

ORIGINAL ARTICLE

## 제주 지역의 30년간 염증성 장질환의 동향

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### Thirty-year Trend in Inflammatory Bowel Disease on Jeju Island, South Korea

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**Background/Aims:** Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), is increasing in South Korea. On the other hand, there are no reports of the incidence and prevalence of IBD specific to Jeju Island, prompting the necessity of this study.

**Methods:** In this retrospective design, the medical records of 453 patients diagnosed with IBD at Jeju National University Hospital from January 1990 to December 2019 were analyzed.

**Results:** Of the 453 IBD subjects (165 CD, 288 UC) included, the UC: CD ratio was 1.75:1. The incidence of IBD increased continuously from 0.19/10<sup>5</sup> in 1990 to 6.39/10<sup>5</sup> in 2017 and after that decreased to 4.92/10<sup>5</sup> in 2019. The male:female ratio was 2.24:1 for CD and 1.29:1 for UC. In the CD subjects, the disease activity included remission (33.3%), mild (25.5%), moderate (30.9%), and severe (6.1%). In UC subjects, the disease activity included remission (24.0%), mild (35.4%), moderate (28.8%), and severe (6.2%). According to the Montreal classification, the cases were as follows: CD: terminal ileum (22.4%), colon (9.7%), ileocolon (66.1%), and upper gastrointestinal involvement (27.3%), and perianal fistula/abscess was present in 43.6% of subjects before or at diagnosis: UC: proctitis (43.4%), left-sided colitis (29.1%), and pancolitis (23.3%) at diagnosis.

**Conclusions:** The incidence of IBD on Jeju Island has increased steadily for approximately 30 years but has exhibited a decline since 2017. Therefore, the incidence of IBD in Jeju is believed to have plateaued. Further study will be needed for clarification. (Korean J Gastroenterol 2023;81:243-252)

**Key Words:** Inflammatory bowel disease; Crohn's disease; Ulcerative colitis; Incidence; Prevalence

## INTRODUCTION

Inflammatory bowel disease (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), is characterized by chronic inflammation with unknown causes, which undergoes repeated improvement and recurrence in the gastrointestinal (GI) tract. CD occurs in any part of the GI tract, and UC occurs

primarily in the rectum and the colon.<sup>1,3</sup> In Asia, the incidence of IBD has different characteristics compared to other regions of the world. For example, the incidence is more prevalent in males than females in Asia, while the opposite is true in other regions. The incidence peaks between the ages of 20-59 in Asia but is a slightly broader range in other regions.<sup>4,6</sup>

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The incidence of IBD has increased worldwide until recently, where studies have shown that the incidence outside of Asia has plateaued or decreased.<sup>7,8</sup> On the other hand, the incidence and prevalence of IBD in the Songpa-Gangdong regions of Korea were on the rise from 1985 to 2015.<sup>9</sup> In contrast, reports from Korea using a Nationwide Health Insurance (NHI) database insisted that the incidence of IBD in Korea reached a plateau or decreased between 2006 and 2016.<sup>10-12</sup> Specifically, epidemiological studies of IBD performed in South Korea are limited to certain areas of Seoul,<sup>9</sup> with few studies being done in other areas<sup>13</sup> and no comparison made across regions has been made. Furthermore, there has been no research on IBD in Jeju Island until recently, despite the increasing incidence.

Therefore, this study examined the 30-year trend for patients with IBD at Jeju National University Hospital from 1990 to 2019. The researchers compared several epidemiologic factors, including the incidence and prevalence of IBD patients in various regions of South Korea. An additional objective was to examine how the recent trend of IBD on Jeju Island, South Korea, differs from that of regions outside of Asia.

## SUBJECTS AND METHODS

### 1. Study area and population

This study was performed on Jeju Island, South Korea. Jeju Island is the largest island in Korea, with a high degree of ethnic homogeneity (96.9% Korean nationals and 3.1% foreign as of 2022). The island's population increased steadily over this study period from 514,608 in 1990 to 670,989 in 2019.<sup>14</sup> This represents a sufficient population to assess the incidence and prevalence of IBD on Jeju Island.

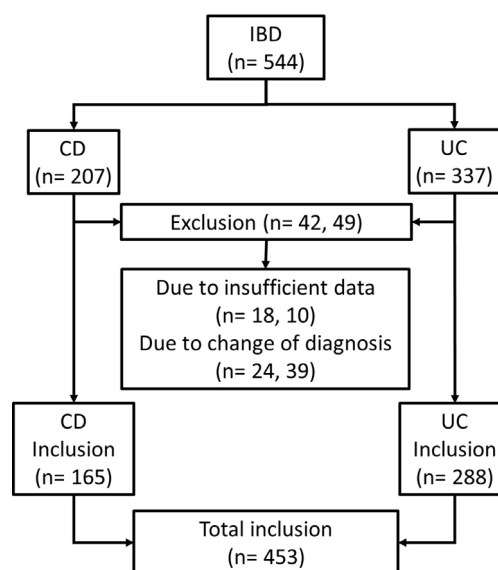
### 2. Data collection

Five hundred and forty-four patients, who underwent treatment in the gastroenterology and pediatric departments of Jeju National University Hospital from March 2009 to December 2019, were initially identified for this study. The diagnosis of IBD began in 1990, as confirmed in medical records. On the other hand, 91 patients were excluded: 63 given alternate diagnoses during treatment and 28 with incomplete medical records. The study ultimately included the records of 453 patients (Fig. 1).

The following data were examined: sex, age, height, weight, BMI, smoking and alcohol status, underlying disease, family history, date of diagnosis of IBD, disease location, behavior and disease activity, and medical and surgical treatment.

A diagnosis of IBD was made by a gastroenterologist or pediatric specialist based on the clinical, endoscopic, radiological, and histopathological criteria. The classification of disease phenotype in IBD was based on age, location of disease, and disease behavior according to the Montreal classification. Age was classified as under 16 years [A1], between 17 and 40 years of age [A2], and over 40 years of age [A3], and patients over 60 years of age at the time of onset were classified further as "elderly-onset" for the initial diagnosis. For CD, the location of the disease was classified as terminal ileum [L1], colon [L2], ileocolonic [L3], and upper GI tract involvement [L4]. In contrast, UC was classified as proctitis [E1], left-sided colitis [E2], and extensive or pancolitis [E3]. A diagnosis of CD was further classified by the subcategory to include inflammatory [B1], stenosis [B2], fistula [B3], stenosis and fistula [B2+B3], and perianal disease [p].

The treating physician evaluated the disease activity using the Crohn's Disease Activity Index (CDAI) for CD and Mayo or Partial Mayo Score for UC. On the other hand, patients treated in pediatrics at the time of diagnosis were evaluated by the treating physician using Pediatric Crohn's Disease Activity Index (PCDAI) for patients with CD and Pediatric



**Fig. 1.** Flowchart for included patients with inflammatory bowel disease. IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis.

Ulcerative Colitis Activity Index (PUCAI) for patients with UC. The disease severity was classified as remission, mild, moderate, or severe.

### 3. Incidence and prevalence trends

The data were collected from the 1990 to 2019 medical records to identify the IBD, CD, and UC trends. The population of Jeju Island was determined in December of each year, as confirmed by the National Statistical Office. The incidence was expressed as the number of cases per 100,000 person-years. The prevalence was also calculated as the number of cases per 100,000 person-years based on the population of Jeju Island in December 2004 and December 2019.

### 4. Statistical analysis

All statistical analyses were conducted using IBM SPSS Statistics version 24.0 (IBM Co., Armonk, NY, USA). The following were analyzed according to the average and proportion: age; sex; smoking and alcohol status; family history; underlying disease; BMI; date of diagnosis of IBD; disease location, behavior, and disease activity; medical and surgical treatment of patients with IBD. The continuous variables are described as mean  $\pm$  standard deviation, comparisons between two

groups using a Student's *t*-test, and non-continuous variables are analyzed using a chi-square test. The linear-by-linear association was used for trend analysis, which was defined as statistically significant with a  $p < 0.05$  value.

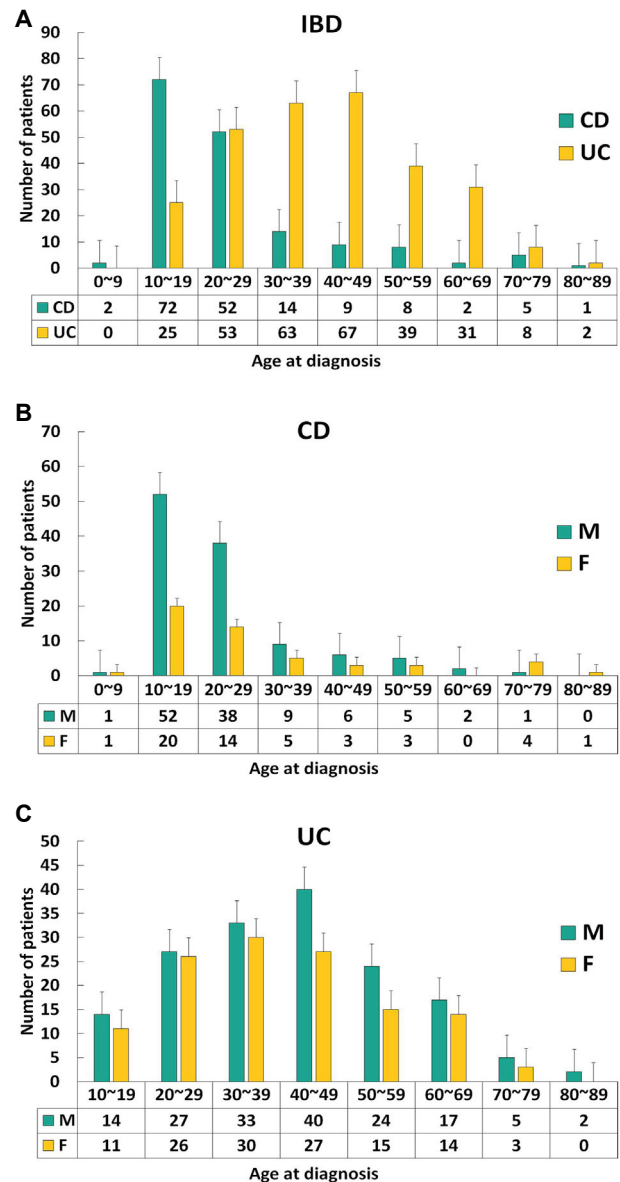
### 5. Ethics statement

The present study protocol was reviewed and approved by

**Table 1.** Baseline Characteristics of IBD Patients

| Characteristics            | CD<br>(n=165)   | UC<br>(n=288)   | p-value |
|----------------------------|-----------------|-----------------|---------|
| Sex                        |                 |                 |         |
| Male                       | 114 (69.1)      | 162 (56.3)      | 0.007   |
| Female                     | 51 (30.9)       | 126 (43.7)      |         |
| Male:Female ratio          | 2.24:1          | 1.29:1          |         |
| Mean age at diagnosis (yr) | 25.7 $\pm$ 15.1 | 40.7 $\pm$ 15.6 | <0.001  |
| Smoking                    |                 |                 |         |
| Smoker                     | 43 (26.1)       | 80 (27.8)       | 0.742   |
| Non-smoker                 | 122 (73.9)      | 208 (72.2)      |         |
| Alcohol drinking           | 48 (29.1)       | 124 (43.1)      | <0.001  |
| Family history of IBD      | 6 (3.6)         | 13 (4.5)        | 0.394   |
| Underlying disease         |                 |                 |         |
| None                       | 157 (95.2)      | 236 (81.9)      | <0.001  |
| Hypertension               | 6 (3.6)         | 39 (13.5)       |         |
| Diabetes                   | 3 (1.8)         | 15 (5.2)        |         |
| Hyperlipidemia             | 2 (1.2)         | 14 (4.9)        |         |
| BMI (kg/m <sup>2</sup> )   | 20.7 $\pm$ 4.0  | 23.3 $\pm$ 3.3  | <0.001  |

Values are presented as number (%) or mean $\pm$ standard deviation. IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis; BMI, body mass index.



**Fig. 2.** Age and sex-specific number of patients with IBD, CD, UC in Jeju island, 1990-2019. (A) Age group-specific number of patients with IBD in Jeju island, 1990-2019. (B) Age and sex-specific number of patients with CD in Jeju island, 1990-2019. (C) Age and sex-specific number of patients with UC in Jeju island, 1990-2019. IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis.

the Institutional Review Board (IRB) of Jeju National University School of Medicine (IRB No. 2020-05-019). Written informed consent was not required because this was a retrospective records-review study.

## RESULTS

### 1. Demographic characteristics of patients

Four hundred and fifty-three patients with IBD were included in this study: 165 patients (36.4%) with CD and 288 patients (63.6%) with UC. The UC: CD ratio was 1.75:1. The

patients were predominantly male at 60.9% overall, with CD at 69.1% and UC at 56.3% ( $p=0.007$ ). The male-to-female ratio was 2.24:1 for CD and 1.29:1 for UC, which was higher for males in CD than in UC.

The mean age at diagnosis of IBD was  $40.7 \pm 15.6$  years for UC and  $25.7 \pm 15.1$  years for CD ( $p<0.001$ ), which showed that UC developed later than CD. The smoking status, including both current and ex-smokers, comprised 43 patients (26.1%) in CD and 80 patients (27.8%) in UC and was similar in the two groups ( $p=0.742$ ). The alcohol intake was higher in UC patients than in CD patients (43.1% vs. 29.1%,

**Table 2.** Incidence of IBD, CD, and UC on Jeju Island, 1990-2019

| Year | Population | Incidence (per 100,000) (n) |           |           | UC:CD ratio |
|------|------------|-----------------------------|-----------|-----------|-------------|
|      |            | IBD (n)                     | CD (n)    | UC (n)    |             |
| 1990 | 514,608    | 0.19 (1)                    | 0         | 0.19 (1)  | N/A         |
| 1991 | 496,119    | 0.20 (1)                    | 0         | 0.20 (1)  | N/A         |
| 1992 | 505,784    | 0                           | 0         | 0         | N/A         |
| 1993 | 510,584    | 0.20 (1)                    | 0         | 0.20 (1)  | N/A         |
| 1994 | 513,905    | 0.39 (2)                    | 0.19 (1)  | 0.19 (1)  | 1:1         |
| 1995 | 518,836    | 0.19 (1)                    | 0         | 0.19 (1)  | N/A         |
| 1996 | 523,022    | 0                           | 0         | 0         | N/A         |
| 1997 | 527,586    | 0                           | 0         | 0         | N/A         |
| 1998 | 534,008    | 0.19 (1)                    | 0         | 0.19 (1)  | N/A         |
| 1999 | 538,744    | 0.37 (2)                    | 0         | 0.37 (2)  | N/A         |
| 2000 | 542,368    | 0.74 (4)                    | 0.18 (1)  | 0.55 (3)  | 3.1:1       |
| 2001 | 546,889    | 0.73 (4)                    | 0.55 (3)  | 0.18 (1)  | 0.3:1       |
| 2002 | 550,831    | 1.27 (7)                    | 0.73 (4)  | 0.54 (3)  | 0.74:1      |
| 2003 | 552,297    | 1.09 (6)                    | 0         | 1.09 (6)  | N/A         |
| 2004 | 555,362    | 1.26 (7)                    | 0.54 (3)  | 0.72 (4)  | 1.3:1       |
| 2005 | 557,569    | 3.95 (22)                   | 1.26 (7)  | 2.69 (15) | 2.1:1       |
| 2006 | 558,496    | 3.04 (17)                   | 1.61 (9)  | 1.43 (8)  | 0.89:1      |
| 2007 | 559,258    | 3.40 (19)                   | 1.43 (8)  | 1.97 (11) | 1.4:1       |
| 2008 | 560,618    | 2.85 (16)                   | 1.43 (8)  | 1.43 (8)  | 1           |
| 2009 | 562,663    | 3.02 (17)                   | 0.36 (2)  | 2.67 (15) | 7.4:1       |
| 2010 | 571,255    | 3.85 (22)                   | 1.93 (11) | 1.93 (11) | 1           |
| 2011 | 576,156    | 3.99 (23)                   | 0.87 (5)  | 3.12 (18) | 3.6:1       |
| 2012 | 583,713    | 5.82 (34)                   | 2.23 (13) | 3.60 (21) | 1.6:1       |
| 2013 | 593,806    | 4.88 (29)                   | 2.69 (16) | 2.19 (13) | 0.81:1      |
| 2014 | 607,346    | 6.09 (37)                   | 2.31 (14) | 3.79 (23) | 1.6:1       |
| 2015 | 624,395    | 5.93 (37)                   | 1.92 (12) | 4.00 (25) | 2.1:1       |
| 2016 | 641,597    | 6.39 (41)                   | 1.87 (12) | 4.52 (29) | 2.4:1       |
| 2017 | 657,083    | 6.39 (42)                   | 1.67 (11) | 4.72 (31) | 2.8:1       |
| 2018 | 667,191    | 4.05 (27)                   | 1.80 (12) | 2.25 (15) | 1.3:1       |
| 2019 | 670,989    | 4.92 (33)                   | 1.94 (13) | 2.98 (20) | 1.5:1       |

IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis; N/A, not applicable.

$p<0.001$ ), which appeared to be related to more advanced age.

The familial history of IBD was 3.6% and 4.5% for CD and UC, respectively, and there was no significant difference between the two groups ( $p=0.394$ ). There were more cases of no underlying disease in CD than in UC patients (95.2% vs. 81.9%,  $p<0.001$ ), which also appeared to be related to the age at the time of diagnosis.

In BMI, the average was  $23.3\pm 3.3$  kg/m<sup>2</sup> in UC patients and  $20.7\pm 4.0$  kg/m<sup>2</sup> in CD, indicating an overweight status in UC patients based on the Asian BMI,<sup>15</sup> while BMI in CD patients was in the normal range, but there was a significant difference between two groups ( $p<0.001$ ) (Table 1).

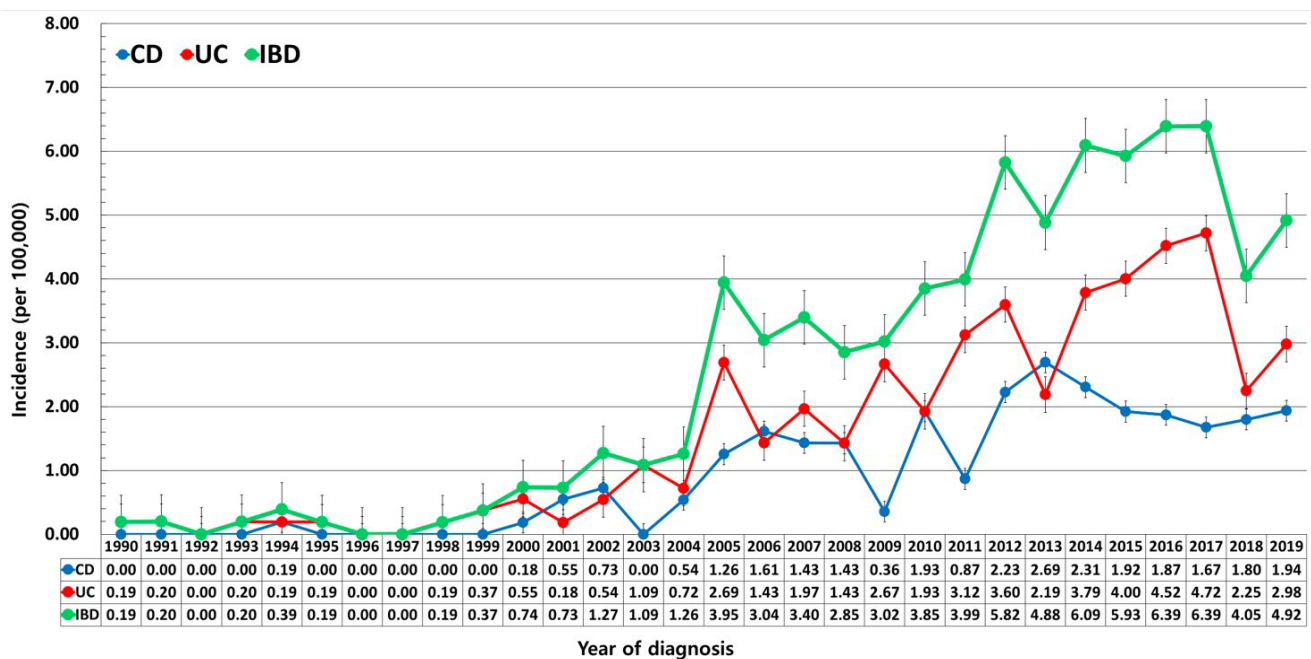
## 2. Age and sex-specific number of patients with IBD in Jeju Island, 1990–2019

Fig. 2A shows the age group-specific number of patients at the time of diagnosis in patients with CD and UC. Of patients with CD, 124 patients (75.2%) were diagnosed between the ages of 10–29. In contrast, most UC patients were diagnosed between the ages of 20–49 for 183 patients (63.5%). At the time of diagnosis, 72 patients (43.6%) under 20 years were diagnosed with CD, which is approximately five times higher than 25 patients (8.7%) with UC. The patients diag-

nosed between the ages of 30–69 years were 33 (20%) for CD and 200 (69.4%) for UC, which was 3.5 times higher than CD. In particular, only two patients (1.2%) were diagnosed between the ages of 60–69 years with CD, but 31 patients (10.8%) were diagnosed with UC, indicating a nine-fold difference in the ratio.

Fig. 2B shows the age and sex-specific number of patients based on the age at the time of diagnosis with CD. Most age groups with CD were also predominantly male, ranging from 10–69 years in age. The largest number of male and female patients were diagnosed between 10–19 years: 52 males (31.5%) and 20 females (12.1%). At the time of the CD diagnosis, between the ages of 10–29, 90 (78.9%) of 114 patients were male, and 34 (66.7%) of 51 patients were female.

Fig. 2C shows the age and sex-specific number of patients based on the age at the time of diagnosis with UC. Patients with UC were predominantly male in all age groups. The peak in diagnosis was between 40 and 49 years for males and between 30 and 39 years for females. Most patients with UC were diagnosed between 20 to 49 years, with 100 males (61.7%) of the 162 patients and 83 females (65.9%) of the 126 patients.



**Fig. 3.** Incidence of IBD, UC, and CD in Jeju island, 1990–2019. IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis.

### 3. Incidence and prevalence of IBD

Table 2 lists the incidence of IBD, CD, and UC. The incidence in 1990 was 0.19/10<sup>5</sup> IBD with 0 CD and 0.19/10<sup>5</sup> UC. The incidence of IBD continued to increase from 0.19/10<sup>5</sup> to 6.39/10<sup>5</sup> between 1990 and 2016, up more than 34 times from the previous period. During the same period, the incidence of CD was 1.87/10<sup>5</sup>, and UC was 4.52/10<sup>5</sup>. During the most recent 2018–2019 period, the incidence was reduced to IBD 4.05/10<sup>5</sup>–4.92/10<sup>5</sup>, CD 1.80/10<sup>5</sup>–1.94/10<sup>5</sup>, and UC 2.25/10<sup>5</sup>–2.98/10<sup>5</sup> (Table 2). The compound annual growth rate (CAGR) for IBD, CD, and UC incidence over 30 years was calculated at 11%, 8%, and 10%, respectively. The UC: CD ratio was 3.1:1 in 2000 but decreased gradually to

1.5:1 in 2019. Fig. 3 presents the incidence of IBD on Jeju Island, which increased steadily for approximately 30 years (1990–2017) but has declined since 2017. Therefore, the incidence of IBD in Jeju is believed to have plateaued.

The prevalence was based on the population of Jeju Island from December 2004 to December 2019. The prevalence of IBD was 6.7/10<sup>5</sup> in 2004 and increased more than 10-fold to 67.5/10<sup>5</sup> in 2019. Similarly, the prevalence of CD and UC also increased tenfold from 2.2/10<sup>5</sup> and 4.5/10<sup>5</sup> in 2004 to 24.6/10<sup>5</sup> and 42.9/10<sup>5</sup> in 2019, respectively. CAGR for IBD, CD, and UC prevalence from 2004 to 2019 was calculated to be 17%, 5%, and 4%, respectively.

**Table 3.** Disease Characteristics of CD and UC Patients

| Characteristics               | CD (n=165)  | UC (n=288)                     | p-value |
|-------------------------------|-------------|--------------------------------|---------|
| Montreal's classification     |             |                                |         |
| Age at diagnosis              |             |                                |         |
| A1 (≤16 years)                | 50 (30.3)   | 10 (3.5)                       | <0.001  |
| A2 (17-40 years)              | 90 (55.2)   | 137 (47.6)                     |         |
| A3 (>40 years)                | 24 (14.5)   | 141 (49.0)                     |         |
| Elderly-onset (≥60 years)     | 8 (4.8)     | 41 (14.2)                      | 0.002   |
| Location at diagnosis         |             |                                |         |
| E1 (Proctitis)                | N/A         | 125 (43.4)                     | 0.128   |
| E2 (Left-sided)               | N/A         | 84 (29.1)                      |         |
| E3 (Pancolitis)               | N/A         | 67 (23.3)                      |         |
| L1 (Terminal ileum)           | 40 (24.2)   | N/A                            |         |
| L2 (Colon)                    | 16 (9.7)    | N/A                            |         |
| L3 (Ileocolon)                | 109 (66.1)  | N/A                            |         |
| L4 (Upper GI)                 | 33 (20.0)   | N/A                            |         |
| Missing data                  | 0 (0)       | 12 (4.2)                       |         |
| Behavior at diagnosis         |             |                                |         |
| B1 (Inflammatory)             | 116 (70.3)  | N/A                            | 0.128   |
| B2 (Stricture)                | 35 (21.2)   | N/A                            |         |
| B3 (Fistula)                  | 8 (4.8)     | N/A                            |         |
| B2+B3 (Stricture & Fistula)   | 3 (1.8)     | N/A                            |         |
| P (Perianal disease)          | 72 (43.6)   | N/A                            |         |
| Missing data                  | 3 (1.8)     | N/A                            |         |
| Disease activity at diagnosis |             |                                |         |
|                               | CDAI, PCDAI | (Partial or) Mayo score, PUCAI |         |
| Remission                     | 55 (33.3)   | 69 (24.0)                      | 0.128   |
| Mild                          | 42 (25.5)   | 102 (35.4)                     |         |
| Moderate                      | 51 (30.9)   | 83 (28.8)                      |         |
| Severe                        | 10 (6.1)    | 18 (6.2)                       |         |
| Missing data                  | 7 (4.2)     | 16 (5.6)                       |         |

Values are presented as number (%).

IBD, inflammatory bowel disease; CD, Crohn's disease; UC, ulcerative colitis; GI, gastrointestinal; CDAI, Crohn's disease activity index; PCDAI, pediatric Crohn's disease activity index; PUCAI, pediatric ulcerative colitis activity index; N/A, not applicable.

#### 4. Disease characteristics of IBD on Jeju Island

According to the Montreal classification, 90 (54.5%) of 165 patients with CD were between the ages of 17 to 40 years [A2]. The next most common were patients with CD under 16 years [A1], which accounted for 50 patients (30.3%), with only 24 patients (14.5%) above 40 years. At the time of diagnosis of CD, the disease location was in the ileocolonic [L3] in 109 patients (66.1%), and 40 patients (24.2%) were limited to the terminal ileum [L1]. In contrast, disease location in patients with CD was 16 (9.7%) for those limited to the colon [L2]. Involvement of the upper GI tract [L4] was confirmed in 33 (20%) of the 165 patients.

At the time of the diagnosis with CD, the disease behavior was inflammatory [B1] in 116 patients (70.3%), while stenosis [B2] and fistula [B3] were identified in 35 (21.2%) and eight (4.8%) patients. In particular, only three patients (1.8%) had stenosis and fistula [B2+B3] at the time of diagnosis of CD. A perianal lesion [P] was identified in 72 patients (43.6%)

at the CD diagnosis. The disease activity of CD was as follows: mild (n=42, 25.5%), moderate (n=51, 30.9%), severe (n=10, 6.1%), and remission for 55 patients (33.3%) (Table 3).

According to the Montreal classification, the UC diagnosis accounted for 141 (49.0%) of 288 patients above 40 years old [A3] at the time of diagnosis. The second was patients diagnosed between the ages of 17 to 40 years [A2], which is equivalent to 137 patients (47.6%) and similar to [A3]. In contrast, only 10 patients (3.5%) were under 16 years of age [A1] at the time of diagnosis, which is approximately one-tenth of that of CD patients in the same age group. According to the Montreal classification, UC was statistically more common than CD in those over 40 years ( $p<0.001$ ). UC was more common than CD in patients aged over 60 years (14.2 % vs. 4.8%,  $p=0.002$ ).

At the time of the UC diagnosis, 125 patients (43.4%) were limited to proctitis [E1], followed by left colitis (n=84, 29.1%) and extensive or pancolitis (n=67, 23.3%). The disease activ-

**Table 4.** Medical and Surgical Treatment of CD and UC Patients

| Characteristics                       | CD (n=165) | UC (n=288) | p-value |
|---------------------------------------|------------|------------|---------|
| Use of medication at diagnosis, n (%) |            |            |         |
| None                                  | 2 (1.2)    | 6 (2.1)    |         |
| 5-ASA                                 | 130 (78.8) | 205 (71.2) |         |
| Steroid                               | 31 (18.8)  | 11 (3.8)   |         |
| Immunomodulator                       | 37 (22.4)  | 0 (0)      |         |
| Biologics                             | 4 (2.4)    | 0 (0)      |         |
| Missing data                          | 28 (17.0)  | 52 (18.1)  |         |
| Use of medication                     |            |            |         |
| 5-ASA                                 | 159 (96.4) | 276 (95.8) | 0.545   |
| Steroid                               | 100 (44.1) | 127 (55.9) | <0.001  |
| Immunomodulator                       | 135 (81.8) | 56 (19.4)  | <0.001  |
| Azathioprine                          | 131 (79.4) | 51 (17.7)  |         |
| 6-Mercaptopurine                      | 7 (4.2)    | 7 (2.4)    |         |
| Methotrexate                          | 3 (1.8)    | 3 (1.0)    |         |
| Biologics                             | 57 (34.5)  | 30 (10.4)  | <0.001  |
| Infliximab                            | 54 (32.7)  | 27 (9.4)   |         |
| Adalimumab                            | 7 (4.2)    | 3 (1.0)    |         |
| Vedolizumab                           | 3 (1.8)    | 5 (1.7)    |         |
| Golimumab                             | 0 (0)      | 3 (1.0)    |         |
| Etrolizumab                           | 1 (0.6)    | 0 (0)      |         |
| Ustekinumab                           | 2 (1.2)    | 0 (0)      |         |
| Abatacept                             | 0 (0)      | 1 (0.3)    |         |
| Intestinal resection                  | 24 (14.5)  | 4 (1.4)    | <0.001  |

Values are presented as number (%).

5-ASA, 5-aminosalicylic acid; Rt, right; Lt, left; T-colon, transverse colon; I&D, Incision and drainage; CD, Crohn's disease; UC, ulcerative colitis.

ity was as follows: mild ( $n=102$ , 35.4%), moderate ( $n=83$ , 28.8%), severe ( $n=18$ , 6.2%), and remission for 69 patients (24.0%) (Table 3).

## 5. Medical and surgical treatment of CD and UC patients

At the initial diagnosis, 5-aminosalicylic acid (5-ASA) and steroids were prescribed to 71.2% ( $n=205$ ) and 3.8% ( $n=11$ ) of patients, respectively. Immunomodulators and biologics were not used in the initial diagnosis of UC. In CD patients, however, 5-ASA, steroids, immunomodulators, and biologics were prescribed in 78.8% ( $n=130$ ), 18.8% ( $n=31$ ), 22.4% ( $n=37$ ), and 2.4% ( $n=4$ ), respectively (Table 4).

During the treatment period after the diagnosis, 5-ASA was the most commonly used drug in both CD and UC; there was no difference between the two groups (96.4% vs. 95.8%,  $p=0.545$ ). Steroids were used more frequently in UC than in CD patients (55.9% vs. 44.1%). In contrast, immunomodulators were used significantly more in CD patients than in UC patients (81.8% vs. 19.4%,  $p<0.001$ ). Azathioprine was the most commonly used immunomodulatory agent for CD and UC, followed by 6-MP and methotrexate. Biological agents were also used more in CD than in UC patients (34.5% vs. 10.4%,  $p<0.001$ ). Infliximab was the most used in both groups, followed by adalimumab, vedolizumab, golimumab, and ustekinumab. Intestinal resection was performed more frequently in CD than in UC (14.5% vs. 1.4%,  $p<0.001$ ) (Table 4).

## DISCUSSION

IBD is on the rise worldwide. In this study, the number of patients with IBD in Jeju has increased steadily for most of the past 30 years. On the other hand, this study indicated that the incidence of IBD has plateaued in recent years, for which further study is recommended.<sup>10-12</sup> Another study suggested that the incidence of IBD may have plateaued or decreased in some Western countries.<sup>7</sup> In addition, the incidence of UC in Korea plateaued from 2018 and CD from 2014.<sup>16</sup> In contrast, a study of the Songpa-Gangdong district, Seoul, in Korea, revealed an increased incidence of IBD and a potential difference in the incidence among regions despite the nation's relative ethnic homogeneity.<sup>9</sup> Therefore, a follow-up study will be needed to confirm the plateau of IBD incidence on Jeju Island.

Over the past 30 years, the incidence of IBD on Jeju Island increased from  $0.19/10^5$  to  $6.39/10^5$ , approximately 34 times higher than at the beginning of 1990, and the prevalence increased from  $6.7/10^5$  to  $67.5/10^5$ , showing a 10-fold increase over 15 years from 2004 to 2019. In addition, the UC:CD ratio showed a decreasing trend over time, which was confirmed to be the same as the results shown in previous studies.<sup>9,17</sup> Similarly, compared to a study conducted in Kuala Lumpur, Malaysia,<sup>18</sup> the number of patients with IBD increased gradually, and the UC:CD ratio decreased, even though both the incidence and prevalence were much higher on Jeju Island. This was attributed to the higher ethnic heterogeneity and lower socioeconomic status of Kuala Lumpur compared to Jeju Island. In contrast, a population-based study from Olmsted County in Minnesota, USA, a developed country, showed a higher incidence and prevalence between 1970 and 2010 than in the present study.<sup>19</sup> Therefore, the incidence and prevalence of IBD are higher in developed countries, which is an important factor in determining the IBD incidence and prevalence. Because IBD is a chronic disease, despite a plateau in the incidence, the prevalence of IBD in Jeju is likely to continue to increase. Accordingly, the medical demand on Jeju Island is also likely to increase.

In the patients with IBD identified in this study, both UC and CD were predominant in males. Compared to previous studies, the overall tendency was the same across all age groups.<sup>9</sup> On the other hand, there was a peculiarity in the age grouping of IBD patients on Jeju Island. In patients with UC or CD over the age of 60, elderly-onset UC (EOUC) or CD (EOCD) accounted for a higher percentage than in previous studies (14.2% vs. 7.4% for EOUC, 4.8% vs. 1% for EOCD).<sup>20,21</sup> In particular, the average age of patients with UC (40.7 vs. 36.4) and CD (25.7 vs. 22.8) at the time of the diagnosis was also higher than that of patients in the Songpa-Gangdong district, Seoul.<sup>20,21</sup> When comparing the populations by age in Seoul and Jeju, the proportion of the population was similar to that of Seoul;<sup>22</sup> thus, IBD occurred more in the elderly population on Jeju Island. The proportion of elderly-onset patients with IBD is increasing. These are difficult to manage because of problems, such as malnutrition, polypharmacy, and cognitive decline. There is also a lack of consensus regarding guidelines for treatment.<sup>23</sup> Therefore, suitable treatment guidelines are needed for the increasing number of elderly-onset IBD patients. The clinical character-



istics of patients according to the Montreal classification were also similar to those in the study conducted in Songpa-Gangdong, Seoul.<sup>9</sup>

Regarding the medication history of IBD patients in this study, most were prescribed 5-ASA at the time of diagnosis, while biological agents were used from the time of diagnosis in some severe CD cases. On the other hand, in the later years of this study, most patients were prescribed steroids, immunomodulators, and biological agents. In a study examining the medication history of IBD patients registered in NHI from 2010 to 2016, immunomodulator was 66.9% nationwide in patients with CD while 81.8% on Jeju Island. Biological agents were administered in patients with CD (19.6%) and UC (6.1%) nationwide,<sup>24</sup> but this was CD 34.5% and UC 10.4% on Jeju Island. Biological agents and other more potent medications increased in parallel to disease prevalence. Recent innovative treatments have emerged, such as fecal material transplantation.<sup>25</sup> Nevertheless, patients with IBD spend more on direct healthcare costs before and after diagnosis; thus, applying new treatments will likely lead to increased medical expenditure.<sup>15,26</sup>

The strengths of this study are as follows. Jeju National University Hospital is the only university hospital on Jeju Island. Therefore, most IBD patients on the island might be identified, and they could statistically represent the IBD incidence of Jeju Island. Furthermore, this study identified medications used for IBD treatment at the time of diagnosis and during the follow-up observations to confirm the difference in medication use according to disease progress.

Among the patients excluded, many diseases mimic IBD, such as indeterminate colitis, intestinal tuberculosis, and radiation colitis, with overlapping clinical and pathological features.<sup>27,28</sup> These patients were initially suspected of IBD but were excluded due to other diagnoses. Microscopic colitis will increase the risk of IBD, and it can be newly diagnosed as IBD in the future.<sup>29,30</sup> Ultimately, the accuracy of diagnosis in this study was confirmed by identifying the misdiagnoses and a change in diagnosis in detail.

The limitations of this study were as follows. As a result of its retrospective cohort design, some patients were excluded because of incomplete medical records. Furthermore, this is a single-center study, and patients undergoing treatment at other hospitals inside and outside Jeju Island were excluded. Therefore, the incidence and prevalence identified

in this study may have been underestimated. In addition, these factors were not analyzed because it was impossible to identify whether IBD patients were hospitalized or experienced exacerbation.

In conclusion, the incidence of IBD on Jeju Island has continuously increased to 6.39 per 100,000 over the past 30 years, increasing approximately 34 times since 1990. On the other hand, the incidence did not increase over the last three years of the study (2017-2019) and has potentially plateaued. Nevertheless, further study will be needed for clarification.

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