A nationwide population-based study of the inflammatory bowel diseases between 1998 and 2008 in Taiwan

Shu-Chen Wei1, Meng-Hung Lin2, Chien-Chih Tung1,3, Meng-Tzu Weng1,4, Jen-Shin Kuo1,5, Ming-Jium Shieh6, Cheng-Yi Wang1, Wen-Chao Ho2, Jau-Min Wong1* and Pau-Chung Chen7,8,9*

Abstract

Background: The incidence of the inflammatory bowel diseases (IBD), ulcerative colitis (UC) and Crohn’s disease (CD), has been increasing in Asia. We probed the nationwide registered database to assess the incidence, prevalence, gender distribution, age of diagnosis and the survival status of IBD patients in Taiwan.

Methods: A retrospective study was conducted to analyze the registered database compiled by the National Health Insurance provided by the Department of Health, Taiwan, from January 1998 through December 2008.

Results: A total of 1591 IBD patients were registered from 1998 to 2008 in Taiwan (CD: 385; UC: 1206). The incidence of CD increased from 0.19/100,000 in 1998 to 0.24/100,000 in 2008. The incidence of UC increased from 0.61/100,000 in 1998 to 0.94/100,000 in 2008. The prevalence of CD increased from 0.19/100,000 in 1998 to 1.78/100,000 in 2008. The prevalence of UC increased from 0.61/100,000 in 1998 to 7.62/100,000 in 2008. Male to female ratio for CD was 2.22 and 1.64 for UC. Age of registered for CD was predominantly between 20 to 39, and for UC between 30 to 49 years of age. The standardized mortality ratio (95% CI) was 4.97 (3.72–6.63) for CD and 1.78 (1.46–2.17) for UC, from 1998 to 2008 in Taiwan.

Conclusions: Using the Taiwan nationwide database for IBD, the incidence and prevalence of IBD in Taiwan significantly increased from 1998 to 2008. The mortality rate was higher for CD patients than UC patients, and both were higher than the general population.

Keywords: Crohn’s disease, Ulcerative colitis, Incidence, Prevalence, Taiwan, Nationwide
health insurance. Since 1997, CD and UC, due to their potential for repetitive admissions and the need for chronic, careful caring, are registered as catastrophic illnesses. When a patient's ailment is diagnosed by a physician as a “catastrophic illness” under Department of Health guidelines, the patient can submit related information and apply for a catastrophic illness certificate/registration. For IBD, the application includes the clinical diagnosis, pathological report as well as the possible image studies to be formally reviewed to validate and register the patient’s diagnosis of CD or UC, as well as for excluding intestinal tuberculosis. In this study, we used this nationwide-based data set to reveal the incidence, prevalence, age/gender distribution and the mortality rate of IBD patients in Taiwan.

Methods
Data source and ethical considerations
The nationwide population-based Taiwanese study of IBD was compiled between January 1998 and December 2008. Data was obtained from the Taiwan National Health Insurance (NHI) research database, which has been routinely collected by the National Health Research Institute (NHRI). These high quality databases have previously been used for epidemiologic research, information on prescription use, diagnoses, and hospitalizations [13-15]. With strict confidentiality guidelines being closely followed in accordance with personal electronic data protection regulations; the NHRI anonymized and maintained the NHI reimbursement data as files suitable for research. In addition, this study was approved by the Ethics Review Board at the National Taiwan University Hospital.

Patient identification
We used the diagnostic code (The International Classification of Diseases, Ninth Revision, Clinical Modification 2001 edition) to retrieve the IBD patients (UC: 556.XX; CD: 555.XX) from the catastrophic illness registration database. For each patient, medical records were collected in the NHI claim database, including date of admission, date of discharge, dates of visits, clinical diagnosis, prescription and total expenditure. The databases also contained patient information, including sex, date of birth and date of death.

Statistical analyses
The characteristics of IBD patients, including the year of diagnosis, sex ratio and age distribution, were described in this study. The annual incidence and prevalence were defined as the number of newly diagnosed patients and the number of patients with IBD per 100,000 persons per year, respectively, namely, the crude incidence and prevalence. We used the Kaplan-Meier method to estimate IBD cumulative survival rate over an eleven year follow-up period. To compare with the general population of Taiwan, the standardized mortality ratio and 95% confidence interval were calculated based on the Poisson assumption. Furthermore, the direct mortality rate was also standardized to the WHO 2000 standard population using 5-year age groups per 1,000 person-years. All statistical analyses were performed with the SAS version 9.3 (SAS Institute, Cary, NC, USA). A P value of less than 0.05 was set to declare statistical significance.

Results
A total of 1,591 IBD patients were registered from 1998 to 2008 in Taiwan. Among them, 385 were diagnosed with CD and 1,206 with UC. As shown in Figure 1, the incidence of CD increased from 0.19/100,000 in 1998 to 0.24/100,000 in 2008. The incidence of UC increased from 0.61/100,000 in 1998 to 0.94/100,000 in 2008. When this period was arbitrarily divided into the first stage as 1998 to 2003 and second stage from 2004 to 2008, the mean incidence for CD in the first stage was 0.16/100,000 and 0.22/100,000 for the second stage; the incidence of CD increased significantly from the first stage to the second stage (p = 0.005). For UC, the mean incidence in the first stage was 0.70/100,000 and 0.88/100,000 for the second stage; the incidence of UC increased also significantly from the first stage to the second stage (p = 0.047).

As shown in Figure 2, the prevalence of CD increased from 0.19/100,000 in 1998 to 1.78/100,000 in 2008. The prevalence of UC increased from 0.62/100,000 in 1998 to 7.62/100,000 in 2008. The mean prevalence for CD in the first stage was 0.51/100,000 and 1.42/100,000 for the second stage; the prevalence of CD increased significantly from the first stage to the second stage (p = 0.0003). For UC, the mean prevalence in the first stage was 2.2/100,000 and 6.12/100,000 for the second stage; the prevalence of UC increased also significantly from the first stage to the second stage (p = 0.0005).

The year of diagnosis and sex-specific number of patients with CD and UC in Taiwan from 1998 to 2008 are
summarized in Table 1. Sex- and age-specific number of patients registered with CD are summarized in Table 2, and for UC in Table 3. The age of registration for CD patients was primarily between 20 to 39 (Figure 3), with the mean and standard deviation of 37.8 and 18.8 years of age, respectively. The age of registration for UC was mostly between 30 to 49 years old (Figure 4), with the mean and standard deviation of 44.5 and 15.8 years old, respectively. Male to female ratios for CD was 2.22 and 1.64 for UC. These ratios reflect a male predominant pattern in Taiwan for CD over UC ($p = 0.01$) (Figure 5).

Table 1 Year of diagnosis and sex-specific number of patients with Crohn’s disease and ulcerative colitis in Taiwan, 1998-2008

| Year of diagnosis | Male | Female | Total | Male to female ratio |
|-------------------|------|--------|-------|----------------------|
| **Crohn’s disease** |      |        |       |                      |
| 1998              | 25   | 13     | 38    | 1.9                  |
| 1999              | 18   | 10     | 28    | 1.8                  |
| 2000              | 22   | 10     | 32    | 2.2                  |
| 2001              | 28   | 12     | 40    | 2.3                  |
| 2002              | 27   | 9      | 36    | 3                    |
| 2003              | 26   | 17     | 43    | 1.5                  |
| 2004              | 37   | 15     | 52    | 2.5                  |
| 2005              | 33   | 15     | 48    | 2.2                  |
| 2006              | 32   | 16     | 48    | 2                    |
| 2007              | 31   | 14     | 45    | 2.2                  |
| 2008              | 41   | 15     | 56    | 2.7                  |

| **Ulcerative colitis** |      |        |       |                      |
| 1998              | 69   | 49     | 118   | 1.4                  |
| 1999              | 91   | 44     | 135   | 2.1                  |
| 2000              | 78   | 42     | 120   | 1.9                  |
| 2001              | 82   | 37     | 119   | 2.2                  |
| 2002              | 113  | 76     | 189   | 1.5                  |
| 2003              | 123  | 72     | 195   | 1.7                  |
| 2004              | 100  | 69     | 169   | 1.4                  |
| 2005              | 136  | 85     | 221   | 1.6                  |
| 2006              | 116  | 85     | 201   | 1.4                  |
| 2007              | 119  | 74     | 193   | 1.6                  |
| 2008              | 123  | 95     | 218   | 1.3                  |

Table 2 Sex- and age-specific number of patients registered as Crohn’s disease in Taiwan, 1998-2008

| Age group | Male | Female | Total |
|-----------|------|--------|-------|
| 0–9       | 18   | 8      | 26    |
| 10–19     | 30   | 16     | 46    |
| 20–29     | 77   | 17     | 94    |
| 30–39     | 72   | 30     | 102   |
| 40–49     | 56   | 26     | 82    |
| 50–59     | 26   | 23     | 49    |
| 60–69     | 22   | 14     | 36    |
| 70–79     | 18   | 7      | 25    |
| ≥80       | 1    | 5      | 6     |

Table 3 Sex- and age-specific number of patients registered as ulcerative colitis in Taiwan, 1998-2008

| Age group | Male | Female | Total |
|-----------|------|--------|-------|
| 0–9       | 8    | 3      | 11    |
| 10–19     | 34   | 26     | 60    |
| 20–29     | 175  | 76     | 251   |
| 30–39     | 290  | 164    | 454   |
| 40–49     | 264  | 162    | 426   |
| 50–59     | 193  | 138    | 331   |
| 60–69     | 109  | 92     | 201   |
| 70–79     | 61   | 58     | 119   |
| ≥80       | 16   | 9      | 25    |

Discussion

Increased incidence and prevalence of IBD in Asia have been reported [1,3-12]. This information is mostly based on hospital-based data except for a report from Japan where there is a nationwide registration system [16]. By using a nationwide registration system in Taiwan,
we confirmed this phenomenon by adding a second
nationwide-based data analysis in Asia, which con-
firmed that the incidence and prevalence of IBD in-
creased from 1998 to 2008 in Taiwan. From our
experience, the true IBD patient number should be more
than the registered number as there are always IBD pa-
tients who have not yet registered or who have not passed
the registration process, therefore, there is no way to know
the real number. The bottom line is that we have at least
the number of cases reported in this study with a con-

dirmed diagnosis of IBD and the number of cases in-
creased significantly over the past years in Taiwan.

Although the incidence (CD: 0.24/100,000; UC: 0.94/
100,000, in 2008) and prevalence (CD: 1.78/100,000; UC:
7.62/100,000, in 2008) increased in Taiwan, they were still
lower than the reports from Japan (prevalence: approxi-
mately 21/100,000 for CD and 63.6/100,000 for UC),
Korea (prevalence: approximately 11/100,000 for CD and
30.9/100,000 for UC), and much lower than those from
Western Countries (prevalence: approximately 200/
100,000 for CD and 400/100,000 for UC) [1,9,16]. And
according to the recently published large scale population-
based epidemiologic study across nine countries in Asia-
Pacific showing geographic variability in disease incidence
even within Asia [17]. Taiwan appeared to have disease in-
cidence that is lower than Hong Kong, some parts of
mainland China, and Macau, and relatively similar to that
of Malaysia and Sri Lanka, but higher than those of
Thailand and Indonesia. One may speculate that different
dergrees of urbanization/socioeconomic status may play a
part in the variation.

The mean age of patients registered with CD was 37.8
and for UC was 44.5 years of age. We previously have
shown that, based on a referral center in Taiwan, the
mean age of diagnosis for CD was 30.5 and for UC was
36 in the National Taiwan University Hospital [11,12].
This difference might be related to the lag between diag-

nosis and registration, as well as the possible gap between
the IBD diagnosis efficiency between an experienced cen-
ter and the other general hospitals. Nonetheless, the mean
age for CD and UC registered patients was still within the
range reported from other countries in Asia [16].

Considering the male to female ratio, in the current
study we found the ratio for CD was 2.22 and for UC was
1.64, which was consistent with our previous results which
showed 1.82 for CD and 1.35 for UC [11,12]. Both diseases
showed a male predominant pattern, especially significant
for CD. This observation was consistent with the reports
from the other Asian countries, most of them revealed a
male predominant prevalence. Interestingly, this differed
from reports from Western countries [16,18].

The survival status, or vice versa, the mortality rate
from this report was quite different from previous re-
ports, even when compared to our previous results
based on a referral center follow-up study which showed
the accumulated mortality rate for CD to be 2.7% (3 of
110) and 1.72% for UC (7 of 406) from 1988 to 2008. In
this study, the survival rate of CD patients after the registration for one year, 5 years and 10 years were: 96%, 90% and 82%, respectively. For UC patients, the survival status after the registration for one year, 5 years and 10 years were: 99%, 95% and 90%, respectively. There was a statistical difference of the survival status between UC and CD patients from 1998 to 2008 in Taiwan ($p = 0.001$). When compared with the general population, the standardized mortality ratio (95% CI) was 4.97 (3.72 – 6.63) and the standardized mortality rate (per 1,000 person-years) was 29.7 for CD; the standardized mortality ratio (95% CI) was 1.78 (1.46 – 2.17) with the standardized mortality rate (per 1,000 person-years) as 9.62 for UC from 1998 to 2008 in Taiwan. Both were higher than the reports from Japan as well as from most Western countries, with the standardized mortality ratio for CD around 1.5 fold the general population. The mortality rate of CD patients was slightly higher than the general population and the mortality rates for UC patients, either from Japan or from Western countries were mostly the same as the general population [19-31].

The higher mortality shown in this study was unexpected. However, as the data was anonymized, only the date of death but not the cause of death nor comorbidity could be traced from this data set. The registered data only provided the diagnosis, no phenotypic information was included. Therefore, we were not able to know whether the higher mortality resulted from the severity of the disease or not. The ages of diagnosis in this cohort were comparable to the reports from other Asian countries [1,17,30], age did not seem to be able to explain the higher mortality. However, when comparing the results from a referral center (National Taiwan University Hospital, for example) with the nationwide population-base, patients tended to be diagnosed at earlier ages and with less mortality when seen in a referral center. This result might reflect the low awareness of IBD in the general practice, since previously in Taiwan, IBD was a relatively low prevalence disease. Experience diagnosing and treating IBD patients when they presented outside the referral center (NTUH, for example) was lagging. Therefore, since 2010, we have started to emphasize the increasing trend of IBD as well as an IBD awareness education program. Hopefully in the future, we can improve the awareness, the quality of care, and the outcome of IBD patients in Taiwan. Our experience might also afford other countries where IBD is low in prevalence, to modify their quality of care in treating IBD patients which should translate into improving the prognosis of IBD patients.

**Conclusion**

Using the Taiwan nationwide database for IBD, the incidence and prevalence of IBD in Taiwan significantly increased from 1998 to 2008.

The mortality rate was higher for CD patients than UC patients, and both were higher than the general population. After our promotion of the disease awareness, we hope the outcome of IBD patients in Taiwan could be improved in the future.

**Competing interests**

The authors declare that they have no competing interests.

**Authors’ contributions**

SCW, CCT, MTW, JSK, MJS, CYW, JMW: study design, data collection, manuscript preparation. MHL, WCH, PCC: statistics analysis and manuscript preparation. All authors read and approved the final manuscript.

**Author details**

1Department of Internal Medicine, National Taiwan University Hospital and College of Medicine, 7 Chung Shan South Road, Taipei, Taiwan. 2Department of Public Health, College of Public Health, China Medical University, Taichung, Taiwan. 3Department of Integrated Diagnostics and Therapeutics, National Taiwan University Hospital and College of Medicine, Taipei, Taiwan. 4Department of Internal Medicine, Far Eastern Memorial Hospital, New Taipei, Taiwan. 5Department of Internal Medicine, Kang-Ning General Hospital, Taipei, Taiwan. 6Department of Oncology, National Taiwan University
