PREVALENCE OF SPONDYLOARTHROPATHY IN PUERTO RICAN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

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Introduction: Inflammatory arthritis is the most common extraintestinal manifestation in patients with inflammatory bowel disease (IBD). Approximately 20% of all IBD patients will present with peripheral arthritis, sacroiliitis, or spondylitis. The purpose of this study was to determine the prevalence of spondyloarthropathy and sacroiliitis in Puerto Rican patients with IBD.

Methods: Patients were obtained from the IBD specialty clinic and all had a diagnosis of ulcerative colitis or Crohn's disease. All the patients who agreed to participate were entered in the study. Patients completed a questionnaire and underwent a physical examination. Radiologic examination of the lumbosacral spine and sacroiliac joints was performed. Blood samples were obtained for determining human leukocyte antigen class I and were serologically analyzed in the pathology department laboratory. Data were analyzed by using SPSS 10.0 for Windows.

Results: One hundred patients were enrolled; 57% had ulcerative colitis, and 43% had Crohn's disease. Fifty percent were female, and the mean age was 37 years (standard deviation 14.96 years). Seventy-seven percent reported history of joint pain, and 47% reported limitation due to joint pain. Physical examination revealed peripheral synovitis in five patients and spinal tenderness in 46 patients. Of the 100 patients, 42 had inflammatory back pain and fulfilled the criteria for spondyloarthropathy. Radiographs were obtained in 76 patients. They revealed grade 2 or greater sacroiliitis in 10 patients (13%) and ankylosing spondylitis in two patients (2.6%). Of the 82 patients with blood samples, human leukocyte antigen B27 was found in five patients (6%).

Conclusions: Of the study population of Puerto Ricans with IBD, 42% had spondyloarthropathy. This prevalence is higher than reported in Caucasians (20%–30%). Sacroiliitis had a similar prevalence as reported in Caucasians, but the prevalence of peripheral arthritis was much lower. (*Ethn Dis*. 2008;18[Suppl 2]:S2-225–S2-229)

Key Words: Spondyloarthopathy, Inflammatory Bowel Disease, Puerto Rican

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INTRODUCTION

Inflammatory bowel disease (IBD) comprises the clinical entities of ulcerative colitis and Crohn's disease. These are chronic, idiopathic, inflammatory diseases of the gastrointestinal tract that share common symptoms such as diarrhea, abdominal pain, fever, and weight loss. Ulcerative colitis involves all or part of the colon, and Crohn's disease commonly involves the terminal ileum and proximal colon.[1] The pathophysiology of IBD is not well understood but involves dysregulation of the intestinal mucosal immune system with subsequent liberation of inflammatory cytokines that initiate and perpetuate the inflammatory response.

The prevalence of IBD in Puerto Rico in 1996 was 106.1 per 100,000 inhabitants: 41.4 per 100,000 for Crohn's disease and 62.2 per 100,000 for ulcerative colitis.[2] The incidence was 3.1/100,000 in 1996 and 7.74/100,000 in 2000.[3] Extraintestinal manifestations occur in 21%–36% of patients with IBD.[4] Almost every organ system can be affected. The pathogenesis of these extraintestinal manifestations is not well understood, but the affected intestinal mucosa may provide an inflammatory immune response that may be the cause of the manifestations. The most common extraintestinal manifestation in IBD is arthritis, which occurs in 2%–20% of patients.[1] It may present as peripheral or axial disease. Peripheral arthritis occurs in 5%–20%, and the risk increases with the extent of the colonic involvement. Axial arthritis occurs in 2%–25% of patients and does not parallel the bowel inflammatory activity. Axial arthritis may be divided into spondylitis or isolated sacroiliitis.[4] Spondylitis is a type of spondyloarthropathy, which includes a group of arthritides that share clinical, biological, and genetic characteristics (presence of the human leukocyte antigen [HLA] B27 gene). Spondyloarthropathy includes ankylosing spondylitis, psoriatic arthritis, and reactive arthritis. The prevalence of spondyloarthropathy in the general population is 2%. However, in patients with IBD the prevalence of spondyloarthropathy increases to 10%–35%.[1,5] Besides arthritis, patients with spondyloarthropathy may also have uveitis, dactylitis, psoriatic lesions on the skin, and the HLA B27 gene.

The most severe subtype of spondyloarthropathy is ankylosing spondylitis, a type of axial arthritis that frequently causes disability. Its prevalence in the general population is .2%–1.2%; in IBD, the prevalence increases to 10%. Ankylosing spondylitis is more common among men and is more frequently associated with Crohn's disease. Until recently, therapeutic armamentarium for patients with ankylosing spondylitis was limited, but the recent discovery of anti-tumor necrosis factor agents as effective therapy for ankylosing spondylitis mandates aggressive early diagnosis of this disease in order to prevent disability.[6,7] The other type of axial arthropathy is isolated sacroiliitis. It occurs in 2%–18% of patients with IBD as evidenced by conventional

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radiography, since it is usually an asymptomatic condition.[5,7–9]

Peripheral arthritis usually responds to treatment of the underlying intestinal inflammation, where axial arthropathy does not.[9] Peripheral arthritis is more frequent in Crohn's disease than in ulcerative colitis, although patients with ulcerative colitis have a higher prevalence of arthralgias. Other joint manifestations seem to be similar in ulcerative colitis and Crohn's disease.[10]

Considerable evidence links HLA B27-associated diseases with gastrointestinal inflammation. Among the most important are the increased prevalence of ankylosing spondylitis in patients with IBD and the presence of microscopic bowel inflammation in patients with HLA B27.[5,11] In arthropathy associated with IBD, axial involvement is associated with HLA B27, but peripheral disease is not.[12]

The prevalence of spondyloarthropathy in Puerto Ricans with IBD is unknown. A recent study of the clinical behavior of IBD in Hispanics compared to Caucasians has revealed several differences among the two groups that raise the issue whether ethnicity plays a role in the clinical manifestations of arthritis in IBD.[13] In this study, we characterize and establish the prevalence of axial and peripheral arthritis in Puerto Ricans with IBD and the presence and association of the arthritis with the HLA B27 gene.

METHODS

One hundred patients with ulcerative colitis or Crohn's disease attending the IBD Clinic at the Puerto Rico Medical Center were evaluated for the presence of clinical and subclinical manifestations of articular involvement. The diagnosis was confirmed by endoscopic, radiologic, and histologic criteria. The patients were selected in a continuous fashion as they came to the outpatient clinic for their regularly scheduled appointments from January 2002 through December 2003.

A comprehensive interview was conducted, which included level of education; duration of disease; co-morbidities; and relevant history of smoking, medications, intestinal surgery, onset of joint pain, sites of joint inflammation, inflammatory and non-inflammatory back pain, ocular symptoms, psoriasis, and Achilles tendonitis. Inflammatory back pain was defined by using the criteria proposed by Calin.[14] These criteria include back pain present for at least three months, insidious in onset, and associated with morning stiffness that improves with exercise and age <40 years.

The subjects underwent a complete physical examination by a rheumatologist, with special emphasis on axial and peripheral joint involvement. Peripheral joints were evaluated for tenderness, joint swelling, and limitation of motion. The axial skeleton was evaluated for vertebral tenderness and axial mobility by using the Schober index, which is measured by asking the subject to bend forward at the waist with the legs straight. The Schober index is considered pathological if the subject's maximal anteflexion of the lumbar spine is <4 cm.[15] Enthesitis, especially of the Achilles tendon, was evaluated by palpation. The presence of psoriatic lesions or dactylitis was recorded.

The European Spondyloarthropathy Study Group (ESSG) criteria were used as additional criteria to establish the diagnosis of spondyloarthropathy. According to the ESSG, any subject with inflammatory spinal pain or peripheral arthritis plus IBD has a spondyloarthropathy.[16]

The following radiologic studies were performed: anteroposterior views of the sacroiliac joints and anteroposterior and lateral views of the lumbosacral joints. The sacroiliac joint was graded for unilateral or bilateral involvement for sacroiliitis. Sacroiliitis was graded according to the New York criteria scale: 0 (normal), 1 (doubtful), 2 (mild irregularity and sclerosis), 3 (marked erosion without ankylosis), and 4 (complete ankylosis).[17] The lumbosacral joint radiographs were evaluated for squaring of the vertebrae, spinal ligament calcification, bamboo spine, and erosions. A single radiologist, who was informed whether the subject had IBD but was blinded to the subjects' symptoms, evaluated all the radiographs.

A blood sample was taken to determine HLA class I. Class I haplotypes were determined by serologic analysis. The HLA haplotype analysis was performed by the histocompatibility laboratory of the pathology department. Results were compared with the general prevalence of HLA-B27 obtained from paternity and pretransplant histocompatibility testing data.

Statistical Analysis

Frequency distributions and descriptive statistics were computed for all the categorical and continuous variables. Prevalence odds ratios and 95% confidence intervals were computed to assess associations between variables. Fisher exact test, χ^2 test, and the Student t test were used for statistical analyses depending on the variable type and the number in cells in the contingency tables; $P<.05$ was regarded as significant. Data were entered and analyzed by using SPSS version 10.0 (SPSS, Inc., Chicago, Ill) for Windows.

RESULTS

A total of 100 subjects with a diagnosis of IBD were enrolled in the study (Table 1); 57% had ulcerative colitis, and 43% had Crohn's disease. The mean duration of disease was 8.4 years (standard deviation [SD] 7.75 years) for ulcerative colitis and 6.7 years (SD 7.00 years) for Crohn's disease. Eighty-six percent were currently on medications for IBD. This percentage was higher for patients with

Table 1. Demographic characteristics in Ulcerative Colitis (UC) and Crohn's Disease (CD) *N*=100

	UC	CD	
	***n*=57**	***n*=43**	***P* value**
Mean years with disease	8.39 (SD=7.75)	6.70 (SD=7.00)	
Women, %	33 (57.9)	17 (39.5)	.70
Men, %	24 (42.1)	26 (60.5)	
Attended college	28 (49.10)	27 (62.8)	.11
Currently using medication for IBD	44 (77.2)	42 (97.7)	.003
Underwent surgery for IBD	22 (38.6)	35 (81.4)	.001
Past history of joint pains	45 (78.9)	32 (74.4)	.594
Presence of joint pains (last 30 days)	32 (55.6)	20 (46.9)	.452
Joint pain causing limitation of movement	24 (42.2)	23 (53.1)	.345
Spinal pain improves with exercise	24 (42.2)	18 (41.9)	.98

Crohn's disease (97.7%) than for patients with ulcerative colitis (77.2%) (P=.0003). A high percentage of patients (57%) required intestinal surgery, and this percentage was higher for Crohn's disease (81.4%) than for ulcerative colitis (38.6%) (P<.001).

Only nine subjects were diagnosed with arthritis (five with ulcerative colitis and four with Crohn's disease) and two with sacroiliitis (both with Crohn's disease) before study entrance. However, 77% of all patients had past history of joint pain (ulcerative colitis 78.9% and Crohn's disease 74.4%, P=.594). Of these 77 subjects, 52% recalled joint pain during the last month. The presence of joint pain during the last month was similar for both groups: 55.6% for ulcerative colitis and 46.9% for Crohn's disease (P=.452). Limitation of movement due to joint pain was reported by 47% of the entire group: 42.2% of the ulcerative colitis patients and 53.1% of the Crohn's disease (P=.345). On physical exam, 5% of the subjects had peripheral arthritis, and spinal tenderness was elicited in 46.3% (Table 2). In 42% the pain improved with exercise and met the criteria of Calin for inflammatory spinal pain (Table 1).

Radiologic studies done in 76 subjects revealed sacroiliitis in 13% and ankylosing spondylitis in 2%. The prevalence of spondyloarthropathy is 2% if ankylosing spondylitis is the sole criterion used for establishing spondyloarthropathy. However, the prevalence increases to 42% when the ESSG criteria are applied.

Table 2 shows clinical manifestations by group of study. No significant differences were seen in uveitis, conjunctivitis, dactylitis, enthesopathy of the Achilles tendon, heel pain, or psoriatic lesions on skin.

HLA analysis for class I haplotypes was performed in 82 of the 100 patients. HLA type I analysis revealed HLA B27 in five subjects (6%): one had ankylosing spondylitis, and the other four did not have any radiologic findings.

DISCUSSION

Even though joint disease is the most common extraintestinal manifestation of IBD, few studies have focused on arthritis in such patients. The peripheral or axial joints may be involved, and although peripheral arthritis is more common, axial arthritis frequently leads to chronic debilitating

Table 2. Clinical manifestations in ulcerative colitis (UC) and Crohn's disease (CD). (*N*=100)

	UC	CD	
Manifestations*	***n*=57**	***n*=43**	***P* value†**
Presence of peripheral arthritis	3 (5.26)	2 (4.65)	.89
Spinal pain in physical exam	39 (50.87)	18 (41.86)	.37
Uveitis	1 (1.75)	1 (2.32)	.84
Conjunctivitis	2 (3.5)	1 (2.32)	.73
Dactylitis	2 (3.5)	1 (2.32)	.73
Achilles tendonitis	1 (1.75)	1 (2.32)	.84
Heel pain	4 (7.0)	2 (4.65)	.62
Psoriatic lesions on skin	19 (1.75)	1 (2.32)	.84

Data are expressed as numbers (%).
* Multiple manifestations may be encountered per person
† P value > 0.05 for all clinical manifestations

disease and is the focus of the present study. Axial arthritis (inflammatory spinal pain or sacroiliitis) in a patient with IBD is, by definition, a spondyloarthropathy.[4–11,16,18]

The overall prevalence of spondyloarthropathy in our sample was 42%. This finding agrees with the published prevalence in Caucasians with IBD: 2%–40%.[5,9,18] Although this discrepancy may be related to ethnic factors, the difference may be the application of the less strict ESSG criteria for the diagnosis of spondyloarthropathy. In a patient with IBD, at least three months of back pain that is worse in the mornings and decreases with mobility is sufficient for the diagnosis of spondyloarthropathy. These data suggest that spondyloarthropathy is probably more common than was initially thought.

Two percent of our subjects had ankylosing spondylitis. These two patients had symptoms of lumbar spinal pain and limitation of movement for years but had never been studied for arthritis. At study entry, both patients presented with marked limitation of lumbar spine mobility and the typical ''bamboo spine'' appearance on lumbosacral radiographs, denoting advanced ankylosing spondylitis. This finding underscores the need to increase awareness that our population of IBD patients need to be monitored for axial complications. Careful clinical and radiological screening of patients with IBD for the development of early ankylosing spondylitis might be considered, especially with the advent of effective therapies, such as infliximab and etanercept, which may halt the progression of ankylosing spondylitis. The overall prevalence of ankylosing spondylitis in this study is within the range reported in other studies (1.1%–10%).[8,18,19]

Thirteen percent of the subjects had sacroiliitis, similar to other studies, which report a 2%–25% prevalence.[5,9,18] Only two (2%) had been diagnosed with sacroiliitis before study entry, suggesting that sacroiliitis is frequently asymptomatic. The presence of sacroiliitis on radiography is frequently the first manifestation of ankylosing spondylitis.[18]

A recent study characterized the clinical expression of IBD in African Americans, Hispanics, and non-Hispanic Whites.[13] It reported a 1.2% prevalence of sacroiliitis in Hispanics, compared to 5.8% in African Americans and 1.7% in Whites, suggesting ethnic differences in the phenotypic expression of sacroiliitis. The Hispanics recruited for that study came mainly from the Los Angeles area. A larger prevalence of sacroiliitis in Puerto Ricans, as compared with other mainland Hispanics, may originate from the ethnic mixture of the present-day Puerto Rican, which is recognized to have important genetic contributions from the African racial group.

Peripheral arthritis of the shoulders, knees, and ankles occurred in 5% of our subjects, lower than in most reported studies (10%–20%).[5,8,15,20] The prevalence of peripheral arthritis was similar among ulcerative colitis and Crohn's disease patients, in contrast to several studies that have shown a higher frequency in Crohn's disease patients.[12] Peripheral arthritis in patients with IBD responds to the treatment of the intestinal disease. The low prevalence of peripheral arthritis in our study group may have been secondary to the high rate of patients who were taking medications for their IBD (86%) and the high percentage of patients who had undergone intestinal surgery (57%). On the other hand, axial arthropathy does not respond to medical or surgical treatment of IBD, with the exception of anti-tumor necrosis factor agents.[9]

The prevalence of HLA B27 in our sample was 6%. The prevalence of HLA B27 in the general Puerto Rican population is .5%. One study reports a frequency of ≤15% in IBD without axial arthritis and 30% with axial arthritis.[1] Therefore, although general prevalence of HLA B27 is much lower in Puerto Ricans as compared with Caucasians, it approaches that of Caucasians when IBD with or without axial arthritis is present.

In summary, spondyloarthropathy prevalence in our group of Puerto Ricans with IBD was found to be high if the ESSG criteria were used, which was similar to other published data, but the prevalence of peripheral arthritis was found to be much lower than reported in other studied populations.

Implications for Improving Health Disparities

This study shows that Hispanics with IBD have a higher prevalence of spondyloarthropathy and that patients with low back pain should be carefully evaluated in order to avoid progression to a debilitating disease. The results demonstrate a need to increase awareness that ethnic groups have different phenotypic expressions of the same disease and that evaluation and management strategies should be tailored to ethnic background.

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REFERENCES

1. Mc Quaid K. Alimentary tract. In: Tierney L, Mc Phee S, Papadakis M, eds. *Current Medical Diagnosis and Treatment.* 44th ed. New York: Mc Graw Hill; 2005. p. 602–611.
2. Torres EA, De Jesus R, Perez CM, et al. Prevalence of inflammatory bowel disease in an insured population in Puerto Rico during 1996. *P R Health Sci J*. 2003;22(3):253–258.
3. Appleyard CB, Hernandez G, Rios-Bedoya CF. Basic epidemiology of inflammatory bowel disease in Puerto Rico. *Inflamm Bowel Dis*. 2004;10(2):106–111.
4. Su C, Judge T, Lichtenstein G. Extraintestinal manifestations of inflammatory bowel disease. *Gastroenterology Clinics*. 2002;31(1):307–327.
5. de Vlam K, Mielants H, Cuvelier C, et al. Spondyloarthropathy is underestimated in inflammatory bowel disease: prevalence and HLA association. *J Rheumatol*. 2000;27: 2860–2865.

6. Sieper J, Rudwaleit M, Khan MA, et al. Concepts and epidemiology of spondyloarthritis. *Best Pract Res Clin Rheumatol*. 2006; 20(3):401–417.
7. Turkcapar N, Toruner M, Soykam I. The prevalence of extraintestinal manifestations and HLA association in patients with inflammatory bowel disease. *Rheumatol Int*. 2006; 26(7):663–668.
8. Gravallese EM, Kantrowitz FG. Arthritic manifestations of inflammatory bowel disease. *Am J Gastroenterol*. 1988;83(7):703–709.
9. Palm O, Moum B, Ongre A, et al. Prevalence of ankylosing spondylitis and other spondyloarthropathies among patients with inflammatory bowel disease: a population study. *J Rheumatol*. 2002;29:511–515.
10. Kethu SR. Extraintestinal manifestations of inflammatory bowel diseases. *J Clin Gastroenterol*. 2006;40(6):467–475.
11. Gaston JSH. Pathogenic role of gut inflammation in the spondyloarthropathies. *Curr Opininion in Rheum*. 1997;9:302–307.
12. Mendoza JL, Lana R, Taxonera C, et al. Extraintestinal manifestations in inflammatory bowel disease: difference between Crohn's disease and ulcerative colitis. *Med Clin (Barc)*. 2005;125(8):297–300.
13. Nguyen GC, Torres EA, Regueiro M. Inflammatory bowel disease characteristics among African Americans, Hispanics, and non-Hispanics Whites: characterization of a large North American cohort. *Am J Gastroenterol*. 2006;101:1012–1023.
14. Calin A, Porta J, Fries JF, et al. Clinical history as a screening test for ankylosing spondylitis. *JAMA*. 1977;237:2613–2614.
15. Taurog J. The spondyloarthritides. In: Fauci A, Langford C, eds. *Harrison's Rheumatology*. New York: Mc Graw Hill; 2006. p. 139–155.
16. Dougados M, van der Linden S, Juhlin R, et al. The European Spondyloarthopathy Study Group preliminary criteria for the classification of spondyloarthropathy. *Arthritis Rheum*. 1991;34:1218–1227.
17. Bennet PH, Burch TA. New York symposium of population studies in rheumatic diseases. *Bull Rheum Dis*. 1967;17:453–458.
18. De Vos M. Review article: joint involvement in inflammatory bowel disease. *Aliment Pharmacol Ther*. 2004;20:36–42.
19. Queiro R, Maiz O, Intxausti JR, et al. Subclinical sacroiliitis in inflammatory bowel disease: a clinical and follow-up study. *Clin Rheumatol*. 2000;19:445–449.
20. Munch H, Purrmann J, Reis HE, et al. Clinical features of inflammatory joint and spine manifestations in Crohn's disease. *Hepatogastroenterology*. 1986;33:123–127.