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Clinical features and treatment of inflammatory bowel disease in a low-incidence area

A hospital-based retrospective cohort study in Taiwan

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Abstract

Inflammatory bowel disease (IBD) has emerged in the Asia–Pacific area over the past 2 decades. There is a paucity of clinical data regarding real-world experience of patients with IBD from low endemic area such as Taiwan. Therefore, the present study aimed to review the clinical features of patients with IBD form a tertiary center from Taiwan.

A total of 163 patients with IBD were identified from the electronic clinical database of Changhua Christian Hospital. Demographic data of the patients and clinical features of the disease pattern were retrospectively reviewed.

There was a higher proportion (62.6%) of patients diagnosed with ulcerative colitis (UC). Patients with Crohn disease (CD) and UC had male predominance. The median age of diagnosis was younger in patients with CD than in patients with UC (CD vs UC: 31 vs 40 years, $P = .0423$). The disease distribution of UC was as follows: E1 (15.7%), E2 (47.1%), and E3 (37.3%). The disease distribution of CD was as follows: L1 (36.1%), L2 (14.8%), L3 (42.6%), and L4 (6.5%). The majority of patients with CD had a complicated presentation with B2 (32.8%) and B3 (32.8%). Patients with CD had a higher bowel resection rate than patients with UC. Patients with CD were more likely to be treated with immunomodulator and biologics and those with UC were more likely to be treated with 5-aminosalicylic acid (5-ASA). A trend of decreased bowel resection for patients with IBD and less severe phenotype of patients with CD were observed after 2015.

UC with male predominance was the predominant type of IBD in the study. Patients with CD are likely to have a complicated disease course, requiring a higher demand of biologic therapy than patients with UC.

Abbreviations: 5-ASA = 5-aminosalicylic acid, CD = Crohn disease, IBD = inflammatory bowel disease, TSIBD = Taiwan Society of Inflammatory Bowel Disease, UC = ulcerative colitis.

Keywords: Crohn disease, inflammatory bowel disease, ulcerative colitis

1. Introduction

Inflammatory bowel disease (IBD) including Crohn disease (CD) and ulcerative colitis (UC) is common in the Western world but relatively uncommon in Asian countries such as Taiwan.[1–4] Both the incidence and prevalence of IBD increased in those low incidence and prevalence countries in the past 2 decades.[1,5,6] The reason for globalization of this Western disease has not been established but is most likely related to environment factors, including improved hygiene, civilization, and the introduction of Western lifestyle diet.

Not only the incidence but also the disease phenotype is different between the Eastern and Western countries.[7] Unlike the data from the Western studies, CD and UC are more likely to be female predominant[22]; data from the Eastern countries showed a male-predominant pattern, especially significant for CD.[5] Although the exact reason is unknown, different genetic background and a male-dominant culture in Asia may lead to sex-specific differences in exposure to breast feeding, antibiotic use in childhood, and subsequent development of IBD.

Since the first case of IBD described in 1969 as ulcerative colitis from the National Taiwan University Hospital,[8] the recent nationwide-based data confirmed the trend of epidemiologic changes of patients with IBD in Taiwan.[2] However, such population-based database study relies on the diagnostic codes used in the National Health Insurance Research Database, there

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Table 1

Clinical characteristics of patients with IBD.

Characteristics	CD (N = 61, 37.4%)	UC (N = 102, 62.6%)	*P*-value
Male sex, n (%)	38 (62.3%)	61 (59.8%)	.7534
Current age (median, IQR)	38.06 (30.18–53.94)	46.67 (36.81–54.61)	.0441
Age at diagnosis (median, IQR)	31 (26–48)	40 (30–50)	.0423
Cigarette smoking (non-smoker/ex-smoker/current smoker)	54/4/3	96/3/3	.4280
Follow-up, months, median, 95% of CI	68 (52.38–76.62)	66 (47–82.5)	.6545
IBD related cancer, n (%)	0 (0%)	4 (3.9%)	.1185
Positivity of HBsAg, n (%)	5 (8.2%)	2 (2%)	.0602
Positivity of anti-HCV Ab, n (%)	1 (1.6%)	3 (2.9%)	.6043
Appendectomy, n (%)	5 (8.2%)	1 (1%)	.0182
Bowel Resection, n (%)	25 (51%)	2 (2%)	<.0001
Peri-anal Disease, n (%)	3 (4.9%)	0 (0%)	.0242
CIC Card, n (%)	57 (93.4%)	86 (85.1%)	.1130

CD = Crohn disease, CI = confidence interval, CIC = critical illness card, HCV = Chronic hepatitis C, IBD = inflammatory bowel disease, IQR = interquartile range, UC = ulcerative colitis.

may be a significant bias for the identification of actual patients with IBD and may not reflect the real-world lifelong care of these patients.[1,9] Therefore, high-quality territory-wide registry data[10] or hospital-based real-world data are required for further understanding the disease features, treatment patterns, and quality of care of patients with IBD in Taiwan.[4,8,11] Therefore, we conducted the present study aimed to review the clinical features of patients with IBD from tertiary referral center in Taiwan.

2. Methods

The medical records of patients diagnosed with IBD in the Changhua Christian Hospital, Taiwan, were retrospectively reviewed. The hospital was the only medical center in Changhua County, with an area of 1074 km^2 and a population of 1.2 million located in central Taiwan. Patients enrolled in the present study met the following inclusion criteria: documented diagnosis of IBD for >6 months with a regular follow-up for at least 3 months in the hospital. We collected clinical data including sex, age at diagnosis, smoking habits, family history, surgical history, disease phenotype, treatment status, and disease behavior according to the Montreal classification, as well as presence of extraintestinal manifestations, colorectal cancer, and hepatitis.

From January 2019, patients diagnosed with IBD, including UC or CD, received care in the hospital from a dedicated IBD nurse (TSH), who helped in reviewing patients' clinical history and symptom, educating patients about the disease, and assessing the effects and/or side effects of treatment during each outpatient clinic visit.[12] The data in this analysis were reviewed by TSH and HHY. This study was approved by the institutional review board of Changhua Christian Hospital (approval number: CCH IRB 190814).

3. Statistical analysis

Extracted data were organized using Microsoft Excel software and analyzed using MedCalc Statistical Software version 19.16 (MedCalc Software bvba, Ostend, Belgium; https://www.medcalc.org; 2020). Continuous data are expressed as mean with standard deviation or median with interquartile range for normally or nonnormally distributed data, respectively. Categorical variables are presented as numbers with percentages. Means with normally distributed variables were compared by independent-samples Student *t* test. The Mann–Whitney *U* and Kruskal–Wallis tests were used, respectively, to compare means of 2 and ≥3 groups of nonnormally distributed variables. The frequencies of categorical variables were compared using the Pearson chi-squared or Fisher exact test, when appropriate. All *P*-values of <.05 were considered significant.

4. Results

4.1. Clinical features of patients with IBD

A total of 163 patients with IBD, with a majority diagnosis of UC (62.6%), who met the inclusion criteria were included. The clinical characteristics of all patients are presented in Tables 1 and 2. Patients with CD were diagnosed at a younger age than those with UC (31 vs 40 years, $P = .0423$). Patients with CD and UC were men predominant and nonsmoker. The overall hepatitis B and hepatitis C rates were similar between patients with CD and UC. Patients with CD had a higher rate of appendectomy and bowel resection rate than patients with UC. Four patients (2.5%)

Table 2

Montreal classification of IBD patients.

	UC (N = 102)	CD (N = 61)
UC disease extent		
E1: Proctitis, n (%)	16 (15.7%)	
E2: Left side colitis, n (%)	48 (47.1%)	
E3: Extensive colitis, n (%)	38 (37.3%)	
CD disease extent		
L1: Ileum, n (%)		22 (36.1%)
L2: Colon, n (%)		9 (14.8%)
L3: Ileo-colon, n (%)		26 (42.6%)
L4: UGI tract, n (%)		4 (6.5%)
CD disease behavior		
B1: non-stricturing, n (%)		21 (34.4%)
B2: stricturing, n (%)		20 (32.8%)
B3: penetrating, n (%)		20 (32.8%)
P: perianal involvement, n (%)		3 (4.9%)
Extraintestinal manifestation	Arthritis (n = 1), rheumatoid arthritis (n = 1), primary sclerosing cholangitis (n = 1)	Rheumatoid arthritis (n = 1), psoriasis (n = 1), arthritis (n = 1)

CD = Crohn disease, IBD = inflammatory bowel disease, UC = ulcerative colitis.

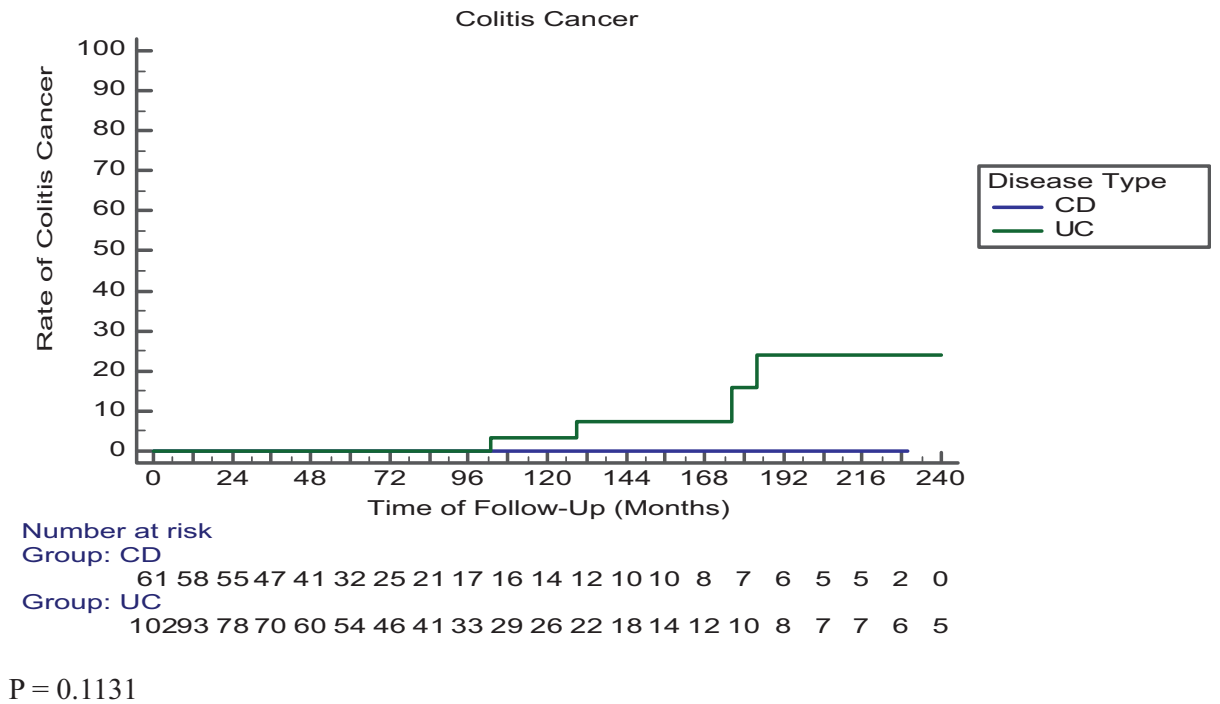

Figure 1. Cumulative rate of colitis cancer in IBD patients. IBD = inflammatory bowel disease.

developed IBD-related cancer during the follow-up period (Fig. 1). There was no family history of IBD.

The Montreal classifications of patients with UC were proctitis (E1, 15.7%), left-sided colitis (E2, 47.1%), and extensive colitis (E3, 37.3%). The Montreal classifications of the anatomical involvement of patients with CD was ileum (L1, 36.1%), colon (L2, 14.8%), ileocolon (L3, 42.6%), and upper gastrointestinal tract (L4, 6.5%). A similar proportion of the Montreal classifications of the behavior of patients with CD was observed. Perianal disease was present in 4.9% of the patients with CD. A higher but nonsignificant proportion of patients with CD (93.4%) were certified for critical illness card than that of patients with UC (85.1%) in this study.

4.2. Past and current treatment of patients with IBD

The medical treatment of all patients is presented in Table 3 and divided into 2 parts. Past treatment included all medications from the time of diagnosis to the current follow-up period and current treatment included all medications used in the last 3 months. Patients with CD and UC received a similar proportion of steroids (CD vs UC: 66.7% vs 55.9%, $P = .1776$) during the treatment course. Patients with UC received a higher rate of 5-ASA but a lower rate of immunomodulator or biologic therapy than patients with CD. Adalimumab was the most commonly prescribed biologic, followed by vedolizumab and infliximab.

The proportion of steroid usage as current prescription was lower than their use as past prescription. 5-ASA medication especially perianal administration was used more frequently in patients with UC than in patients with CD. The requirement of biologic therapy was significantly higher in patients with CD than in patients with UC (62.3% vs 18.6%, $P < .0001$).

4.3. Comparison of clinical features of patients with IBD diagnosed before and after 2015

Based on the increase in awareness of IBD in Taiwan after 2015,[1] we divided our patients into 2 time periods (before and after 2015[1]) for further analysis (Table 4). The ratio of UC-to-CD, median age at diagnosis, CD disease location, UC disease extent, and current and past medical treatment were comparable between the 2 time periods. However, there is a trend of decreased bowel resection rate in patients with IBD diagnosed after 2015 (before and after 2015 21.1% vs 11%, $P = .0839$).

Table 3

Medical treatment of patients with IBD.

Past treatment	CD (N = 61)	UC (N = 102)	*P*-value
5-ASA, n (%)	54 (88.5%)	102 (100%)	.0005
Steroid, n (%)	40 (66.7%)	57 (55.9%)	.1776
Immune modulator, n (%)	49 (80.3%)	24 (23.5%)	<.0001
Any biologics, n (%)	43 (70.5%)	21 (20.6%)	<.0001
Infliximab, n (%)	6 (9.8%)	2 (2.0%)	.0247
Adalimumab, n (%)	39 (63.9%)	18 (17.6%)	<.0001
Vedolizumab, n (%)	8 (13.1%)	3 (2.9%)	.0125
Current treatment			
Oral 5-ASA, n (%)	35 (57.4%)	92 (90.2%)	<.0001
Anal 5-ASA, n (%)	1 (1.6%)	60 (58.8%)	<.0001
Steroid, n (%)	16 (26.6%)	23 (22.5%)	.5952
Immune modulator, n (%)	36 (59%)	19 (18.6%)	<.0001
Any biologics	38 (62.3%)	16 (15.7%)	<.0001
Infliximab, n (%)	5 (8.2%)	2 (2.0%)	.0581
Adalimumab, n (%)	27 (44.3%)	11 (10.8%)	<.0001
Vedolizumab, n (%)	6 (9.8%)	3 (2.9%)	.0630

5-ASA = 5-aminosalicylic acid, CD = Crohn disease, IBD = inflammatory bowel disease, UC = ulcerative colitis.

Table 4

Comparison of clinical features of IBD diagnosed before and after 2015.

	Before 2015	After 2015	*P*-value
UC/CD	57/33	45/28	.8251
Median age at diagnosis	37	37	.1092
Male sex, n (%)	57 (63.3%)	42 (57.5%)	.4523
CD location (L1/L2/L3/L4)	13/5/13/2	9/4/13/2	.9337
CD behavior (B1 vs B2/B3)	7/26	14/14	.0193
UC extent (E1/E2/E3)	7/28/22	9/20/16	.5670
Bowel resection (%)	19 (21.1%)	8 (11.0%)	.0839
5-ASA, n (%)	86 (95.6%)	70 (95.9%)	.9167
Steroid, n (%)	57 (63.3%)	40 (55.6%)	.3171
Immune modulator, n (%)	45 (50%)	45 (61.6%)	.1383
Any biologics, n (%)	36 (40%)	28 (38.4%)	.8313

5-ASA = 5-aminosalicylic acid, CD = Crohn disease, IBD = inflammatory bowel disease, UC = ulcerative colitis.

Patients with CD had a less severe phenotype (inflammatory vs structuring/penetrating disease) after 2015 (before and after 2015 21.2% vs 50%, $P = .0193$).

5. Discussion

In this hospital-based real-world cohort study from a low-endemic area, 62.6% of the patients with IBD were diagnosed with UC and both UC and CD had a male predominance. Additionally, 42% of the patients with CD were diagnosed with ileocolonic disease, and 6.5% of the patients with CD had only upper gastrointestinal involvement. The most frequent disease location in patients with UC was left-sided colitis (47.1%). None of the patients with IBD had a family history. Biologic therapy was required for most of the patients with CD. Patients with CD diagnosed after 2015 had a less severe disease phenotype.

With the increasing incidence of IBD in the world, there is a significant difference between the disease phenotype between the East and West.[7,13–15] In our study, we found a low rate of family history and extraintestinal manifestations among our patients with IBD than among those in the Western reports. This is explained by the complex interplay of different environmental exposures, genetic predisposition, and intestinal dysbiosis underlying IBD. In addition, the average age of disease onset in adult cases was 31 to 34 years in the Western country[15] and is different from reports from Asia (Table 5). The reported median age of diagnosis of CD and UC was 30 and 41 years in a territory-wide registry study from Hong-Kong[10] and 22 and 36 years in Korea.[16,17] In our results and other hospital-based reports, the disease onset age was younger (CD vs UC, 30.5–36 vs 36–40 years)[3,4,8] than that in a population based-study in Taiwan[1] (CD vs UC, 35 and 44 years). Western studies have reported that CD and UC are more prevalent among female patients.[15] By contrast, we found a male predominance especially for CD.[14] Although the exact reason for these disparate patterns is unclear,[14,15] further studies are required to investigate the influence of genetic background and sex hormone that contributed to the IBD susceptibility.

The present study provided real-world data that allowed further understanding the disease behavior in Taiwan, which in turn helps the society and the government for future policy making for these patients. Patients with CD from the Western population presented with ileal disease (27%–42%), colonic disease (28%–35%), ileocolonic disease (22%–33%), and upper GI disease (1%–6%).[13] Our study found that the proportion of colonic CD disease was lower than that of ileal or ileocolonic disease, which is similar to reports from Taiwan,[4,11] China,[18] or Korea.[16] Endoscopic monitoring is more difficult for small intestinal CD,[4,19] and the treatment strategy may differ from that of colonic disease.[4] When looking at the disease behavior of CD, inflammatory pattern was most common (54%–88%)[13] from the Western countries and Hong-Kong[10] or Korea.[16] A complex CD disease phenotype (stricturing or penetrating disease) at diagnosis was observed in the present study and studies from Taiwan[4,11] and China.[18] This difference might be explained by a delay in disease diagnosis. The clinicians are not familiar with the disease before the foundation of Taiwan Society of Inflammatory Bowel Disease (TSIBD) in 2013. The development of treatment guidelines and increased studies[3,20–22] from Taiwan improved the public awareness of IBD; thus, clinicians can diagnose IBD in an earlier stage. This may explain our finding of less complicated disease pattern and bowel resection rates observed since 2015.[23]

As biologic is more effective but also expensive than conventional therapy for moderate-to-severe IBD, the Taiwan National Health Insurance system reimbursed patients for anti-TNF antibody treatment of CD since July 2011 and for that of UC since October 2016.[24] The reported rate of biologic therapy for CD (15.3%–37%) and UC (0.6%–1.6%) from Asia[10,18,24] was lower than that for CD (14%–69.4%) and UC (8%–45.2%) from Western reports.[25–27] Therefore, the proportion of biologic therapy is not an indicator for disease severity among different countries but reflects the balance between disease severity and patient accessibility to the medication.[20,28,29] While using population-based study, we can only observed the overview

Table 5

Comparison of recent IBD literature reports from Asia.

Country	Study type	CD (n)	UC (n)	UC/CD	CD: male	UC: male	CD: age	UC: age	CD disease (L1/L2/L3/L4)	CD behavior (B1/B2/B3)	UC disease (E1/E2/E3)	Colitis cancer	CD biologic	UC biologic	Author, report year
Taiwan	H	61	102	1.67	62.30%	59.80%	31	40	36.1/14.8/42.6/6.5	34.4/32.8/32.8	15.7/47.1/37.3	2.50%	70.50%	20.60%	Current study, 2020
Taiwan	H	80	110	1.38	75.00%	67.70%	36	40	57.5/7.5/33.8/1.3	18.8/60/21.3	18.2/42.7/39.7	2.10%	85.00%	42.70%	Chou JW,[4] 2019
Taiwan	H	110	406	3.69	64.55%	57.40%	30.5	36	30/26.4/38.2/NA	41.8/33.6/27	21.1/37.9/41	1.50%	N/A	N/A	Wei SC,[8,11] 2012
Taiwan	P	919	2887	3.14	68.60%	61.80%	35	44	NA	N/A	N/A	N/A	N/A	N/A	Yen,[1] 2019
Hong Kong	P	983	1541	1.57	65.00%	56.10%	30	41	24.5/32.3/43.1/8.4	65.2/25.1/16.1	34.5/32/33.5	1.30%	15.30%	1.60%	Ng SC,[10] 2016
Korea	H	2414	2798	1.16	72.25%	53.72%	22	36	21.5/5.5/72.5/NA	N/A	28.7/29.6/40.9	0.58%	N/A	N/A	Lee HS,[16] 2015
Korea	P	418	1013	2.42	76.10%	53.60%	22	36	21.9/9.3/65.8/22.5	81.1/8.1/10.8	54.3/22.5/23.2	N/A	N/A	N/A	Park SH,[15] 2019

CD = Crohn disease, H = hospital-based study, IBD = inflammatory bowel disease, P = population-based study, UC = ulcerative colitis.

of medical therapy but not the actual practice pattern in the daily practice.[7,9,18,24] Delayed use of immunosuppressive therapy with increased corticosteroid therapy will lead to long-term corticosteroid use complications and reduced quality of care.[24,30,31] In this study, we observed that patients with CD received more immunomodulator and biologic therapy than patients with UC, suggesting the fact that patients with CD were more difficult to treat with conventional therapy.[4,19] A low rate of steroid usage among our patients with IBD, similar to the Western reports,[30,32,33] may reflect the improved quality of IBD care in Taiwan in the past one decade.[2,8,11]

There are several limitations to this study. First, the study was retrospective and hospital based. There are few centers that have a dedicated IBD care team[8,11,34] or a special IBD nurse for patient care as in our hospital in Taiwan. Therefore, the findings of the present study revealed the clinical practice pattern of a single center and cannot be generalized to other centers in Taiwan. Second, the study is limited to a small number of cases in a medical center, which was not enough for the evaluation of risk factors or protective factors of the disease. Patients with mild disease may be cared in the community hospital or the clinic. The estimated disease severity and the need of biologic therapy may be an overestimation. Third, our hospital has no dedicated IBD care team; thus, the care of the patients may be varied among different physicians. For patients with unclassified inflammatory bowel disease,[35,36] close observation by physicians is required, and such patients were not included in this analysis. A dedicated IBD nurse with a recently build electronic patient care system in our hospital may help the physician to follow the updated society treatment guideline[3,20] for their patient care.

6. Conclusion

The increasing prevalence of IBD in Taiwan increased the need for understanding and teamwork care of this complicated disease. Patients with CD are likely to have a complicated disease pattern, requiring a higher demand of biologic therapy than patients with UC. Further prospective population-based registry studies at the national level are needed to further understand the clinical characteristics, treatments, and patient outcomes of this disease in Taiwan.

Author contributions

Conceptualization: Hsu-Heng Yen, Tsui-Chun Hsu, Mei-Wen Chen, Pei-Yuan Su, Yang-Yuan Chen.
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