United States (standard-
ized rate ratio (SRR) in Hong Kong, 4.3; incidence rate and
rate ratio (IRR) in the United States, 3.07). However, etiol-
ogy of the male predominance in MCL still remains unclear.
Interestingly, despite the male predominance noticed in most
subtypes of lymphoma, no such phenomenon was observed in

DLBCL (sex ratio, 1.11-1.29), MZBCL (sex ratio, 0.64-1.28),
and FL (sex ratio, 0.87-1.44). These findings are consistent
with the results in Hong Kong, where SRRs of DLBCL,
MZBCL, and FL were 1.3, 1.1, and 1.1, respectively. As for
the United States, though IRRs of MZBCL (1.05) and FL
(1.18) were the lowest among all subtypes as well, DLBCL
was a bit more male-predominated than Taiwan and Hong
Kong instead with IRR of 1.49. Further research concern-
ing subtype-specific etiology of lymphoma is still urgently
required to elucidate the sex difference.

While we provide tremendous epidemiologic informa-
tion of lymphoma, the present study has some limitations.
First, the incidence of some TCL in Taiwan was extremely
low, such as MF, CTCL, and ATLL. Therefore, it should
be very cautious when making comparisons with the inci-
dences in other countries. Second, the subtype-specific in-
cidences of lymphoma in the South Korea population were
adjusted according to Segi world population, which is dif-
ferent from the standard applied in our study. The slight
discrepancies may therefore be arisen when we try to make
the comparisons with the data in South Korea. Nevertheless,
there are still merits of our study. Using population-based
data source, our results are representative enough of the
Taiwanese population. Moreover, adjustments made on in-
cidence rates according to the 2000 world standard popu-
lation let us be able to evaluate the dissimilarity existing
among countries. In this way, our data are worth helping
unveil the rather mysterious etiology of lymphoma.

Conclusively, our study is the first population-based study
conducted in Taiwan aiming to investigate subtype-specific
epidemiology of lymphoma. Most of the incidence rates of
lymphoid malignancies in Taiwan are lower than those in the
United States, and higher than or comparable to those in Japan
except that the ASRs of some TCL are the highest, including
PTCL/NOS, AITL, and NK/TCL. The researches regarding
the subtype-specific epidemiology of lymphoid malignan-
cies in different countries or regions are crucial to elucidate
the etiologies of lymphoma. Further investigations about
the subtype-specific survival of lymphoid malignancies in Taiwan
are required to clarify the natural history of lymphoma and the
impact of ever-advancing therapies.
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CONFLICT OF INTERESTS

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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