

## Arthritic Manifestations of Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) is commonly associated with arthritic manifestations. They are divided into three clinical categories; peripheral arthritis, spondylitis, and sacroiliitis. To evaluate the incidence of arthritis associated with IBD in Korea, we retrospectively reviewed one hundred and twenty-nine patients with IBD, 77 with ulcerative colitis (UC) and 52 with Crohn's disease (CD). Arthritis occurred in twenty-two patients (17.1%); 15 with UC (19.6%), 7 with CD (13.5%). Patients with arthritis had more active inflammations and all were seronegative except one patient. Peripheral arthritis was found in twenty patients (15.5%) and more common in UC (19.6%) than in CD (9.6%). Joint involvements tended to be monoarticular or pauciarticular, and most frequently developed in the knee and ankle. Spondylitis was diagnosed in one patient (1.6%) who showed HLA B27 positivity. Radiographic sacroiliitis was observed in eight patients (6.2%) who revealed HLA B27 negativity. Both peripheral arthritis and sacroiliitis were found in six patients (4.6%). In CD, arthritis occurred in 20% of the patients with colonic involvement but in none of the patients without colonic involvement. In conclusion, arthritis was frequent in patients with IBD. Peripheral arthritis was more common in patients with UC than CD. All the patients with CD and arthritis had colonic involvement.

**Key Words :** Arthritis, Inflammatory bowel disease, Korea

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### INTRODUCTION

Inflammatory bowel disease (IBD) is a chronic inflammatory disorder of unknown cause involving gastrointestinal tract. Chronic IBD may be divided into two major groups, ulcerative colitis (UC) and Crohn's disease (CD). UC has a prevalence about twice that of CD (1). Recently, the increased incidence of CD has been reported (2). IBD is complicated by many local and systemic disorders. Among the extraintestinal complications of IBD, arthritic manifestations were the most common (3, 4). Arthritis associated with IBD may be divided into three clinical categories; peripheral arthritis, spondylitis, and sacroiliitis (5-8).

Peripheral arthritis occurs in 15-20% of patients with IBD. The arthritis tends to be asymmetrical, often migratory nature running more or less parallel with the inflammatory bowel disease and should not be confused with rheumatoid arthritis. Joint involvements are monoarticular or oligoarticular and occur most often in the knee and ankle. Spondylitis occurs in 3-6% of patients with IBD. In contrast to the peripheral arthritis, spondylitis usually follows a chronic progressive course unrelated

to exacerbation and remission of bowel disease (9). Most patients show an increased incidence of HLA B-27 (10). Radiographic sacroiliitis is seen in 4-18% of patients but usually asymptomatic and may not progress to ankylosing spondylitis. Unlike spondylitis, sacroiliitis in IBD is not associated with HLA B-27 (11).

The purpose of the present study was to establish the incidence and clinical characteristics of arthritis in a large group of non-selected patients, suffering from UC and CD at a tertiary referral center in Korea.

### MATERIALS AND METHODS

One hundred and twenty-nine patients with IBD, seen at Yonsei University Medical Center during the decade of 1987-1996, were retrospectively studied. The hospital records of all patients were reviewed in detail, together with roentgenograms and laboratory data.

Diagnoses of UC and CD were made by one of our authors (WH Kim), or confirmed at surgery. In UC, patients were subdivided into two groups; patients with the involvement of only the rectosigmoid region (recto-

sigmoid) and beyond the rectosigmoid region (pancolitis). In CD, patients were also subdivided into two groups; patients with colitis and without colitis.

Except for the hip, arthritis was defined as joint pain associated with tenderness and swelling. Hip arthritis was considered to be present if pain on hip motion was elicited during the examination. Arthritis was subdivided into peripheral arthritis and spondylitis. Roentgenograms of sacroiliac joint were available from barium enema films or simple pelvis AP films. If these were in any way abnormal, radiographic sacroiliitis was considered and HLA B-27 result was recorded. The result of a latex fixation test for rheumatoid factor (RF) was recorded in patients with joint symptom.

The mean and standard deviation were calculated. Differences between the groups were tested for their statistical significance using non-paired Student's t-test and Mann-Whitney U-Wilcoxon Rank Sum test. A p value less than 0.05 was considered statistically significant.

## RESULTS

Of the one hundred and twenty-nine patients with IBD, 77 patients had UC (mean age  $38.5 \pm 16.8$  yrs) and 52 patients had CD (mean age  $34.0 \pm 15.4$  yrs). There were more female patients in UC (m: f = 34 : 43), but more males in CD (m: f = 31 : 21). Mean disease duration was not different between both disease. Predominant symptoms at the time of diagnosis are summarized in Table 1. Diarrhea and hematochezia were more common presenting symptoms in UC than CD ( $p < 0.05$ ). But abdominal pain was more common in CD ( $p < 0.05$ ). Arthritis occurred in 22 patients (17.1%). Of these, 15 patients had UC (19.6%) and 7 had CD (13.5%) ( $p > 0.05$ ).

The mean age of patients with arthritis was  $35.1 \pm 14.8$  yrs and mean disease duration was  $29.2 \pm 26.9$

**Table 1.** Clinical manifestations of patients with inflammatory bowel disease

	Ulcerative colitis (n=77)	Crohn's disease (n=52)
Age, yr	$38.5 \pm 16.8$	$34.0 \pm 15.4$
Sex, m : f	34 : 43	31 : 21
Disease duration, mo	$32.0 \pm 35.9$	$25.4 \pm 27.7$
Diarrhea, no(%) <sup>#</sup>	72(94)	36(69)
Hematochezia, no(%) <sup>#</sup>	62(81)	7(14)
Abdominal pain, no(%) <sup>#</sup>	55(71)	50(96)
Weight loss, no(%)	43(56)	30(58)
Arthritis, no(%)	15(20)	7(14)

<sup>#</sup>  $p < 0.05$

**Table 2.** Clinical characteristics of patients with arthritis of inflammatory bowel disease

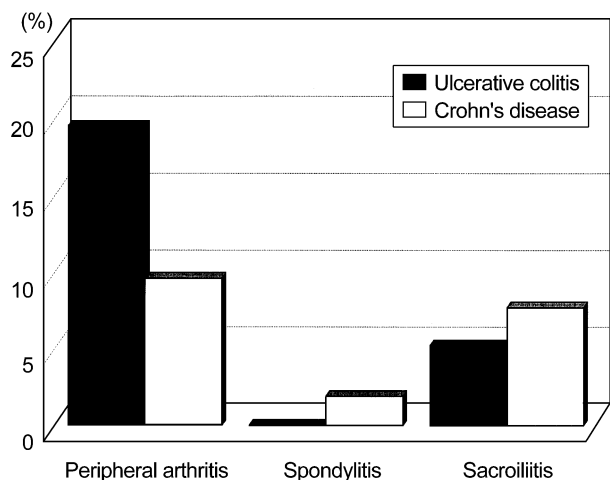
	With arthritis (n=22)	Without arthritis (n=107)
Age, yr	$35.1 \pm 14.8$	$37.0 \pm 16.7$
Sex, m : f <sup>#</sup>	5 : 17	60 : 47
Disease duration, mo	$29.2 \pm 26.9$	$29.5 \pm 34.2$
RF, positive no/total no	1/13	2/16
ESR, mm/hr <sup>#</sup>	$37.0 \pm 25.4$	$17.5 \pm 12.5$
CRP, mg/dl <sup>#</sup>	$2.15 \pm 2.50$	$0.74 \pm 1.54$

<sup>#</sup>  $p < 0.05$

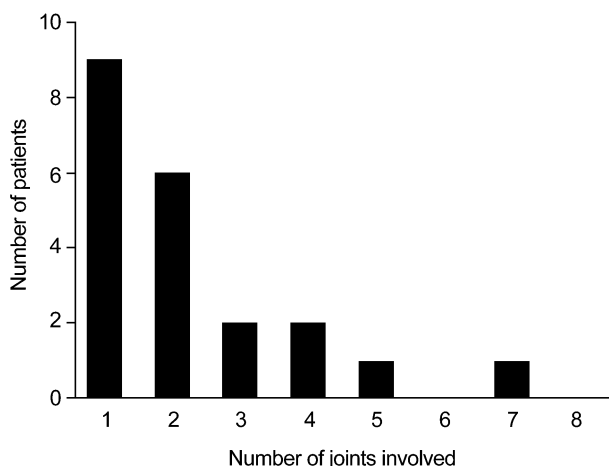
months (Table 2). The patients with arthritis were more females compared to the patients without arthritis ( $p < 0.05$ ). The arthritis in IBD was seronegative (negative RF) except one patient who showed low titer RF and monoarticular involvement (knee). Four patients with sacroiliitis showed HLA B-27 negativity, but one patient with spondylitis revealed HLA B-27 positivity. The patients with arthritis showed a higher erythrocyte sedimentation rate and C reactive protein compared to the patients without arthritis ( $p < 0.05$ ).

Those patients with arthritis were classified into the categories previously used by Gravalles and Kantrowitz (8) for IBD: peripheral arthritis, spondylitis, and sacroiliitis. Their incidence is shown in Fig. 1.

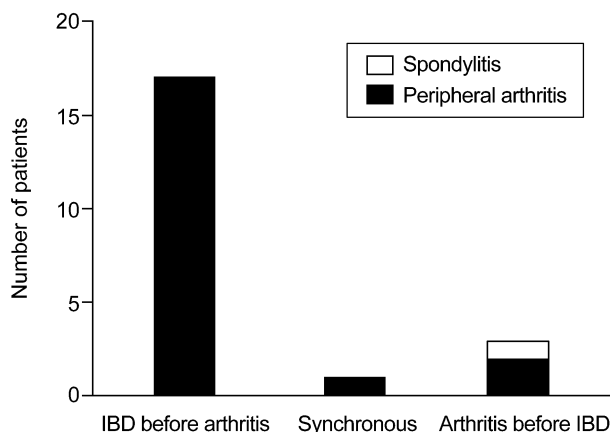
Peripheral arthritis was found in 20 patients (15.5%); 15 patients with UC (19.6%) and 5 patients with CD (9.6%) ( $p > 0.05$ ). Articular involvement tended to be monoarticular or pauciarticular, but two patients had polyarticular involvement (Fig. 2). The most frequently involved joint was the knee joint (14 patients), followed by the ankle (6 patients), elbow (3 patients), wrist (3 patients), proximal interphalangeal (3 patients), shoulder (2



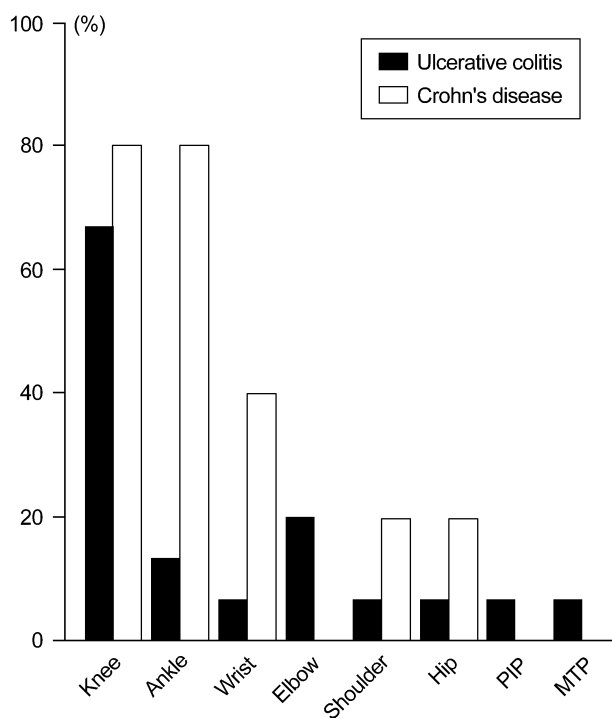
**Fig. 1.** Joint manifestations of IBD. There was no significant difference in the prevalence of arthritis between UC and CD.



**Fig. 2.** The number of involved joints in patients with arthritis and inflammatory bowel disease.



**Fig. 4.** Onset of inflammatory bowel disease related to arthritis.



**Fig. 3.** Joint involvement of peripheral arthritis in IBD.

patients), hip (2 patients), and metatarsophalangeal joint (1 patient) (Fig. 3). Spondylitis was diagnosed in one patient (1.6%) with inflammatory back pain and radiologic sacroiliitis grade 3, who developed CD two years later. Sacroiliac joint abnormality was observed in eight patients (6.2%); four with UC and four with CD. Of these, two patients were classified as suspicious sacroiliitis (grade 1). Radiographic sacroiliitis grade 2 was diagnosed in six patients. Both peripheral arthritis and sacroiliitis were found in six patients; four with UC and two with CD.

In most patients, arthritis appeared after the onset of bowel symptoms with mean duration of 21 months in UC and 25 months in CD. But arthritis preceded the onset of bowel symptoms in three patients for one month, three months, and two years respectively and was concurrent in one patient (Fig. 4).

An attempt was made to delineate involvement of bowel affected by IBD in patients with arthritis (Table 3). There was no difference in the incidence of arthritis between the patients with colitis of rectosigmoid region and with pancolitis in UC. In Crohn's disease, arthritis occurred in seven patients (20%) with colonic involvement, but not in patients without colitis.

**Table 3.** Arthritis according to the extent of bowel disease

	Ulcerative colitis		Crohn's disease	
	pancolitis n=42	rectosigmoid n=35	with colitis n=35	without colitis n=17
Arthritis, no (%)	9 (21)	6 (17)	7 (20)	0 (0)
Peripheral arthritis, no (%)	9 (21)	6 (17)	5 (14)	0 (0)
Spondylitis, no (%)	0 (0)	0 (0)	1 (3)	0 (0)
Sacroiliitis, no (%)	3 (7)	1 (2)	4 (11)	0 (0)

## DISCUSSION

The articular manifestations of IBD have been characterized by many investigators since they were first described by Bagen in 1929 (3-9,12-17). Most series of patients with IBD have estimated the frequency of joint involvement to be 4-26% in UC and 2-16% in CD (3-8, 13, 14). Several reports (3, 6, 8, 13) suggested the articular complications of UC and CD were similar, but more common in patients with CD. In the present study, the overall incidence of arthritis in IBD was 17.1%. It was more common in patients with UC than CD, but the difference did not reach statistical significance.

McEwen *et al.* (5) reviewed the arthritic manifestations in 84 patients with UC and 3 patients with CD. In that study, there were slightly fewer females (46%) than males (54%) in the patients with arthritis. However, their series had a relatively large number of patients with spondylitis, most of whom were males. More recent studies have supported a nearly equal incidence between both sexes (4, 14, 16). In our patients with IBD, the patients with arthritis were more commonly female compared to the patients without arthritis.

Gravallese and Kantrowitz (8) divided the arthritic manifestations of IBD into three clinical categories. First, a unique form of peripheral arthritis occurs in 15-20% of patients with IBD. This is self-limited, non-deforming arthritis that waxes and wanes with bowel flares and characteristically involves the lower extremities, especially the knees and ankles. The incidence of RF positivity is not higher in patients with IBD and peripheral arthritis than in the general population (9). Second, spondylitis, clinically and radiographically indistinguishable from idiopathic ankylosing spondylitis, occurs in 3-6% of patients with IBD. HLA B27 positivity occurs in 53-73% of cases, fewer than in idiopathic ankylosing spondylitis (18). Third, bilateral, symmetrical sacroiliitis is found in 4-18% of patients. This asymptomatic radiographic sacroiliitis is not associated with an increased incidence of HLA B-27, and may not progress to true spondylitis with spinal involvement (11).

The features of arthritis associated with IBD in this series were typical. Peripheral arthritis occurred in 15.5% of patients. Joint involvement tends to be monoarticular or pauciarticular and to affect most commonly the knee and ankle. Except one patient who showed low titer RF and monoarthritis (knee), all patients with peripheral arthritis showed RF negativity. Spondylitis occurred in only one patient (1.6%) with Crohn's disease, who revealed HLA B27 positivity. This was slightly lower than the incidence of spondylitis (3.7%) reported by Dekker-Saeys *et al.* (7). Radiographic sacroiliitis occurred in 6.2% of patients. Those patients were asymptomatic and show-

ed HLA B27 negativity. If technetium pyrophosphate bone scanning is used to evaluate such patients, the incidence of sacroiliac abnormalities may be as high as 52% (19). Results with bone scanning, however, are difficult to interpret, and probably overestimate the incidence of sacroiliitis.

Interestingly, cases have been reported in which arthritis predates documented bowel disease (6, 15). In all recent studies, including this one, the peripheral arthritis either followed the onset of IBD or appeared simultaneously with it in the majority of patients. This was true in 82% of the present series and 89% of all the collected from the literature (5, 9, 13, 16).

Few data are available regarding the cases of spondylitis. McEwen *et al.* (5) suggested that colitis preceded joint disease in only slightly lower percentages (74%) in patients with spondylitis than with peripheral arthritis. Hanslock (13) described that majority of the spondylitis patients developed articular symptoms before gastrointestinal ones. Schorr-Lesnick and Brandt (4) concluded that spondylitis usually occurred before the onset of overt intestinal diseases. In our patient with spondylitis, joint manifestation preceded the onset of IBD by two years. Recently, Mielants *et al.* (20) reported that gut inflammation, mainly subclinical, could be demonstrated in 68% of patients with spondyloarthropathy, and chronic gut lesion is related to the inflammation of Crohn's disease. They demonstrated the close relationship between gut and peripheral arthritis (21).

In their study of 108 patients with UC, Wright and Watkinson (17) found arthritis in 22% of patients with involvement of the entire colon, and 12% when colitis was limited to the left side. Scarpa *et al.* (22), however, showed a strong reverse relationship between the affected joint number and the extent of colitis and suggested that the extent of the intestinal lesion in ulcerative colitis seems to be important in the expression of the articular complications. In the fifteen of our patients with peripheral arthritis associated with IBD, pancolitis was involved in nine (21%) and rectosigmoid in six (17%). There was no difference in the incidence of arthritis according to the extent of bowel involvement in ulcerative colitis.

It is well known that there is a tendency for patients with arthritis to have more involvement of large bowel in CD (3, 6, 13). Interestingly, all our patients with arthritis associated with CD showed colonic involvement. However, no support is lent to the theory that such involvement is an essential associate of the articular disorders.

The basis for the arthritis associated with IBD is unknown. Both infection and immune mechanisms have been postulated. Hodgdon *et al.* (23) have demonstrated anticomplementary activity, suggesting immune com-

plexes, in the serum of patients with active IBD and acute arthritis.

In summary, arthritis occurred in 17.1% of patients with IBD in our series. The patients with arthritis associated with IBD were more females than males and had more active inflammations. Peripheral arthritis was found in 15.5% of patients and joint involvements were monoarticular or pauciarticular, frequently in the knee and ankle. Spondylitis was diagnosed in 1.6% and radiographic sacroiliitis was observed in 6.2% of patients with IBD. There was more common peripheral arthritis in patients with UC than CD. All the patients with arthritis and CD had colonic involvement. Generally, joint manifestations appeared after onset of bowel symptoms except spondylitis.

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