

Increasing Incidence of Inflammatory Bowel Disease Among Young Men in Korea Between 2003 and 2008

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Abstract

Background and Aims Temporal trends in incidence rates of Crohn's disease (CD) and ulcerative colitis (UC) can provide valuable clues about etiology. Korea has a draft system, and every male must fulfill his military service. However, according to military rules, patients with CD and UC are not conscripted into the army, and when the disease is diagnosed during military service, patients are relieved from military duties. Such policies provide a unique opportunity to determine the incidence of CD and UC among young men in Korea. We studied the incidence of

CD and UC over time in Korea, a rapidly developing country.

Methods The Armed Forces Medical Command of the Republic of Korea Army provided lists of members who were relieved from military duties due to diagnoses of CD and UC between 2003 and 2008.

Results During this 6-year period, there were 96 incident cases of CD and 104 incident cases of UC. For the 6-year period, the adjusted mean annual incidence rates of CD and UC per 100,000 persons were 3.2 and 3.5, respectively. When analyzed by 2-year intervals, the mean annual incidence of CD and UC increased, from 1.8 and 1.7 per 100,000 persons in 2003–2004, to 2.7 and 3.3 per 100,000

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persons in 2005–2006, and to 5.1 and 5.4 per 100,000 persons in 2007–2008, respectively.

Conclusions Incidence of CD and UC among young men is rapidly increasing in Korea, which strongly suggests an environmental contribution to the disease.

Keywords Inflammatory bowel disease · Crohn's disease · Ulcerative colitis · Incidence

Abbreviations

CD Crohn's disease

UC Ulcerative colitis

IBD Inflammatory bowel disease

Introduction

Crohn's disease (CD) and ulcerative colitis (UC), collectively termed inflammatory bowel disease (IBD), are heterogeneous chronic relapsing disorders of unknown etiology [1]. Although IBD occurs worldwide, its epidemiologic and clinical characteristics vary depending upon the geographic location and the ethnicity of the population [2]. Studying temporal trends in incidence rates in a given area can provide valuable clues about etiology [3]. However, accurate data about the incidence of IBD in Asian countries are scarce, because of lack of population-based registries, limited access to health care facilities, limited availability of diagnostic devices, and occurrence of infectious diseases that mimic IBD [2].

This is the first report involving the incidence of IBD among young soldiers in the Republic of Korea Army. Because of the following reasons, there is a unique advantage of this study to study the trend in incidence of IBD. First, Korea has a draft system, and every male must fulfill his military service before 30 years of age. Most males enlist in the army between 19 and 25 years of age and serve in the army for 2 years. Second, men with CD or UC are not conscripted into the army according to military rules. Third, members who are diagnosed with IBD during military service are relieved from military duties, and it is mandated to report every case that has been relieved from military duties to the Department of Preventive Medicine in the Armed Forces Medical Command of the Republic of Korea Army. Fourth, there has been no change of this policy in the army during the study period. Thus, the cohort of this study consists of all healthy (or previously undiagnosed) males of a certain age group in Korea, and patients with IBD in this cohort are completely recruited. This provides a unique opportunity to study the trend in incidence of IBD among young males in Korea. The aim of

the present study is to determine the trend of CD and UC among young soldiers in the Republic of Korea Army.

Methods

Patient Identification

For a member who is diagnosed with IBD during military service, a committee comprising a physician, surgeon, radiologist, and pathologist would form at the Armed Forces Hospital of the respective region to review the medical record. When all committee members agree with the diagnosis of IBD, the member is relieved from military duties. It is mandated to report every case that has been relieved from military duties to the Department of Preventive Medicine in the Armed Forces Medical Command of the Republic of Korea Army. The Armed Forces Medical Command provided a list of members ($n = 200$) who were relieved from military duties under the diagnosis of CD and UC between 2003 and 2008. This study was conducted in accordance with the Declaration of Helsinki, Good Clinical Practice.

Clinical Characteristics of IBD

The database of the Armed Forces Medical Command [Defense Medical Information System (DEMIS)] was reviewed for 186 patients at 13 major Armed Forces Hospitals. The clinical information pertaining to 14 patients diagnosed at the other two Armed Forces Hospitals was not available.

The case records of 186 patients recruited from each source were reviewed, and patients were classified as definite cases and incomplete cases. For a definite case of CD, at least two of the following criteria were required: (1) clinical history of abdominal pain, weight loss, malaise, diarrhea, and/or rectal bleeding; (2) endoscopic findings of mucosal cobblestoning, linear ulceration, skip areas, or perianal disease; (3) radiologic findings of stricture, fistula, mucosal cobblestoning, or ulceration; (4) macroscopic appearance of bowel wall induration, mesenteric lymphadenopathy, and "creeping fat" at laparotomy; and (5) pathologic findings of transmural inflammation and/or epithelioid granulomas [4, 5]. Patients were diagnosed with definite cases of UC if all three of the following criteria were present: (1) typical history of diarrhea or blood and pus or both in stools for ≥ 4 weeks; (2) typical sigmoidoscopic or colonoscopic picture of diffusely granular, friable, or ulcerated mucosa without rectal sparing or skip lesions or radiologic signs of characteristic continuous granular or ulcerated mucosa; and (3) characteristic histopathologic signs of inflammation on biopsy [5, 6].

For the 186 patients, we recorded the gender, age at time of diagnosis, location of disease at time of diagnosis, presenting symptoms, and the interval from onset of symptoms to diagnosis. CD was classified by location as isolated small bowel disease, isolated colonic disease, or both small bowel and colonic disease. We also evaluated whether CD involved the perianal area, and the type of involvement as follows: (1) stricturing, (2) penetrating, and (3) nonstricturing and nonpenetrating. For UC, disease extent was categorized as proctitis if present up to 15 cm from the anal verge, left-sided colitis if present up to but not beyond the splenic flexure, or extensive colitis if present beyond the splenic flexure.

Data Analysis

The annual incidence of IBD, defined as the number of newly diagnosed patients per 100,000 soldiers per year, was estimated for each year. The population during the study period (2003–2008) was constant, being approximately 500,000 soldiers. Incidence was calculated from year of diagnosis not onset of symptoms. To evaluate temporal trends in incidence rates, the study period was divided into three 2-year periods (2003–2004, 2005–2006, and 2007–2008). Differences in numeric variables between the 2-year periods were tested using a Kruskal–Wallis test. Differences in numeric variables between CD and UC were tested using the Mann–Whitney test. For categorical variables, a chi-square test or Fisher's exact test was used as appropriate. Statistical analysis was conducted using PASW Statistics 17.0 (SPSS, Inc., Chicago, IL, USA).

Results

Patient Characteristics

During the 6-year study period (2003–2008), 200 new cases of IBD were diagnosed among soldiers of the Republic of Korea Army. There were 96 incident cases of CD and 104 incident cases of UC. Median age at time of diagnosis of CD and UC was 21 years (range 19–24 years) and 21 years (range 18–28 years; $P = 0.803$), respectively. The median interval from symptom onset to diagnosis was 3 months (range 0.3–76 months) and 1 month (range 1–48 months; $P = 0.002$) for CD and UC, respectively.

Incidence of IBD

The mean annual incidence rate of CD for the entire study period was 3.2. The annual incidence of CD increased progressively throughout the study period (Fig. 1). The annual incidence of CD was 1.6, 2.0, 2.0, 3.4, 5.2, and 5.0

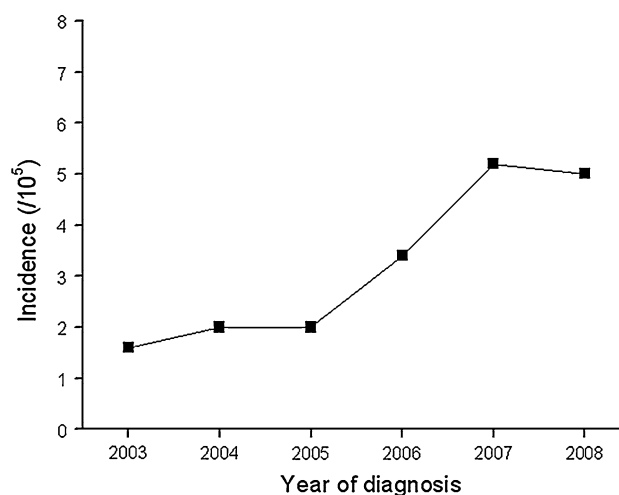


Fig. 1 Annual incidence of Crohn's disease in the Republic of Korea Army (2003–2008). Incidence of Crohn's disease is increasing in Korea

per 100,000 persons in 2003, 2004, 2005, 2006, 2007, and 2008, respectively. The mean annual incidence rate of UC for the entire study period was 3.5. The annual incidence of UC also increased progressively throughout the study period (Fig. 2), being 1.0, 2.4, 2.0, 4.6, 4.0, and 6.8 per 100,000 persons in 2003, 2004, 2005, 2006, 2007, and 2008, respectively. The UC-to-CD ratio was 1.08 during the entire study period, being 0.94, 1.22, and 1.05 in 2003–2004, 2005–2006, and 2007–2008, respectively (Table 1).

Characteristics of CD

Of the 96 incident cases of CD, clinical information was available for 87 patients. Seventy-three of these 87 patients (84%) were definite cases. Fifty-eight patients (67%) had disease in the small bowel and colon, 10 patients (11%) had isolated small bowel disease, and 19 patients (22%) had isolated colonic disease at time of diagnosis. The number of new patients with isolated small bowel disease increased progressively (Table 2). The type of CD was stricturing in 4 patients (5%), penetrating in 3 patients (3%), and nonstricturing, nonpenetrating in the remaining 80 patients (92%). Perianal lesions were noted in 40 patients (46%).

Characteristics of UC

Of the 104 incident cases of UC, clinical information was available for 99 patients. Of these 99 patients, 24 (24%) had proctitis, 26 (26%) had left-sided colitis, and 43 (44%) had extensive colitis at time of diagnosis (Table 3). For six patients (6%), extent of disease was not fully evaluated at time of diagnosis. All 99 patients were definite cases of UC.

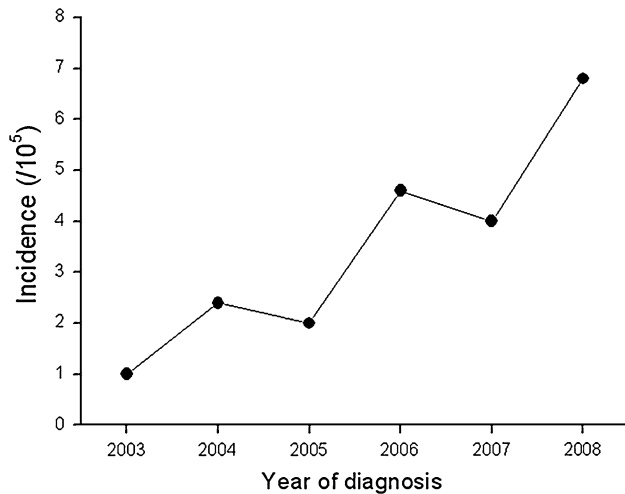


Fig. 2 Annual incidence of ulcerative colitis in the Republic of Korea Army (2003–2008). Incidence of ulcerative colitis is increasing in Korea

Table 1 Temporal trends in annual incidence of ulcerative colitis and Crohn’s disease, and their ratio, in the Republic of Korea Army (2003–2008)

	Year of diagnosis		
	2003–2004	2005–2006	2007–2008
Incidence (/10 ⁵)			
Ulcerative colitis	1.7	3.3	5.4
Crohn’s disease	1.8	2.7	5.1
UC-to-CD ratio	0.94	1.22	1.05

Table 2 Temporal trends in age at diagnosis, interval from symptom onset to diagnosis, and location of disease at diagnosis in 87 patients with Crohn’s disease in the Republic of Korea Army (2003–2008)

	Year of diagnosis		
	2003–2004	2005–2006	2007–2008
Number of patients	13	26	48
Age at diagnosis [years, median (range)]	21 (19–22)	21 (19–24)	21 (18–24)
Interval from onset to diagnosis [months, median (range)]	3 (0.2–12)	5 (1–72)	2 (0.2–36)
Location of disease, <i>n</i> (%)			
Small bowel and colon	11 (85%)	18 (69%)	29 (60%)
Small bowel only	0 (0%)	1 (4%)	9 (19%)
Colon only	2 (15%)	7 (27%)	10 (21%)

Discussion

In the current study, we documented a rapid increase in CD and UC over time in young men in Korea. As mentioned in the “Introduction,” this cohort has advantage in identifying

Table 3 Temporal trends in age at diagnosis, interval from symptom onset to diagnosis, and location of disease at diagnosis in 99 patients with ulcerative colitis in the Republic of Korea Army (2003–2008)

	Year of diagnosis		
	2003–2004	2005–2006	2007–2008
Number of patients	15	32	52
Age at diagnosis [years, median (range)]	21 (20–28)	21 (19–26)	20 (19–25)
Interval from onset to diagnosis [months, median (range)]	2 (1–6)	1.5 (1–24)	1.5 (1–48)
Location of disease <i>n</i> , (%)			
Proctitis	0 (0%)	11 (34%)	13 (25%)
Left-sided colitis	6 (40%)	4 (13%)	16 (31%)
Extensive colitis	9 (60%)	14 (44%)	20 (39%)
Unknown	0 (0%)	3 (9%)	3 (5%)

temporal trends in the incidence rate of IBD in Korea, since this cohort consisted of almost every healthy male of a certain age group (primarily 20–25 years) in Korea. In the current study, the number of cases of CD with isolated small bowel disease, which is relatively difficult to diagnose, was also on the rise. Although this finding may suggest that the increased incidence of CD over time is a result of the availability of new diagnostic modalities, such as capsule endoscopy or double-balloon enteroscopy, we showed that the number of new patients with small bowel and colonic disease, the predominant type of CD in the current study, is also increasing. Thus, it is unlikely that the increased incidence of CD is a result of improved diagnostic sensitivity alone. The number of cases of ulcerative proctitis also increased over time. This may represent increased physician awareness of the disease. However, the number of new patients with left-sided colitis or extensive colitis is also increasing. The time interval from symptom onset to diagnosis of IBD was also constant during the study period. This finding indicates that the increased incidence is not caused by increased awareness alone. The progressive increase in incidence of CD and UC appears to be real, and is consistent with other reports from Korea, all of which have shown increasing incidence of IBD in Korea [3, 5, 7].

This temporal trend in incidence rates may provide valuable clues to the etiology of IBD, as well as useful information for implementation of health care policy. The rising incidence over time in Korea strongly suggests an environmental contribution to the expression of disease. Increasing incidence of IBD has also been reported in many other parts of the world, including South America and Eastern Europe [8, 9]. These areas as well as Korea are industrializing areas, suggesting that urbanization may be a risk factor for IBD [2].

In the current study, the most common location of CD involved the small bowel and colonic disease. This is consistent with other reports from Korea and Japan [5, 7, 10], but is different from the pattern normally seen in Western countries [11–13]. The location of CD in East Asian countries may be different from in Western countries.

The UC-to-CD ratio in Korea has been reported to be decreasing [5]. As it has in several Western countries [14–16], the incidence rate of CD is expected to catch up with or even surpass UC over time in Korea. In a previous report from Korea, the UC-to-CD ratio was 2.3 in the interval between 2001 and 2005 for all ages [5]. In the current study, the UC-to-CD ratio was 1.08, much lower than the report from Yang et al. [5]. This discrepancy may be attributed to the characteristics of our cohort, which consisted of young males; however, this discrepancy may also be due to the diagnostic criteria for CD. In the current study, all cases of UC were definite cases, as described in the “Methods” section. However, for CD, 84% of the cases were definite cases when the diagnostic criteria described in the “Methods” section were used.

Our data are limited by several factors. First, the data in this study were retrospective, which has inherent limitations. Second, of 200 listed patients, review of the medical records was not possible for 14 patients (7%). Third, as mentioned in the “Methods” section, the diagnosis of CD in this study was made by a committee comprising a physician, surgeon, radiologist, and pathologist. The aim of this committee was to provide members with a fair and definitive diagnosis of IBD. However, since there is no gold standard for diagnosis of CD and the committee consisted of many physicians with different experiences, the diagnosis of CD was debatable for some members. Thus, the definite cases of CD with the diagnostic criteria described in the “Methods” section accounted for 84% of the CD patients in our study. In the other 16% of patients, diagnosis of CD was made after empirical treatment with antituberculosis therapy, by capsule endoscopic findings in the small bowel along with clinical history, or by presence of intractable perianal disease along with aphthous erosions in the colon. Thus, the true incidence rate of CD among young males might be somewhat lower than the incidence rate of CD in the current study. Fourth, the incidence data of this study only apply to the age and sex range of the military sample and not to the Korean population as a whole.

In conclusion, we found that incidence of UC and CD is increasing rapidly among young men in Korea. The progressive increase in the incidence of CD and UC in Korea appears real. Korea is a rapidly developing country, and these trends are explained best by one or more environmental factors. Research to clarify the etiologies in

association with the increasing number of patients, as well as a strategy to manage this growing disease, is needed in Korea, as well as for countries facing similar issues.

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Conflict of interests The authors have no commercial associations that might represent a conflict of interest in relation to this manuscript.

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