Fibromyalgia and Chronic Widespread Pain in Patients with Inflammatory Bowel Disease: A Cross Sectional Population Survey

ØYVIND PALM, BJØRN MOUM, JØRGEN JAHNSEN, and JAN TORE GRAN

ABSTRACT. ***Objective.*** To assess the prevalence of fibromyalgia (FM) and chronic widespread pain (CWP) in a population based cohort of patients with inflammatory bowel disease (IBD).

Methods. Patients in a prospective survey on newly diagnosed IBD were, 5 years after study entry, invited to a clinical examination including the investigation of musculoskeletal manifestations. A total of 521 patients were examined, corresponding to 80% of surviving cases with definite diagnoses of ulcerative colitis (UC) and Crohn's disease (CD). The diagnoses of FM and CWP strictly followed the American College of Rheumatology classification criteria of 1990.

Results. At clinical examination, FM was diagnosed in 18 patients (3.5%), 3.7% with UC and 3.0% with CD. The prevalence was 6.4% in females and 0.4% in males. Thirty-eight patients (7.3%) had CWP (8.5% with UC; 4.8% with CD). The female:male ratio was 27:3 in the UC group and 8:0 in CD. In 19 patients (50%), CWP occurred after onset of IBD. No correlation with the extent of intestinal inflammation and the occurrence of FM and CWP was found.

Conclusion. The prevalences of FM and CWP in patients with IBD were similar to those of the general population. There were no differences in prevalence of FM and CWP between UC and CD. Chronic idiopathic inflammation of the intestine does not appear to predispose to chronic widespread pain. (J Rheumatol 2001;28:590–4)

Key Indexing Terms:
CHRONIC WIDESPREAD PAIN CROHN'S DISEASE FIBROMYALGIA
INFLAMMATORY BOWEL DISEASE ULCERATIVE COLITIS

Inflammatory bowel diseases (IBD), including ulcerative colitis (UC) and Crohn's disease (CD), are debilitating diseases of unknown etiology with a variety of extraintestinal manifestations. Due to the intestinal disease itself and the accompanying extraintestinal manifestations, few chronic diseases can be more annoying and severe in their course than these bowel disorders. Among extraintestinal manifestations, symptoms and signs from the musculoskeletal system occur frequently in IBD. The presence of inflammatory rheumatic disease manifestations such as peripheral arthritis and spondyloarthropathy has been carefully described[1,2]. Significantly less knowledge has emerged regarding the incidence and implications of noninflammatory rheumatic manifestations.

Fibromyalgia (FM) is a chronic form of nonarticular rheumatism characterized by widespread pain, stiffness, and multiple tender points. It is regarded as part of a spectrum of chronic widespread pain (CWP). The etiopathogenesis of both conditions remains unknown. The prevalences of FM estimated in previous studies have shown significant variations, the results depending on the methods of selecting cases for study, age and sex group investigated, and the use of different criteria[3]. FM may exist as a primary syndrome or coexist with a variety of chronic disorders. Studies in patients with inflammatory diseases like rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) attending outpatient clinics have revealed a high prevalence of FM[4,5]. Such findings may indicate a role of stress related factors of chronic disease in the etiopathogenesis of FM. Similarly, a recent study reported a frequency of FM of 30% in patients with IBD. In that study, patients with CD were particularly prone to develop FM (49%)[6]. However, there are few investigations of the extent, prevalence, and possible prognostic significance of FM and chronic widespread pain in IBD. We assessed the prevalence of FM and CWP in a population based cohort of patients with IBD.

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MATERIALS AND METHODS

Study population. All newly diagnosed cases of IBD or possible IBD between January 1, 1990, and December 31, 1993, in 4 well defined areas in southeastern Norway (the counties of Oslo, Østfold, Telemark, and Aust-Agder) were recorded by the local departments of gastroenterology. To ensure complete ascertainment, all the 1236 general practitioners and clinicians at the 14 hospitals of the 4 participating counties received information about symptoms consistent with IBD, and were invited to refer all potential cases of UC or CD to the local gastroenterological outpatient clinic. The information was given prior to the start of the study by 3 written reminders. In addition, information about the study was presented at local meetings; as well, practicing gastroenterologists, internists, surgeons, and pediatricians were informed of the study. The total study population was 966,427 on January 1, 1992.

Endoscopy was chosen as the main instrument for diagnosis and for determining the distribution of disease in the colon. A total of 618 cases of UC and indeterminate colitis (IND) and 225 cases of CD were diagnosed[7,8]. In a followup between one and 2 years later, the diagnoses were reevaluated. Ninety-eight percent were available for followup; 4% were excluded as the diagnosis of IBD could not be definitely confirmed[9].

In a followup 5 years after inclusion, all patients in whom the clinical course, symptoms, and examination including endoscopy and histology confirmed the diagnosis of UC or CD[10] were invited to a structured interview and clinical examination by a rheumatologist.

However, 133 patients were excluded as followup could not verify a definite diagnosis of UC or CD. Moreover, 56 patients had died and 56 patients were not able to attend the followup (33 patients had moved out of the area, 23 due to concomitant serious illness or advanced age), and 77 did not respond to the invitation. Consequently, out of 654 patients with a definite diagnosis of UC or CD, 521 patients were clinically examined. Additionally, 155 evaluations were based on hospital records, telephone interviews, or mailed questionnaires.

Diagnostic criteria. Uniform methods and diagnostic criteria were applied. The initial classification of UC and CD required symptoms consistent with IBD for more than 4 weeks, excluding infections and other acute or chronic non-IBD.

The diagnosis of UC was based on the presence of at least 3 of the following criteria: (1) a history of diarrhea and/or blood/pus in stool; (2) macroscopic appearance by endoscopy, with continuous mucosal inflammation affecting the rectum in continuity with some or all of the colon; (3) microscopic features on biopsy compatible with UC; and (4) no suspicion of CD in small bowel radiograph or ileoscopy or in biopsy[7].

The diagnosis of CD was based on established criteria[11], as follows: (1) typical clinical features including abdominal pain, diarrhea, and weight loss; (2) macroscopic appearance at surgery or endoscopy; segmental, discontinuous, and/or patchy lesions with or without rectal involvement; discrete or aphthous ulcerations; fissuring and penetrating lesions, cobblestone, or strictures; (3) radiological evidence of stenosis in the small bowel, segmental colitis, or findings of fistulae; and (4) histologic evidence of transmural inflammation or epithelial granulomas with giant cells. Two or more of these criteria were required for the diagnosis of CD.

The extent and localization of colonic disease were based on endoscopic findings with characteristic histological signs of inflammation. Proctitis was defined as mucosal changes in the rectum up to 15 cm from the anus, left side colitis up to the splenic flexure, and, finally, inflammation beyond the splenic flexure was classified as extensive colitis. When the extent of disease changed during followup, the maximum extent of bowel involvement was recorded. The patients with CD were classified according to the Vienna classification[12].

Pain was considered chronic and widespread if present for at least 3 months on both the left and the right side of the body and below and above the waist. Axial skeletal pain had to be present, following the American College of Rheumatology (ACR) criteria of 1990[13].

The diagnosis of FM also followed ACR criteria of 1990 requiring a history of CWP and pain in 11 or more of 18 tender point sites on digital palpation[13].

The study was approved by the Regional Ethics Committee and the Norwegian Data Registry. Confidentiality of patient identity and records was maintained using guidelines suggested by the National Health Department.

Statistics. Fisher's exact test, chi-square test, and Student t test were used for statistical analyses, and a p value < 0.05 was regarded as significant.

RESULTS

Demographics and bowel diagnoses. A total of 521 patients were clinically examined, which corresponded to 80% of the surviving cases with a definite diagnosis of IBD. There were 353 patients with UC and 168 with CD. Patient characteristics are shown in Table 1.

Fibromyalgia. Of the 521 patients with UC or CD, 18 patients (3.5%) fulfilled the criteria for FM. The prevalences of FM in UC and CD were similar, 3.7% and 3.0%, respectively. Among the 266 women with IBD, 17 patients (6.4%) had FM compared to one patient (0.4%) among 255 male

Table 1. Characteristics of patients with ulcerative colitis (UC) and Crohn's disease (CD).

	UC, n = 353	CD, n = 168	Total, n = 521
Sex, M/F	176/177	79/89	255/266
Age, yrs, mean (range)*	46 (15–86)	39 (16–81)	43 (15–86)
Disease duration, mo, mean			
Symptoms	85	84	85
Diagnosis	73	74	73
Disease localization and extension, n (%)			
Proctitis	100 (28)		
Left side colitis	122 (35)		
Extensive colitis	131 (37)		
Upper GI		3 (2)	
Ileitis		41 (24)	
Colitis		62 (37)	
Ileocolitis		62 (37)	

*p = nonsignificant.

Table 2. Prevalence and epidemiological data of FM and chronic widespread pain (CWP) in clinically investigated patients with ulcerative colitis (UC) and Crohn's disease (CD).

	UC		CD	
	Male, n = 176	Female, n = 177	Male, n = 79	Female, n = 89
Fibromyalgia				
Number of patients (%)*	1 (0.6)	12 (6.8)	0 (0)	5 (5.6)
Age, yrs, mean (range)	37	46 (26–66)	—	44 (33–57)
Chronic widespread pain				
Number of patients (%)**	3 (1.7)	27 (15.3)	0 (0)	8 (9.0)
Age, yrs, mean (range)	46 (37–58)	49 (24–73)	—	40 (30–55)

*$p < 0.01$ in UC and $p < 0.05$ in CD (females vs males). **$p < 0.001$ in UC and $p < 0.05$ in CD (females vs males).

IBD patients ($p < 0.001$) (Table 2). In UC, 7 of the 13 patients (54%) developed symptoms of FM after onset of IBD (mean 5 yrs, range 3–11). In CD, 4 of the 5 patients developed symptoms of FM prior to onset of IBD. In the remaining patient, FM occurred 6 years after initial symptoms of IBD. The difference in onset of FM in UC and CD was not significant.

In patients with UC, proctitis was found in 8 of 13 cases (62%) with FM and in 92 of 340 cases (27%) without FM ($p < 0.05$). The distributions of left side colitis and extensive colitis in UC, and upper gastrointestinal involvement, ileitis, colitis, and ileocolitis in CD with and without FM were not significantly different. Systemic drug therapy included corticosteroids (5% of UC patients, 18% of CD patients), 5-aminosalicylic acid (22% of UC patients, 39% of CD patients), and sulfasalazine (22% of UC patients, 13% of CD patients). There were no differences in medical therapy and surgical interventions between patients with and without FM.

Chronic widespread pain. According to the criteria applied[13], all patients with FM also had CWP. In addition, 20 cases of CWP were found, hence 38 patients (7.3%) fulfilled the criteria of CWP. The prevalence was 8.5% in UC (30 patients) and 4.8% in CD (8 patients) ($p > 0.05$) (Table 2). In 19 patients (50%), CWP occurred after onset of IBD, of whom 6 patients (32%) developed CWP within one year, 9 patients (47%) within 1–5 years. Four patients (21%) developed CWP more than 5 years after onset of IBD. No significant difference was found concerning systemic medical treatment or rate of surgery in patients with and without CWP.

DISCUSSION

In patient cohorts, FM is frequently found in RA (13.6%)[4], SLE (22%)[14], hepatitis C virus infection (16%)[15], and human immunodeficiency virus infection (29%)[16]. In patients with IBD, few studies have addressed the occurrence of noninflammatory rheumatic manifestations. We are aware of only one study, in which FM was diagnosed in 30% of the patients[6]. This figure contrasts sharply with the overall prevalence of FM of 3.5% that we found. The disease duration, the male/female ratio, and the mean age of patients in these 2 studies were rather similar, and thus cannot explain the apparent discrepancy. Variations in social, cultural, and educational background of the patients studied may have influenced the results[17], but more likely, difference in study design appears to be the main reason for the differences in estimated prevalence rates.

Our study was based on patients recruited from the general population, whereas the study by Buskila and co-workers[6] was based on patients attending a hospital unit. Studies have shown differences between patients treated by general practitioners and those attending hospital units concerning disease severity (measured by global severity, Health Assessment Questionnaire Disability Index, and visual analog scales for pain) — hospital patients yielded higher scores[18]. Moreover, patients selected through population based studies have, in general, a lower incidence of concurrent disorders[19-21], perhaps suggesting a less frequent concurrence of FM and IBD than that revealed in hospital patients. This may explain why our estimates are close to the prevalence of FM of 2% found in a general US population[18] and 3.3% among noninstitutionalized adults in Canada[18a]. Finally, the estimated prevalence of FM of 8.5–10.5% in a general Norwegian female population[22] is not far from the prevalence of 6.4% among our women with IBD. We therefore conclude that among unselected cases of IBD, the occurrence of FM is similar to that of the general population.

In contrast to Buskila and co-workers[6], we found the same prevalence of FM in UC and CD patients. Further, we found no differences in usage of drugs and need for surgery in patients with and without FM. This is in agreement with surveys that found no differences of disease severity in patients with and without FM in RA[4] and SLE[14]. These findings further emphasize the difference between hospitalized

patients and patients selected through population surveys. The findings also indicate that the development of FM in IBD is not associated with the extent or severity of the intestinal disease.

In UC, proctitis was statistically more prevalent in patients with FM than in cases without FM. The difference is difficult to explain, and is likely not to be of real clinical significance.

Due to the criteria applied[13], the occurrence of CWP is obviously higher than that of FM. However, the prevalence of CWP in patients with IBD has to our knowledge not been previously ascertained. In the general adult population in the United Kingdom, the prevalence of CWP was estimated at 11.2%[23], whereas a Norwegian survey estimated a prevalence of 22% among middle aged women[24]. However, in our study, information was obtained through direct interview and not by mailed questionnaires, as in other studies[23,24]. The latter screening method may result in a higher response rate[22] and could partly explain the lower rates of CWP we found.

In spite of rather low prevalences, the occurrence of FM and CWP may have certain clinical implications. The clinical features of these chronic pain syndromes may in some patients imitate increased IBD activity and thus be misinterpreted as a disease relapse. Such a mistake may occasionally result in increased administration of drugs[25]. Clinicians should also be aware of the frequent occurrence of gastroenterological symptoms in FM. According to some authors, as many as 70% of patients with FM may exhibit symptoms consistent with irritable bowel syndrome[26]. Although our study revealed a low prevalence of FM in IBD, it is important to be aware of coexistence in some patients.

Our findings show that the occurrence of syndromes like chronic widespread pain and fibromyalgia is the same in inflammatory bowel disease as in the general population, suggesting that patients with IBD are not more likely to develop FM than individuals without IBD. The stress and pain accompanying IBD do not appear to be putative triggering agents for the development of FM and CWP. More studies are warranted to evaluate the relationship further, particularly investigations of cases with IBD of long disease duration. This study cannot rule out a possible effect of longstanding IBD upon musculoskeletal pain development.

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