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ORIGINAL ARTICLE

Temporal Trends of Inflammatory Bowel Diseases in Taiwan from 2016 to 2020: A Population-Based Study

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Abstract

Background There are scanty population-based studies investigating the incidence and prevalence rates of inflammatory bowel disease (IBD) in Taiwan.

Aims This study aimed to estimate the nationwide prevalence and incidence of IBD and identify its noticeable trends in Taiwan between 2016 and 2020.

Methods A retrospective study by analyzing the data from the National Health Insurance Research Database of Taiwan.

Results A total of 2595 patients with catastrophic IBD illness were registered from 2016 to 2020 in Taiwan (CD, 880; UC, 1715). The male-to-female ratio in the study sample was 1.83:1 for CD and 1.69:1 for UC. The median age of those registered with CD and UC was 37 and 47 years, respectively. The incidence rate of CD was 0.65 per 100,000 persons in 2016 and it was increased to 0.81 per 100,000 persons in 2020. The incidence rate of UC was 1.16 per 100,000 persons in 2016 and it was increased to 1.53 in 2020. Overall, the incidence of IBD was increase from 1.81 per 100,000 persons to 2.34 per 100,000 persons between 2016 and 2020. Overall, the prevalence rates of IBD was increase from 14.95 per 100,000 persons to 20.02 per 100,000 persons between 2016 and 2020.

Conclusion The epidemiological stages of IBD in Taiwan was considered in the acceleration in incidence stage, during which incidence rises and prevalence is relatively low. Understanding these geographical differences is important for the rising global burden of IBD.

Keywords Crohn's disease · Ulcerative colitis · Epidemiology

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Introduction

Inflammatory bowel disease (IBD) is characterized by chronic and repetitive inflammation of the gastrointestinal tract [1, 2].Crohn's disease (CD) and ulcerative colitis (UC) are the two major forms.

IBD is thought to be caused by a complex interactions between diet, environmental factors, genetic predisposition, immune dysregulation, and gut dysbiosis, but comprehensive understanding of the underlying pathophysiological mechanisms is still lacking [1, 2]. Over time, many patients with IBD experience disease progression from primarily inflammation to bowel damage such as intestinal obstruction, strictures, fistula, and abscess.

The characteristics of IBD are different between Asia and Western patients with regard to epidemiology, nature course, phenotype, and genetic susceptibility [3]. Comparison of population-based data in East and West reveals that the incidence of IBD has risen rapidly in East while plateauing in West [4–6]. The prevalence and incidence of IBD is increasing in Asia, including Taiwan [5, 7–11]. Today, IBD is recognized as a global disease. The growing number of IBD patients is likely to substantial increase in the burden of health care system.

However, the latest data about epidemiological trend in IBD in Taiwan was 2015. In the current study, we would report the epidemiological trend of IBD in Taiwan from 2016 to 2020.

Materials and Methods

A retrospective study was conducted to analyze data recorded from January 2016 to December 2020 in the registered database compiled by the National Health Insurance and provided by the Ministry of Health and Welfare, Taiwan. The Taiwan National Health Insurance (NHI) is a centralized and compulsory health insurance system covering > 99% of Taiwan's citizens.

We identified the patients who received catastrophic illness certificates for IBD by their associated International Classification of Diseases, 10th revision (ICD-10) codes. The following ICD-10, Clinical Modification (ICD-10-CM) codes were used to identify patient records in this study: K50.x for CD and K51.x for UC. Catastrophic illness certification is initiated by a physician. Physicians have to submit patients' histopathological and endoscopic (or radiologic) examination data to the Taiwan National Health Insurance (NHI), and IBD patients would be registered in Registry for Catastrophic Illness (RCI) after approval by the NHI's Expert Committee.

The prevalence rate of IBD was computed by year. Prevalence rate was calculated as the number of cases between 2016 and 2020 divided by the total number of person-years at risk. Incidence rate was calculated as the number of new cases between 2016 and 2020 divided by the total number of person-years at risk.

The present study was approved by the Ethics Review Board of the Chang Gung Memorial Hospital (IRB No. 202201150B1) and informed consent was waived.

Results

Incidence

Between 2016 and 2020, there were 880 incident cases of CD and 1715 incident cases of UC respectively, corresponding to an overall incidence rate ratio of UC to CD was 1.95 (Table 1).

The incidence rate of CD was 0.65 per 100,000 persons in 2016 and it was increased to 0.81 per 100,000 persons in 2020. The incidence rate of UC was 1.16 per 100,000 persons in 2016 and it was increased to 1.53 in 2020. Overall, the incidence of IBD was increase from 1.81 per 100,000 persons to 2.34 per 100,000 persons between 2016 and 2020 (Table 2; Fig. 1).

Table 1 Clinical features of patients with newly registered IBD in 2016 to 2020

	CD		UC		
	N	%	*N*	%	*p*-value
No. of cases	880		1715		
Age (yr)					
Mean	40.15		46.6		< 0.0001
Median	37		47		
Age groups					< 0.0001
< 20	97	11.02	67	3.91	
20–39	388	44.09	517	30.15	
40–59	228	25.91	739	43.09	
60–79	159	18.07	365	21.28	
> = 80	8	0.91	27	1.57	
Male/female ratio	1.83		1.69		0.3526
2016	2.45		1.44		0.0134
2017	1.69		1.74		0.8907
2018	1.45		1.88		0.1957
2019	1.59		1.84		0.4269
2020	2.25		1.53		0.0473

Prevalence

The prevalence rates of CD increased from 3.91 in 2016 to 6.06 per 100,000 persons in 2020. The prevalence rates of UC increased from 11.04 in 2016 to 13.96 per 100,000 persons in 2020. Overall, the prevalence rates of IBD was increase from 14.95 per 100,000 persons to 20.02 per 100,000 persons between 2016 and 2020 (Table 3; Fig. 2).

Age

During 2016 to 2020, the median age of those registered with CD and UC was 37 and 47 years, respectively (Table 1).

Table 2 Incidence rate of IBD

Year	Population		IBD		CD		UC
			No	IR	IR	No	IR
2016	23,515,945		426	1.81	0.65	273	1.16
2017	23,555,522		508	2.16	0.68	347	1.47
2018	23,580,080		506	2.15	0.7	342	1.45
2019	23,596,027		605	2.56	0.9	393	1.67
2020	23,582,179		552	2.34	0.81	361	1.53
p-value for trend test		0.0125			0.0144		0.0177

IR Incidence rate

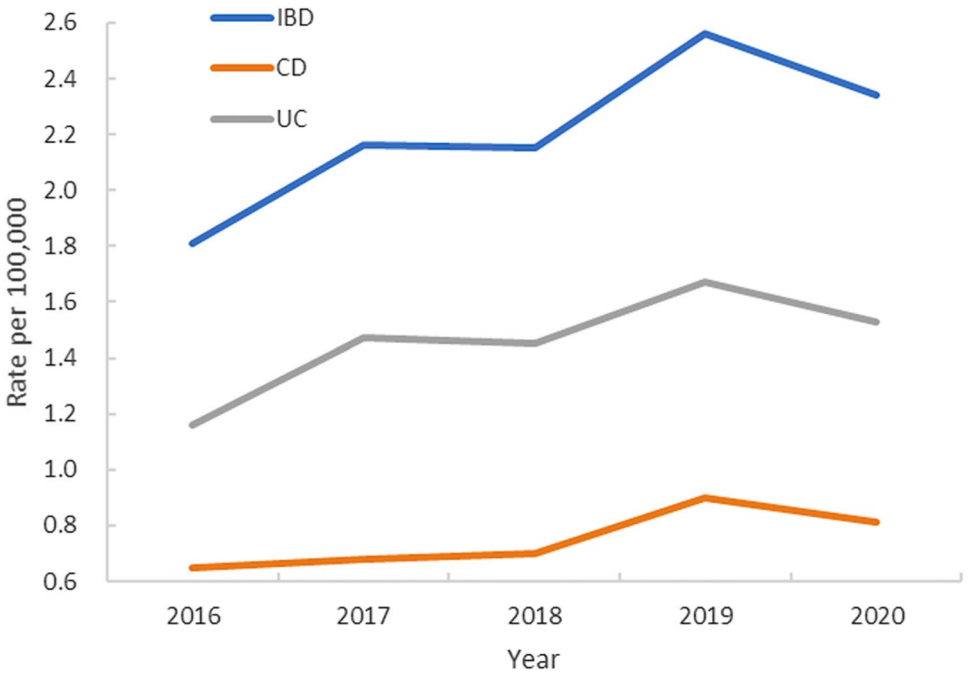

Fig. 1 Incidence rate of IBD between 2016 and 2020

Table 3 Prevalence rate of IBD

Year	Population	IBD		CD		UC	
		No	Prevalence rate	No	Prevalence rate	No	Prevalence rate
2016	23,515,945	3515	14.95	919	3.91	2596	11.04
2017	23,555,522	3890	16.51	1053	4.47	2837	12.04
2018	23,580,080	4209	17.85	1181	5.01	3028	12.84
2019	23,596,027	4544	19.26	1331	5.64	3213	13.62
2020	23,582,179	4722	20.02	1430	6.06	3292	13.96
p-value for trend test		< 0.0001		< 0.0001		< 0.0001	

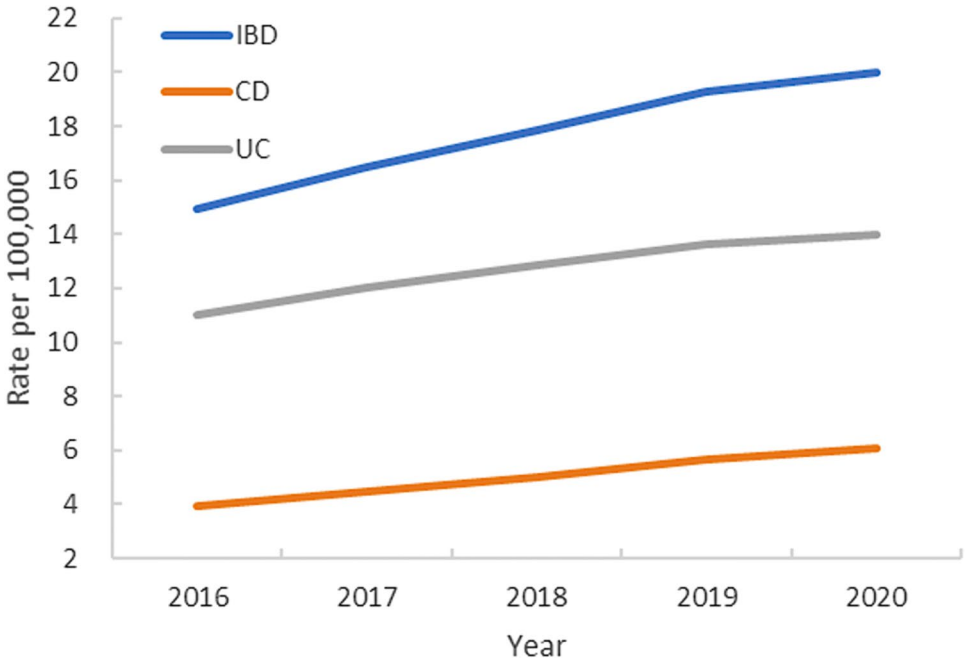

Fig. 2 Prevalence rates of IBD between 2016 and 2020

For CD, the incidence case peaked at age 25–29 and dropped thereafter with a second smaller peak at age 55–69. For UC, the incidence case peaked at age 40–44 and dropped thereafter with a second smaller peak at age 50–59 (Fig. 3).

For CD, 11.02% of patients was registered at age under 20, 44.09% at age 20–39, 25.91% at age 40–59, 18.07% at age 60–79 and 0.91% at age over 80. For UC, 3.91% of patients was registered at age under 20, 30.15% at age 20–39, 43.09% at age 40–59, 21.28% at age 60–79 and 1.57% at age over 80 (Table 1).

Male-to-Female Ratio

The male-to-female ratio in the study sample was 1.83:1 for CD and 1.69:1 for UC. The male-to-female ratio in 2016 was 2.45:1 for CD and 1.44:1 for UC. The male-to-female ratio in 2017 was 1.69:1 for CD and 1.74:1 for UC. The male-to-female ratio in 2018 was 1.45:1 for CD and 1.88:1 for UC. The male-to-female ratio in 2019 was 1.59:1 for CD and 1.84:1 for UC. The male-to-female ratio in 2020 was 2.25:1 for CD and 1.53:1 for UC. A

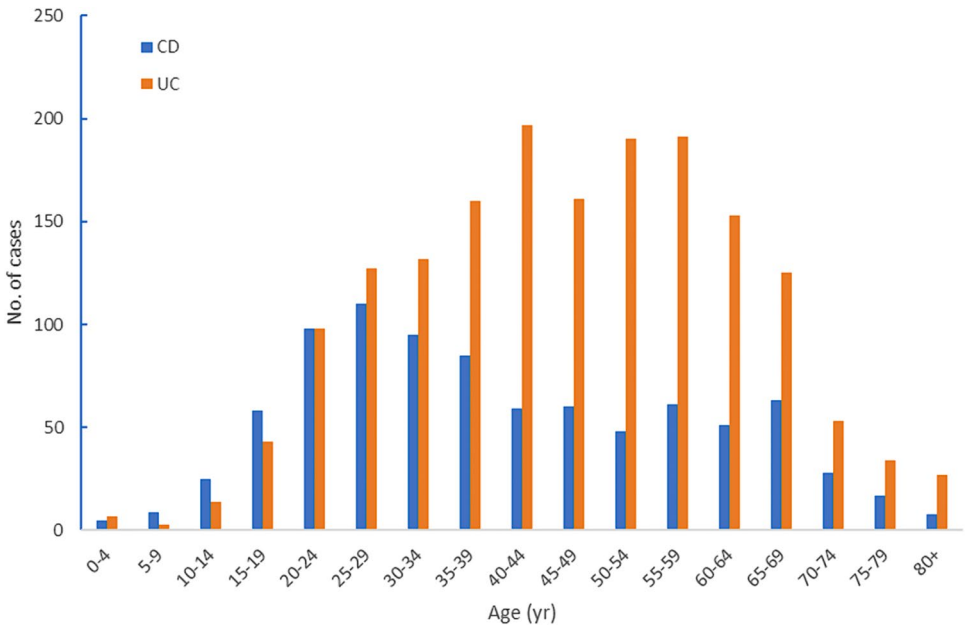

Fig. 3 Age-specific incidence rate CD and UC between 2016 and 2020

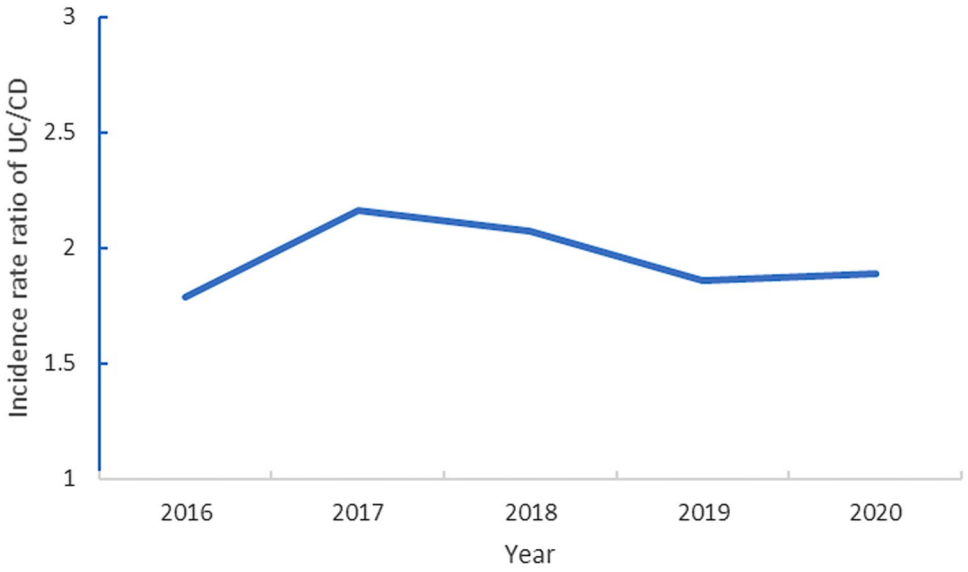

Fig. 4 Incidence ratio of UC to CD between 2016 and 2020

Table 4 CD with catastrophic illness card on biologics

Years	CD with catastrophic illness card on biologics
2016	231
2017	320
2018	430
2019	526
2020	574

Table 5 UC with catastrophic illness card on biologics

Years	UC with catastrophic illness card on biologics
2016	73
2017	234
2018	354
2019	481
2020	594

male-predominant pattern for IBD was observed in Taiwan (Table 1).

UC-to-CD Incidence Ratio from 2016 to 2020 in Taiwan Was Steady

We compared the incidence ratio of UC to CD from 2016 to 2020 and no significant difference was observed during this period. UC is twice as common as CD (Fig. 4).

Burden of Biologic Use in IBD Patients Is Increasing

Among CD, the number of patients who received biologics treatment was increased from 231 in 2016 to 574 in 2020 (Table 4). Among UC, the number of patients who received biologics treatment was increased from 73 in 2016 to 594 in 2020 (Table 5).

Among CD, the most prescribed biologics were Adalimumab (52.27%) and Vedolizumab (28.96%) in 2020. Among UC, the most prescribed biologics were Vedolizumab (43.89%) and Adalimumab (35.89%) in 2020.

Discussion

IBD is believed to be related to the activation of the intestinal mucosal immune system in response to dysbiosis of the gastrointestinal tract in genetically susceptible individuals [1]. This disease most commonly occurs in young and middle-aged adults and still has a certain disability rate even with recent advances in treatment.

Taiwan CD and UC incidence and prevalence rates are lower than in the West. However, in recent decades, Taiwan's CD and UC disease incidence and prevalence rates have been increased rapidly [10, 11]. The crude incidence of CD increased from 0.17 per 100,000 persons in 2001 to 0.47 per 100,000 persons in 2015, whereas that of UC increased from 0.54 per 100,000 persons in 2001 to 0.95 per 100,000 persons in 2015. The prevalence of CD increased from 0.6 per 100,000 persons in 2001 to 3.9 per 100,000 persons in 2015, whereas that of UC increased from 2.1 per 100,000 persons in 2001 to 12.8 per 100,000 persons in 2015 [11]. In our current study, the incidence rate of CD was 0.65 per 100,000 persons in 2016 and it was increased to 0.81 per 100,000 persons in 2020. The

incidence rate of UC was 1.16 per 100,000 persons in 2016 and it was increased to 1.53 in 2020. The prevalence of CD increased from 3.91 per 100,000 persons in 2016 to 6.06 per 100,000 persons in 2020, whereas that of UC increased from 11.04 per 100,000 persons in 2016 to 13.96 per 100,000 persons in 2020. In Taiwan, the incidence and prevalence of IBD were increased steadily from 2001 to 2020.

In Western country, the average age of onset in adult incident cases was a median 31–34 years [12–16]. In both CD and UC, incidence peaked in the age interval 20–30 years; however, a second peak between the ages of 60 and 79 years was reported in UC. A similar age distribution has been reported in Asia, where the median age of diagnosis in patients with CD and UC was 34 and 42 years, respectively [17, 18]. In contrast to findings in West, a bimodal distribution was only seen in CD and not in UC in most Asian populations, where the incidence rate of CD peaked in the age ranges of 20–24 years and 40–44 years [19]. In our current study, the bimodal distribution was seen in CD but not obvious in UC.

The proportion of IBD cases diagnosed in older adults in each population has practical implications and will vary not only with changes in age-specific incidence rates but also with changes in the age structure of the population. In the Danish National cohort [20], 21% of UC cases and 17% of CD cases were diagnosed above 60 years of age. In our current study, 22.85% of UC cases and 18.98% of CD cases were diagnosed above 60 years of age. In the future, the health care system will face increasing IBD patent number while simultaneously managing an aging population that will have a mixture of complications of longstanding IBD and age-related comorbidities [6].

The overall incidence of UC in Western country is independent of gender. In CD, less consistent findings have been reported, with some cohorts suggesting a female predominance in the incidence of CD and others failing to find any gender difference [12–16]. In a pooled analysis of studies in the West, females predominated among CD patients from adolescence to middle-age, while a higher risk of UC was found among males aged 45 years and older [21]. These findings contrast with those from Asia, where male gender was associated with a higher risk of both CD and UC. In mainland China, the risk ratio of CD and UC in males versus females is 1.15:1 and 2.4:1, respectively [22]. An increased risk of UC among males was also found in Korea [23]. A pooled analysis confirmed the association between male Asians and an increased risk of both CD and UC among those in the range of 10–50 years old [24]. In our current study, male-to-female ratio of CD and UC is 1.83:1 and 1.69:1, respectively. The male-to-female ratio in Taiwan from 2001 to 2015 was 2.19 for CD and 1.62 for UC. The trend of male predominance continued between 2016 and 2020 [10] The precise mechanism underlying the differences in the sex distributions between Asian and Western IBD patients is still unknown.

As we known, the UC/CD ratio in East Asian countries has reduced because of the accelerating incidence of CD. According to previous study [10], the UC/CD ratio decreased from 4.32 in 2001–2005 to 4.17 in 2006–2010 to 2.03 in 2011–2015 in Taiwan and decreased to 1.95 in 2016–2020 in present data. In Korea, the UC/CD ratio was 5.03 in 1986–1990, and it reduced to 2.57 in 2006–2010, to 2.39 in 2011–2015[25]. The decreasing slope of UC/CD ratio has became flattened. We compared the incidence ratio of UC to CD from 2016 to 2020 and no significant difference was observed during this period. Currently, UC is twice as common as CD in Taiwan.

The definite reason for decrease of UC/CD ratio after 2000 is not clear, but may reflect the improvement of diagnosis for CD. Capsule endoscopy, which was introduced in 2000, and double-balloon enteroscopy, which was introduced in 2001, had made it possible to explore the entire small intestine. The diagnosis of CD is more complex and improvement of diagnostic methods make physician more aware of CD.

IBD is a global disease and its evolution can be divided into four epidemiological stages: emergence, acceleration in incidence, compounding prevalence and prevalence equilibrium. In the stage of acceleration in incidence, there is a dramatic increase in the number of incident cases but overall prevalence remains low [6].

Incidence of IBD is increasing in emerging populations in Asia suggesting that changing environmental factors play an important part. Various environmental risk factors have been implicated in the pathogenesis of IBD, including diet and lifestyle which may perturbations of the gut microbiota [26, 27] Certain nutrients and food additives can impact on the gut microbiome and their interactions with the host may play a role in the pathogenesis of IBD [28] Consumption of ultra-processed food had increased over the last decade in industrialized countries, and epidemiological studies had found associations between ultra-processed food consumption and chronic diseases [29]. Understanding the underlying determinants of development of IBD is very important. By modification of the underlying determinants, particularly around diet and other modifiable behaviors, may prevent disease development in subject with genetic susceptibility.

The epidemiological stage of IBD in Taiwan was considered in the acceleration in incidence stage. High cost of caring for patients with IBD will have a considerable financial effect on the health care system.

Limitations

By analyzing data from the National Health Insurance registration system, we found a steady increase in the incidence and prevalence of IBD in Taiwan from 2016 to 2020. The strength of this study was the availability of a nationwide cohort that provides access to healthcare and registration for near all its citizens. But the incidence and prevalence level may be underestimated due to relatively strict criteria by using the number of patients who completed a catastrophic disease registry, which required clinical records, endoscopic images, and pathological findings. Additionally, there was no information about the disease phenotype.

Conclusion

The epidemiological stages of IBD in Taiwan was considered in the acceleration in incidence stage, during which incidence rises and prevalence is relatively low. Understanding these geographical differences is important for the rising global burden of IBD.

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Author's contribution All authors have made substantial contributions as following: Developed the study concept and design: CT Chiu, CJ Chang, CJ Kuo, PH Le. Provided the critical revision of the manuscript for important intellectual content: WR Lin, ML Chang, MY Su. Wrote the main manuscript text: CJ Kuo, CY Lin. Prepared figures : YW Kuo, CM Hsu, MW Lai. All authors approved the final version of the manuscript. The authors thank Yu-Yang Lin and Tse-Chih Chou for their assistance with statistical analysis

Data availability No datasets were generated or analysed during the current study.

Declarations

Conflict of interest The authors declare no competing interests.

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