CLINICAL OUTCOMES STUDIES

Epidemiology and Disease Burden of Ulcerative Colitis in Taiwan: A Nationwide Population-Based Study

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A B S T R A C T

Objectives: A rising trend of incidence and prevalence of ulcerative colitis (UC) had been noticed in Asian countries. We conducted this study to investigate the epidemiology and medical burden of UC in Taiwan. **Methods:** In this 10-year retrospective database study, we identified cases of patients with UC during 1998 to 2008 from the Taiwan National Health Insurance Research Database. Patients who had a catastrophic illness certificate were included in epidemiology and medical burden calculation. **Results:** There were 1522 cases identified in our study period. The incidence increased twofold from 0.37 per 100,000 in 1998 to 0.78 per 100,000 in 2008. The incidence and prevalence had an increasing trend in our population. The cases onset age was 45.0 years on average. In our survey, most of the top 20 coexisting diseases were gastrointestinally relevant diseases, anemia (9.99%), and hypertension (7.69%). There were more than 70% patients using

mesalamine, and the medical expenditure on mesalamine occupied the highest position in patients with UC. The average medical expenditure of patients with UC had a decreasing trend after 2001. **Conclusions:** This study had the largest sample and the longest study period for the epidemiology and medical burden estimation of UC in Taiwan. The incidence rates and medicine use of patients with UC had a definite rising trend across the years in Taiwan. Patients with anemia or choric diseases were observed in our population. More surveillance of UC-related diseases and health care costs need to be conducted in the future.
Keywords: disease burden, epidemiology, medical expenditures, ulcerative colitis.

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Introduction

Ulcerative colitis (UC) is a rare idiopathic inflammatory disease of the colon and the rectum that makes the estimation of incidence and prevalence rates difficult in Asians. A number of studies have shown that the prevalence and incidence of UC are increasing in Asians, especially in East Asian countries, including Hong Kong, Korea, and Japan [1–5], although the exact etiology and mechanisms for this trend are not clear [6–8]. Multiple factors may be involved, including lifestyle [9,10], environment factors [11], genetics [12–17], gender, and the immunological system [18,19]. Upon reviewing previous research, we found that only one study had reported the prevalence rates of UC by using data from a tertiary referral center in Taiwan [20]. As a result, the current report on UC epidemiologic outcome in Taiwan was limited [21–24].

Furthermore, a number of studies noted that the clinical features and natural history of Asian patients with UC may be different from those of Western patients, including extent of

disease, relapse rate, incidence of colorectal cancer (CRC), and mortality [7,25,26]. The symptoms and signs of UC include distal colitis, extensive colitis, diarrhea mixed with blood and mucus, constipation, weight loss, crampy pain, abdominal pain, low-grade fever, and anemia [27,28]. Moreover, a recent study showed that anemia is very common in inflammatory bowel disease and the prevalence in patients with inflammatory bowel disease ranged from 9% to 74% [29]. UC can also be associated with local and extraintestinal complications. There are some severe local complications of UC, including fulminant colitis, intestinal perforation and stricture, massive hemorrhage, and the development of CRC [2,30]. A numbers of studies have also indicated that UC may be associated with a number of extraintestinal complication, including iritis, arthritis, panniculitis, and deep venous thrombosis [31–33]. Therefore, appropriate diagnosis and treatment are important in UC. In most cases of UC, the treatment goals are prolonging remission, decreasing prognosis of disease severity, and increasing quality of life as previous reports have shown that patients with UC are associated with decreasing

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quality of life and high morbidity [34–36]. The published literature on the economic burden of patients with UC is currently limited. A previous report in the United States described the mean annual costs of $5066 for UC in 10,364 patients from year 2003 to 2004, with 73% of the costs being attributable to hospitalization and outpatient care and 27% to pharmaceutical claims [37]. Despite the study demonstrating the substantial economic burden of UC, the time trend of medical costs in managing patients with UC could not be observed in this study.

The aims of this study were 1) to investigative the incidence, prevalence, and coexisting diseases of UC in Taiwan, using a 10-year nationwide population-based database, and 2) to describe the distribution of drug utilization and medical expenditures of treatment of UC in Taiwan between inpatients and outpatients.

Methods

This is a population-based retrospective study for which data on patients with UC were extracted from the list of catastrophic illness (CI) certificates published during 1997 to 2008 by the Department of Health, Executive Yuan of Taiwan. UC cases were identified by using the *International Classification of Diseases, Ninth Revision* code 556. A UC diagnosis on a CI certificate needs to be strictly evaluated by at least two gastroenterologists according to the laboratory data and images from applied hospital (sigmoidoscopy and biopsies of the mucosa is the standard criterion used by the Taiwan government), and all documents are rechecked by a third physician in the Department of Health before a CI certificate is issued. Patients with CI certificates are eligible for exemption from insurance premiums and co-payments in National Health Insurance. The approval of the CI certificate needs strict evaluation by the Department of Health, and it may lead to underestimation of the actual number of cases. Although the actual number of cases may be underestimated, UC diagnosis and coding are accurate. We extracted the medical records of UC cases from the National Health Insurance Research Database (NHIRD). The National Health Research Institute provided the database, and the database includes information on outpatient, ambulatory, hospital inpatient care, dental services, and prescription drugs. Because this study was based in part on data from the NHIRD, which in this study consisted of de-identified secondary data released to the public for research purposes, this study was exempt from full review by the ethical committee, and informed consent did not need to be obtained from study subjects. In this study, subjects with UC CI certificates were included for the calculation of incidence and prevalence rates (1998–2008).

The following data were included for analysis: gender, onset of diagnosis age, and top 20 coexisting diseases after UC diagnosis. The new case numbers in each year were recorded to calculate the annual incidence rate from 1998 to 2008. The incidence rate for the CI certificates was calculated to track their first UC medical claim date. The prevalence rate for the CI certificates was also calculated to track their first yearly UC medical claim date.

For assessing time trend of medical costs in the treatment of patients with UC, we focused on drug utilization and medical expenditures in each year, and categorized medication into the following categories: 5-aminosalicylic acid derivate (including mesalamine and sulfasalazine, which were common use in Taiwan), corticosteroids, and immunosuppressant agents (azathioprine, cyclosporine, 6-mercatopurine, and Tacrolimus). Otherwise, each medical claim was classified as inpatient or outpatient. To compare the average medical expenditure in the treatment of patients with UC with that of the general Taiwan population in each year, we quote the average medical

expenditure per UC patient fold to average expenditure on medicine per capita from National Health Expenditure, published by the Department of Health, Executive Yuan of Taiwan (http://www.doh.gov.tw/EN2006/DM/DM2.aspx?now_fod_list_no=12117&class_no=390&level_no=2).

Statistics

The crude incidence rate was calculated by using the total number of residents in each year from 1998 to 2008 as the denominator and the total number of new cases of patients with UC in each year as the numerator. The crude prevalence rate was calculated by using the total number of residents in each year as the denominator and the total number of cases of patients with UC in each year as the numerator. The incidence and prevalence rates were expressed as the number of cases per 100,000. We adjusted incidence and prevalence rates by age by using the standard population of the year 2000. Medical expenditure was calculated in each category (mesalamine, sulfasalazine, corticosteroids, and immunosuppressant agents) by outpatient, inpatient, and total medical claims each year. Average medical expenditure per patient with UC in each year from 1998 to 2008 was calculated by using all medical services expenditure in that year as the denominator and the total number of medical users in that year as the numerator. We also compared the average medical expenditure per UC patient fold to the average medical expenditure per capita in Taiwan from 1998 to 2008. All statistical analyses were carried out by using SAS 9.2.

Results

Among 10-year follow-up in Taiwan population, 1522 cases (945 males and 577 females) were identified. During 1998 to 2008, there were 1518 new cases. The 10-year average crude incidence rate was 0.66 patients with UC per 100,000 (Table 1). The crude incidence rate in 1998 was 0.37 per 100,000 and in 2008 was 0.78 per 100,000 in our population. The age-adjusted incidence rate in 1998 and 2008 was 0.38 and 0.72 per 100,000, respectively. Despite the fact that the incidence rate over the past decade had risen twofold from 1998 to 2008 in Taiwan, there was quite a lot of variation in the rate from year to year. The crude incidence rate increased by 84% from 1998 to 2003 and slightly increased by 10% from 2003 to 2008. The peak incidence rate during 1998 to 2008 in this population was 0.81 per 100,000 in 2007. From 1998 to 2008, the male to female ratio of new cases ranged from 1.25 to 2.18. The crude prevalence rate in 1998 and 2008 was 0.39 per 100,000 and 4.62 per 100,000, respectively. Over the 10-year period, the UC incidence and prevalence rates had an increasing trend in our populations.

The onset age (mean ± SD) of new UC cases was 45.08 ± 15.04 years on average during 1998 to 2008. The onset age was stable with each year, with the lowest ranging from 42.76 ± 15.09 years in 2005 to the highest ranging from 46.97 ± 15.77 years in 2000. The onset age for females (46.21 ± 13.1 years) was slightly more than that for males (44.42 ± 15.08 years) on average during 1998 to 2008 (Table 2). On the onset age distribution of UC, the disease onset of UC was found to range from children to elderly and predominant at the 30 to 49 years age group for both males and females. The peak age-specific incidence and prevalence of UC was in the 50 to 59 years age group (Table 3). The age of patients with UC showed a stable trend during 1998 to 2008 (Table 4). However, the age gap between the most young and the most old had sustained, rising over the past decade for both males and females.