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Observational Study

Recent Trends in the Epidemiology and Clinical Outcomes of Inflammatory Bowel Disease in South Korea, 2010–2018

Kim SJ *et al*. Recent trends of IBD in South Korea

Abstract

BACKGROUND

Inflammatory bowel disease (IBD) was previously regarded as a Western disease; however, its incidence is increasing in the East. The epidemiology of IBD in Asia differs significantly from the patterns in the West.

AIM

We aimed to comprehensively investigate the epidemiology of IBD in South Korea, including its incidence, prevalence, medication trends, and outcomes.

METHODS

We analyzed claims data from the Health Insurance Review and Assessment Service and Rare and Intractable Diseases (RIDs), operated by the National Health Insurance Service of South Korea. Patients with IBD were identified based on the International Classification of Diseases, Tenth Revision, and RID diagnostic codes for Crohn's disease (CD) and ulcerative colitis (UC) from 2010 to 2018.

RESULTS

In total, 14,498 and 31,409 patients were newly diagnosed with CD and UC, respectively, between 2010 and 2018. The annual average incidence of CD was 3.11 cases per 10^5 person-years, and that of UC was 6.74 cases per 10^5 person-years. Since 2014, the incidence rate of CD has been stable, while that of UC has steadily increased, shifting the peak age group from 50-year-olds in 2010 to 20-year-olds in 2018. The CD and UC prevalence increased consistently over the study period; the use of 5-aminosalicylates and corticosteroids gradually decreased, while that of immunomodulators and biologics steadily increased in both CD and UC. The clinical outcomes of IBD, such as hospitalization and surgery, decreased during the study period.

CONCLUSION

The CD incidence has been stable since 2014, but that of UC has increased with a shift to a younger age at peak incidence between 2010 and 2018. IBD clinical outcomes improved over time, with increased use of immunomodulators and biologics.

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

Core Tip: Inflammatory bowel disease (IBD) was previously regarded as a Western disease; however, its incidence is increasing in the East, with a different epidemiological pattern. This nationwide cohort study analyzed claims data from South Korea between 2010 and 2018. The incidence of ulcerative colitis increased continuously, particularly among younger demographic groups, during this period, whereas the incidence of Crohn's disease remained stable from 2014. Additionally, in this period, hospitalization

and surgery rates for IBD decreased as the use of immunomodulators and biologics increased.

INTRODUCTION

Inflammatory bowel disease (IBD), which includes Crohn's disease (CD) and ulcerative colitis (UC), is a chronic relapsing inflammatory disease of the gastrointestinal tract. Although it was previously regarded as a Western disease, its incidence has increased in newly industrialized countries, including South Korea, since the start of the twenty-first century[1,2].

South Korea is a representative Asian country in which the incidence and prevalence of IBD are rapidly increasing[1]. According to a longitudinal population-based study conducted in the Songpa-Kangdong (SK) district of Seoul, South Korea, the incidence rates of both CD and UC have rapidly increased since the first diagnosis of a patient with IBD in Korea in 1986 (from 0.06/10[3] inhabitants/year in 1986–1990 to 2.44/10[3] inhabitants/year in 2011–2015 for CD, and from 0.29/10[3] inhabitants/year in 1986–1990 to 5.82/10[3] inhabitants/year in 2011–2015 for UC)[4]. Several nationwide population-based studies have investigated the epidemiology of IBD in South Korea[3,5,6]. Jung et al[3] reported the average annual incidence of UC and CD to be 5.0 and 2.8 per 10^5 person-years, respectively, from 2011 to 2014, and Kwak et al[6] reported that both the prevalence and incidence of CD and UC showed an increase between 2007 and 2016 (1.9-fold and 1.2-fold increase in the prevalence and incidence of CD, respectively, and 1.6-fold and 1.3-fold increase in the prevalence and incidence of UC, respectively). However, despite the previous epidemiological data on IBD in South Korea, studies on recent trends are still lacking. Furthermore, although the clinical course of IBD has changed due to the recent introduction of various new therapeutic agents, there are very few demographic studies on its clinical outcomes.

The current study aimed to explore the incidence and prevalence of IBD using a nationwide population-based cohort from the National Health Insurance Service

(NHIS) database and to investigate the temporal changes in medication and clinical outcomes of IBD in South Korea.

MATERIALS AND METHODS

Data source

The NHIS is a mandatory nationwide insurance system operated by the government that covers approximately 97% of the entire population of South Korea. It contains medical claims data, including patient demographics, principal diagnosis, and comorbidities, using the International Classification of Disease 10th revision (ICD- 10) codes and prescriptions, admissions, and procedures[7]. All the information from the NHIS is integrated into the Health Insurance Review and Assessment Service (HIRA) claims database, which is a comprehensive data source for epidemiological studies in South Korea[3,5,6].

The NHIS established the Rare and Intractable Disease (RID) registration program in 2006 to provide a medical copayment reduction of 10% to patients with RIDs, including IBD. To register in this program and obtain a special code (V code), patients must obtain diagnostic approval from a physician based on the strict diagnostic criteria defined by the NHIS[5]. Because it is directly related to the government's support for medical expenses, RID registration is conducted strictly to ensure a high reliability in RID diagnosis.

The current retrospective nationwide cohort study used claims data from HIRA and RIDs (operated by the NHIS) and was approved by the Seoul National University Hospital Institutional Review Board (1806-060-949). Because there are no personal identifiers, informed consent was waived.

Patient identification

Patients diagnosed with IBD between 2010 and 2018 were included in this study. To establish an accurate definition for identifying patients with IBD, we compared two different definitions: one defined patients with IBD using only ICD-10 codes, whereas the other used both ICD-10 and V codes. Finally, we identified patients with CD as

those with both ICD-10 code K50 and RID code V130 and patients with UC as those with ICD-10 code K51 and RID code V131. The diagnostic accuracy of each definition for identifying patients with IBD was assessed using data from the SK-IBD study in which all IBD cases were strictly identified through a medical record review conducted by two experts[4].

The following information was collected from the HIRA claims database: date of diagnosis, comorbidities, prescription records, and IBD-related clinical outcomes, including emergency room (ER) visits, hospitalizations, and surgery.

Definition of IBD-related medication and outcomes

IBD-related medications included 5-aminosalicylates (5-ASA), immunomodulators (azathioprine or 6-mercaptopurine), systemic corticosteroids (including both oral and intravenous corticosteroids), and biologics (infliximab, adalimumab, vedolizumab, ustekinumab, or tofacitinib), prescribed at least once, along with the diagnostic codes. ER visit was defined as a visit to the ER for a primary diagnosis of IBD. Hospitalization was defined as an admission for ≥ 3 days with the principal diagnosis of IBD. Surgery was defined as resection of the small bowel, colon, or rectum in patients diagnosed with IBD.

Statistical analysis

The annual incidence of IBD was defined as the number of newly diagnosed cases of IBD per 10^5 individuals in the respective year, based on the registered resident population for that year. Prevalence was defined as the number of patients with IBD per 10^5 person-years based on the registered resident population for that year. Incidence and prevalence were calculated for different age and sex groups, and each value was expressed as the number of cases per 10^5 person-years.

Trends in IBD-related prescriptions and clinical outcomes, including ER visits, hospitalization, and surgery, between 2010 and 2018 were examined. Trends in prescriptions and clinical outcomes were described based on the number of patients who were prescribed IBD-related medications or had an ER visit, hospitalization, or surgery annually. Statistical analyses were performed using SAS version 9.4 (SAS

Institute, Cary, NC, USA) and R version 3.4.3 (The R Foundation for Statistical Computing, Vienna, Austria). Figure 1 provides an overview of the study's selection process.

RESULTS

Accuracy of diagnostic definitions

To assess the accuracy of the diagnostic definitions, we identified patients with IBD from the healthcare data of the SK district, using only ICD-10 codes or both ICD-10 codes and V-codes, and compared them with the published results of the SK-IBD study from 2011 to 2015[4]. Compared to using ICD-10 and V codes for identifying patients with IBD, using only ICD-10 codes overestimated the incidence and prevalence (mean annual incidence rate per 10^5 inhabitants: 17.34 for CD and 109.05 for UC). However, when V-codes were applied in addition to the ICD-10 codes, the results (mean annual incidence rate per 10^5 inhabitants: 3.79 for CD and 7.40 for UC) were similar to the incidence rates reported in a previous study for the SK district (mean annual incidence rate per 10^5 inhabitants: 2.44 for CD and 5.82 for UC) (Supplementary Table 1).

Incidence

Between 2010 and 2018, 45,907 patients were newly diagnosed with IBD; specifically, 14,498 (31.6%) and 31,409 (68.4%) patients were diagnosed with CD and UC, respectively. Table 1 and Figure 2 present the incidence of IBD in South Korea between 2010 and 2018. The mean annual incidence rates during the study period were 3.1 per 10^5 and 6.7 per 10^5 for CD and UC, respectively. The incidence of UC increased steadily throughout the study period from 5.3 to 8.2 per 10^5 between 2010 and 2018, with an annual increase of approximately 0.4%. Meanwhile, the incidence of CD increased from 2.5 to 3.3 per 10^5 between 2010 and 2014 and remained relatively stable thereafter at approximately 3.3 per 10^5. In 2018, the UC-to-CD incidence ratio was 2.5.

Age-specific incidence rates showed different patterns for CD and UC throughout the study period (Figure 3). For CD, the peak incidence was observed in individuals aged 10–19 years. The incidence rate remained relatively high in the 20–29-year-olds but

decreased significantly after age 30, exhibiting a consistent pattern over time. In contrast, there was a shift in the peak incidence age for UC, decreasing from 50–59 years in 2010 to 20–29 years in 2018.

Both CD and UC showed higher incidence rates in men than in women over the study period, with sex differences being more prominent in patients with CD than in those with UC. In 2018, the male-to-female ratios for CD and UC were 2.4 and 1.7, respectively. Additionally, age- and sex-specific incidence rates demonstrated distinct patterns for CD and UC in 2018 (Figure 4). The peak incidence of CD occurred in patients aged 10–19 years in both men and women. In contrast, while the incidence of UC peaked in the 20–29-year-olds for both men and women, the second peak incidence of UC was observed only in males in the 60–69-year-old age group.

Prevalence

The prevalence of IBD steadily increased between 2010 and 2018, reaching 17,168 and 34,420 patients with CD and UC, respectively, in 2018. CD and UC showed more than double the prevalence over the study period, from 15.1 per 10^5 in 2010 to 32.7 per 10^5 in 2018 for CD, and from 31.6 per 10^5 in 2010 to 65.5 per 10^5 in 2018 for UC. The prevalence rate was higher in men than in women for both CD and UC, with a greater sex difference observed, especially for CD; the values were 46.8 per 10^5 in men and 18.5 per 10^5 in women for CD, and 77.1 per 10^5 in men and 53.9 per 10^5 in women for UC (Supplementary Figure 1). Furthermore, the prevalence of IBD increased in all age groups throughout the study period. The peak prevalence of CD occurred in the 20–29-year-old age group, whereas that of UC occurred in the 60–69-year-old age group, which was consistent for both men and women (Supplementary Figures 2 and 3).

Changes in prescription patterns of IBD medications

5-ASA, immunomodulators, systemic corticosteroids, and biologics were administered to 12,435 (72.4%), 10,516 (61.3%), 4,323 (25.2%), and 6,278 (36.6%) patients with CD, respectively, in 2018. In the UC group, 5-ASA was administered to almost all patients (32,323; 93%), whereas immunomodulators, systemic corticosteroids, and biologics were administered to 5,789 (16.8%), 6,271 (18.2%), and 2,822 (8.2%) patients, respectively.

Figure 5 shows the temporal changes in the use of IBD medications between 2010 and 2018. The number of patients using immunomodulators and biologics increased in both the CD and UC groups during the study period. In patients with CD, the use of immunomodulators increased from 52.1% in 2010 to 61.3% in 2018, and that of biologics increased from 11.9% in 2010 to 36.6% in 2018. Moreover, in patients with UC, the use of immunomodulators increased from 13.1% in 2010 to 16.8% in 2018, whereas that of biologics increased from 0.7% in 2010 to 8.2% in 2018. Conversely, the use of steroids decreased during the same period, from 32.1% in 2010 to 25.2% in 2018 for CD and from 23.8% in 2010 to 18.2% in 2018 for UC. Finally, the use of 5-ASA decreased from 87.9% in 2010 to 72.4% in 2018 in CD while remaining relatively unchanged in UC patients throughout the study period.

Clinical outcomes

Figure 6 shows the trend in IBD outcomes, including IBD-related ER visits, hospitalizations, and surgeries, between 2010 and 2018. In 2018, 1,991 (11.6%) and 1,081 (3.1%) patients with CD and UC, respectively, visited the ER at least once with a diagnosis of IBD. The rate of ER visits did not change significantly during the study period.

A total of 3,448 (20.1%) and 2,440 (7.1%) patients with CD and UC, respectively, were hospitalized in 2018. The hospitalization rates for CD and UC showed a decreasing trend during the study period, from 24.1% in 2010 to 20.1% in 2018 for CD and from 8.9% in 2010 to 7.1% in 2018 for UC.

Regarding surgery, 399 patients with CD (2.3%) and 42 patients with UC (0.1%) underwent bowel resection for complications related to IBD in 2018. The surgery rate for patients with CD decreased from 3.4% in 2010 to 2.3% in 2018. Regarding UC, there was a decreasing trend in the surgery rate, from 0.4% in 2010 to 0.2% in 2014; however, it remained relatively unchanged thereafter.

DISCUSSION

This nationwide population-based study investigated the comprehensive epidemiological data on IBD in South Korea from 2010 to 2018. To the best of our knowledge, this was the first study to analyze the epidemiology of IBD in an Asian population, considering medication use and IBD-related clinical outcomes, such as ER visits, hospitalizations, and surgeries. Throughout the study period, the incidence of UC increased continuously, with a shift towards the younger age group, whereas that of CD plateaued from 2014 onwards. Furthermore, patients with more recently diagnosed IBD showed higher use rates of immunomodulators and biologics and lower rates of hospitalization and surgery.

The average annual incidence rates of IBD in this study from 2010 to 2018 were 3.1 per 10^5 for CD and 6.7 per 10^5 for UC, comparable to the findings of previous studies conducted in Korea using the nationwide HIRA database. In such studies, the incidence of CD and UC ranged from 2.6 to 3.2 per 10^5 people and from 4.3 to 5.3 per 10^5 people, respectively, during 2005–2016[3,5,6,8]. The incidence of IBD in the present study was lower than that in North America (Olmsted County, Minnesota; the incidence of CD was 10.7 per 10^5 people and that of UC was 12.2 per 10^5 people) and Europe (Denmark; incidence of CD was 9.1 per 10^5 people and that of UC was 18.6 per 10^5 people)[9,10]. However, this was the highest estimate among Asian countries, representing the economic advancement and Westernization of society with rapid industrialization in Korea[11,12].

Remarkably, the incidence of UC increased continuously over the entire study period, whereas that of CD plateaued from 2014 onwards. Although the SK cohort study showed an increased incidence of IBD, the increase has slowed down recently[4]. Moreover, recent studies using a nationwide database have reported the incidence of IBD to have plateaued or even decreased[3,5,6]. The global evolution of IBD could explain this trend; IBD in Korea has recently accelerated through the incidence stage to the stage of compounding prevalence[2]. Unlike other industrialized countries in Asia that experienced a rising incidence of IBD in the 2020s, Korea and Japan transitioned into an accelerated incidence stage earlier owing to rapid industrialization[6,13]. Studies with

more recent data may show a trend toward a decrease or plateau in incidence. Importantly, our study included the most recent data from previous epidemiological studies in Korea and confirmed a stabilizing incidence and an increasing trend in the prevalence of IBD. Longitudinal studies with long-term follow-ups would be necessary to evaluate the transition of this epidemiological stage accurately.

One of the interesting findings of this study was the shift in the peak age of UC incidence to a younger age, which changed from individuals in their 50s to those in their 20s, during the study period. This trend has also been observed in several previous studies in Korea[6,8,14]. Although the exact reason for this shift is still unclear, changes in dietary habits and lifestyle factors may be linked. Furthermore, the increased frequency of eating out and using delivered food, especially among young people, and the rise in coffee and sugar-sweetened beverage consumption, could play a role[15,16]. Moreover, reduced exposure to green areas and increased time spent in urban living and working environments may have contributed to this trend[17,18]. Finally, with improved access to healthcare over the past few decades, the rate of endoscopic examinations among young people may have increased, leading to a higher rate of early diagnosis of UC[19]. Further studies are recommended to elucidate the underlying reasons for this trend.

Another interesting finding of this study was that the rates of hospitalization and surgery in patients with IBD decreased over the study period, in line with the increased use of immunomodulators and biologics. Temporal changes in IBD outcomes following the use of new therapeutic agents have been addressed in previous studies. In a hospital-based cohort study of patients with UC, conducted in Korea between 1986 and 2015, the rates of hospitalization and surgery decreased over time; in particular, the rate of surgery significantly decreased after the introduction of anti-TNF agents[20]. A meta-analysis of 44 population-based cohort studies revealed a decreasing trend in the risk of surgery, which was significantly lower in patients diagnosed in the 21st century than in those diagnosed in the 20th century for both CD and UC[21].

 The ER visits and hospitalization rates in this study were comparable to those reported in previous Korean studies[3,20]. However, the surgery rate was much lower than that in

previous studies[7,21,22]. This discrepancy could be attributed to differences in the methods used to calculate the surgery rate. Two Western studies have reported that the risk of surgery is highest within the first 1 or 2 years after the diagnosis of UC, and one South Korean study has reported that the rate of surgery is low between 5 and 10 years after the diagnosis of UC, increasing slightly thereafter[20,23,24]. Our current study analyzed the rate of surgery in patients with IBD each year, irrespective of the time of diagnosis, so it did not reflect the cumulative probabilities of surgery after IBD diagnosis. Furthermore, considering that previous studies reported a gradual decrease in the surgery rate over time, the lower rate in this study could have been due to our consideration of a more recent time period[21,25].

This study had some limitations. First, the certainty of the IBD diagnosis was limited owing to the nature of the claims data. To overcome this concern, we defined patients with IBD more accurately using both ICD-10 codes and V-codes rather than relying only on ICD-10 codes based on a comparative analysis of patients with IBD in the SK-IBD study. Our definition was further validated internally at a tertiary referral hospital in Korea (Seoul National University Hospital), demonstrating sensitivity rates of 94.5% and 96.4% for CD and UC, respectively. Second, since we used claims data, we could not obtain detailed clinical information, such as symptoms, disease phenotype, or severity, which may have influenced the clinical outcomes of IBD. Thus, we could not establish a causal relationship between using immunomodulators and biologics and IBD-related clinical outcomes. Third, the present study included a study cohort that was retrospectively enrolled with a diagnostic code for IBD during the study period from 2010 to 2018 and was followed up until 2018. Therefore, the duration of the disease and follow-up within the cohort showed heterogeneity; moreover, the follow-up duration may be too short to reflect the entire clinical course of IBD, particularly among subjects diagnosed recently. Finally, although we carefully devised an operational definition of clinical outcomes to encompass IBD-related results, inherent uncertainty remained since the NHIS does not provide detailed clinical data of individual patients or information on individual identifiers.

CONCLUSION

In conclusion, our study indicated a distinct shift in the epidemiology of the Korean population with IBD towards a stabilizing incidence and a younger age at diagnosis. The incidence of CD has been stable since 2014, whereas that of UC has continuously increased, peaking at a younger age. Moreover, the use of immunomodulators and biologics increased notably, aligning with a reduction in the rates of hospitalization and surgery during the study period. Our findings shed light on the evolving landscape of IBD in Korea and reveal changes in its incidence, treatment patterns, and clinical outcomes.

ARTICLE HIGHLIGHTS

Research background

Over time, IBD has become a global disease with changing epidemiological patterns. Traditionally, IBD has been considered a Western disease; however, its incidence has increased in newly industrialized countries, including Asia, since the turn of the twenty-first century.

Research motivation

Although the epidemiology of IBD differs between the Western and Eastern worlds, and understanding the epidemiology of IBD is crucial for better management of patients and healthcare resources, data on IBD epidemiology in Asia remain limited.

Research objectives

We aimed to evaluate the incidence and prevalence of IBD using a nationwide population-based cohort in South Korea. Additionally, we sought to investigate the temporal changes in the medications and clinical outcomes of IBD.

Research methods

This study used claims data from the National Health Insurance Service of South Korea. We identified IBD patients using the International Classification of Diseases, Tenth Revision, and RID diagnostic codes for Crohn's disease (CD) and ulcerative colitis (UC). The incidence, prevalence, medication use, and clinical outcomes of IBD were assessed from 2010 to 2018.

Research results

Over the study period, from 2010 to 2018, 14,498 and 31,409 patients were newly diagnosed with CD and UC, respectively. The incidence of CD has stabilized in South Korea, while that of UCD has steadily increased with a shifted peak age from the 50s to the 20s since 2014. The prevalence rates of both CD and UC increased consistently. Over the study period, the use of immunomodulators and biologics increased, but that of 5-ASA and steroids decreased in both CD and UC patients, which was accompanied by decreased IBD-related hospitalizations and surgeries.

Research conclusions

The nationwide study revealed the recent epidemiology of IBD in South Korea. The incidence of CD has been stable since 2014, but that of UC has increased with a shift to a younger age at peak incidence between 2010 and 2018. Additionally, the clinical outcomes of IBD improved over the study period, in parallel with the increased use of immunomodulators and biologics.

Research perspectives

Future studies are required to evaluate the long-term prognosis of IBD according to changes in IBD treatment medications, including indicators such as disease activity and quality of life.

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