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ORIGINAL ARTICLE

Axial Pain and Arthritis in Diagnosed Inflammatory Bowel Disease: US National Health and Nutrition Examination Survey Data

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Abstract

Objective: To estimate the nationally representative prevalence of chronic axial pain, inflammatory back pain (IBP), axial spondyloarthritis (axSpA), and peripheral arthritis in persons diagnosed with inflammatory bowel disease (IBD).

Patients and Methods: US National Health and Nutrition Examination Survey (NHANES) data from the 1976-1980 and 2009-2010 survey cycles.

Results: In NHANES 1976-1980, the chronic axial pain prevalence in participants with diagnosed ulcerative colitis (UC) was 19.5% vs 7.2% in the general population ($P<.01$). Neck or upper back, lower back, and Amor criteria-based axial pain were also significantly increased (11.2%, 14.5%, and 13.0%, respectively, vs 3%-5% in the general population ($P<.01$). In those with diagnosed UC, 40% had axial pain onset at an age older than 45 years; 30.2% reported peripheral arthralgias, and 12.2% reported peripheral arthritis. Arthritis findings on examination were uncommon. In NHANES 2009-2010, axial pain in those diagnosed with IBD had similar patterns.

Conclusion: Despite high rates of chronic axial pain in those with IBD, few cases met the IBP and axSpA classification criteria. This apparent discrepancy is unexplained. However, in IBD, axial pain onset at an age older than 45 years is common; and these may not meet IBP and axSpA age criteria. Also, neck pain was increased in those with IBD but is not included in most IBP and axSpA criteria. Peripheral arthralgias and chronic arthritis symptoms were common, but examination findings were not, suggesting that tenosynovitis or enthesitis is more likely than frank arthritis to occur in patients with UC.

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Inflammatory bowel disease (IBD), including ulcerative colitis (UC) and Crohn's disease, has high morbidity, burdening patients, families, and the health care system. The global IBD prevalence rates vary widely.[1] The 1999 and 2015 US National Health Interview Surveys estimated the prevalence of medically diagnosed IBD to be 0.9% and 1.3%, respectively, or 1.8 and 3.1 million persons, respectively.[2,3] Extraintestinal, musculoskeletal complications add significantly to IBD morbidity. The chief complication among these is spondyloarthritis, inflammation of appendicular, entheseal, and axial or spinal structures. The classical phenotype of ankylosing spondylitis (AS) develops in some patients; however, the preferred term is axial spondyloarthritis (axSpA). Alternately, patients may have only peripheral joint involvement, termed as peripheral spondyloarthritis (pSpA). Patients may have both axSpa and pSpA. Currently, there is uncertainty about the prevalence of IBD-related axSpA and pSpA. The published rates vary widely: 3%-46% for pSpA and 1%-10% for AS.[4,5] Reviews have noted that the spectrum of IBD-related spondyloarthritis phenotypes remains incompletely

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TABLE 1. Prevalence of Chronic Axial Pain, Inflammatory Bowel Disease, Axial Spondyloarthritis, and Arthritis Diagnosis in Patients With inflammatory Bowel Disease[a,b]

NHANES 1976-1980	n	UC cases, % (95% CI)	n	No UC, % (95% CI)	*P*
Axial pain >3 mo	30	19.5 (12.9-27.6)	808	7.2 (6.4-8.1)	<.01
Neck or upper back pain	19	11.2 (5.8-18.9)	366	3.2 (2.8-3.7)	.01
Mid back pain	3	2.3[c]	113	1.0 (0.9-1.2)	[c]
Lower back pain	16	14.5 (8.5-22.6)	381	5.1 (4.5-5.7)	<.01
Amor axial pain positive	15	13.0 (7.4-20.5)	447	4.3 (3.7-4.9)	<.01
Medical diagnosis of arthritis	89	41.1 (31.3-51.5)	3756	21.1 (19.1-22.3)	<.01
NHANES 2009-2010		IBD cases		No IBD	
Axial pain >3 mo	21	27.7 (11.1-44.3)	959	19.1 (17.1-21.2)	.11
Neck or upper back pain	13	19.0[c]	443	8.5 (7.6-9.4)	[c]
Mid back pain	3	1.0[c]	222	4.0 (3.3-4.6)	[c]
Lower back or buttock pain	16	20.0[c]	778	15.5 (13.8-17.1)	[c]
Amor axial pain positive	13	17.2[c]	637	12.4 (11.2-13.7)	[c]
Medical diagnosis of arthritis	26	30.6 (17.8-47.3)	1041	19.1 (17.8-20.3)	.08
Calin or ESSG IBP criteria	3	6.1[c]	271	5.6 (4.7-6.5)	[c]
Rudwaleit IBP criteria positive	2	7.8[c,d]	235	4.8 (4.2-5.5)	[c]
Any axSpA criteria positive	4	10.0[c]	89	1.8 (1.2-1.3)	[c]
Amor axSpA criteria positive	3	5.8[c]	40	0.8 (0.5-1.1)	[c]
ESSG axSpA criteria positive	1	4.4[c]	69	1.4 (.09-1.9)	[c]

[a]axSpA, axial spondyloarthritis; CI, confidence interval; ESSG, European Spondyloarthropathy Study Group; IBD, inflammatory bowel disease; IBP, inflammatory back pain; NHANES, US National Health and Nutrition Examination Survey; UC, ulcerative colitis.
[b]Sample sizes: NHANES 1976-1980: 13,566 (UC cases: 164); NHANES 2009-2010: 5041 (IBD cases: 62).
[c]Estimate not statistically reliable, variance estimate not shown.
[d]Criteria 7B or 8A positive on the basis of the age group of 20-39 years (subsample size = 3188).

characterized. There is high patient-to-patient variability and significant heterogeneity in the methodologies used to define its features.[6,7]

Currently, there are no US nationally representative estimates for the prevalence of IBD-related axial pain, inflammatory back pain (IBP), axSpA, and pSpA. The US National Health and Nutrition Examination Survey (NHANES) routinely provides US population-based arthritis surveillance data for rheumatoid arthritis, osteoarthritis, and others.[8] Although not designed as IBD-arthritis studies, 2 NHANES cycles (2009-2010 and 1976-1980) collected nationally representative data on medically diagnosed IBD, axial pain, and peripheral arthritis. The NHANES 2009-2010 cycle was specifically designed to estimate the US prevalence of IBP and axSpA.[9,10]

The NHANES 1976-1980 cycle collected interview and examination data for UC, axial pain, and peripheral joint arthritis. In both the surveys, the US prevalence of self-reported, physician-diagnosed IBD or UC was consistent with previously reported national survey estimates; furthermore, IBD or UC diagnosis was supported by NHANES clinical data.[2,3,11]

This report estimates the US national prevalence of chronic axial pain, IBP, axSpA, and pSpA in patients diagnosed with IBD on the basis of disease classification criteria and NHANES data. These data provide an opportunity to examine how existing IBP and axSpA classification criteria may or may not apply in the IBD setting, potentially bearing on the issues of the underdiagnosis of IBD-related arthritis and the feasibility of fielding future, specifically designed NHANES-based national surveillance studies on IBD arthritis.

MATERIALS AND METHODS

The US National Health and Nutrition Examination Survey is a series of nationally representative, cross-sectional surveys monitoring US population health, including in-person household interviews and health

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TABLE 2. US National Health and Nutrition Examination Survey 1976-1980 Interview-Based Prevalence of Peripheral Arthralgia and Arthritis[a,b]

	Peripheral arthralgias					Peripheral joint arthritis[c]				
	All UC		No UC			All UC		No UC		
Joint distributions	n	% (SE)	n	% (SE)	*P*	N	% (SE)	n	% (SE)	*P*
Any joint involved	55	30.2 (5.4)	2163	19.0 (0.7)	.02	23	12.2 (3.4)	771	6.5 (0.4)	.01
Pauciarticular	32	19.1 (4.4)	1678	16.2 (0.6)	.12	18	9.9 (2.8)	626	5.6 (0.4)	.02
Polyarticular	22	14.8 (4.0)	468	4.3 (0.4)	.01	5	3.3[d]	130	1.0 (0.1)	[d]
Symmetric	43	26.1 (5.4)	1104	10.0 (4.5)	.01	18	7.6[d]	405	3.1 (0.2)	[d]
Asymmetric	11	6.3[d]	1042	10.5 (0.5)	[d]	5	5.1[d]	351	5.2 (0.4)	[d]
Upper extremities	39	21.9 (4.6)	1371	13.3 (0.7)	.03	16	7.8[d]	452	4.1 (0.3)	[d]
Hand-wrist	32	16.9 (3.2)	819	8.3 (0.6)	.01	14	6.9[d]	379	3.4 (0.3)	[d]
Elbow	18	14.2 (4.1)	469	5.4 (0.4)	.03	6	3.7[d]	102	1.0 (0.1)	[d]
Shoulder	23	16.6 (4.5)	759	7.6 (0.4)	.01	4	2.9[d]	127	1.1 (0.1)	[d]
Lower extremities	44	28.7 (5.4)	1462	13.1 (0.6)	.01	16	9.5[d]	489	4.4 (0.3)	[d]
Hips	24	19.0 (4.9)	532	5.1 (0.4)	.01	4	2.5[d]	74	0.6 (0.1)	[d]
Knee	29	22.8 (5.3)	1057	9.8 (0.5)	.02	10	5.5[d]	323	2.9 (0.2)	[d]
Foot ankle	21	17.2 (4.8)	586	5.8 (0.4)	.03	7	5.5[d]	167	1.4 (0.1)	[d]

[a]NHANES, US National Health and Nutrition Examination Survey; SE, standard error; UC, ulcerative colitis.
[b]Sample sizes: UC = 131cases; no UC = 10,272 persons.
[c]Reported peripheral joint arthralgia plus joint swelling and palpable tenderness for 6 weeks or more. Symmetric joint involvement is 1 or more pair of symmetrically involved joints. Pauciarticular and polyarticular definitions are from the study by Orchard et al[14] (≤5 joints and >5 joints involved, respectively).
[d]Estimate potentially not reliable, variance estimate not shown.

examinations. It uses a complex, demographically based, multistage survey design to ensure nationally representative samples and minimize biases.[12] The US National Center for Health Statistics Ethics Review Board approves protocols, operations, and data releases. Written informed consent is obtained from all participants. Publicly available NHANES data were used for analysis.[13]

Details about the history of physician-diagnosed UC (both the surveys) and Crohn's disease (NHANES 2009-2010) were obtained via interviews; these self-reports are generally consistent with actual physician-diagnosed IBD. Cases of IBD from NHANES 2009-2010 had high colonoscopy rates at diagnosis, increased rates of characteristic IBD gastrointestinal symptoms, and IBD-related extraintestinal manifestations (uveitis, colon cancer, osteoporosis, and AS). Cases of UC from NHANES 1976-1980 had increased gastrointestinal symptoms, including bleeding, transfusions, anemia, and abdominal operations.[11] Cases of IBD had increased clinical visits and hospitalizations. The sample sizes were as follows: NHANES 2009-2010: 5105 persons, 62 IBD cases; NHANES 1976- 1980: 13,566 persons, 164 UC cases.

Both the surveys collected axial pain data; peripheral arthritis data were only collected in 1976-1980. Chronic axial pain was defined as pain on most days for 3 or more months. Data on peripheral joint symptoms were obtained for a duration of 6 weeks or more. Oxford criteria were used for analysis.[14] In NHANES 2009-2010, a cognitively tested questionnaire with pain diagrams was used to estimate the prevalence of axial pain; IBP on the basis of the Calin criteria, European Spondyloarthropathy Study Group (ESSG) criteria, and criteria described by Rudwaleit et al; and axSpA on the basis of the ESSG and Amor criteria.[15-18] The axial levels were as follows: neck, C1-C7; upper back, T1-T7; mid back, T8-T12; lower back, L1-L5; and buttocks: sacrum and buttocks.

Amor criteria-based axial pain was characterized by lumbar or dorsal pain (T1-L5) at night or by lumbar or dorsal stiffness in the morning. Assessment of Spondyloarthritis International Society criteria for IBP or axSpA were published after the 2009-2010 survey was

TABLE 3. US National Health and Nutrition Examination Survey 1976-1980 Peripheral Joint Symptoms and Examination Findings[a]

	All UC		No UC		
	n	% (95% CI)	n	% (95% CI)	*P*
Reference interview data					
Current SR arthralgias[b]	44	26.9 (16.6-39.4)	1318	12.0 (10.9-13.2)	.01
Current SR arthritis[b]	19	7.4[c]	688	4.1 (3.5-4.7)	[c]
Physical examination data					
Any positive exam finding	31	11.7 (6.4-19.2)	1096	8.2 (5.7-11.3)	.02
Upper extremity joints	17	5.0[c]	563	5.1 (3.2-7.0)	[c]
Lower extremity joints	21	8.6[c]	753	5.4 (3.6-7.6)	[c]
Palpable joint tenderness	19	9.7[c]	641	5.5 (2.7-8.3)	[c]
Joint pain, passive motion	25	9.2 (4.9-15.6)	868	6.5 (4.3-9.5)	.02
Palpable joint swelling	9	3.9[c]	391	3.4 (2.3-4.4)	[c]
Exam pain and swelling	7	3.3[c]	289	2.4 (1.4-3.4)	[c]
Heberden's nodes—DIP joints	35	12.4 (6.5-20.9)	1386	10.2 (6.9-14.4)	.07
Symptomatic Heberden nodes	2	0.7[c]	54	0.5[c]	[c]

[a]CI, confidence interval; DIP, distal interphalangeal; NHANES, US National Health and Nutrition Examination Survey; SR, self-reported; UC, ulcerative colitis.
[b]Self-reported arthralgia and arthritis. Overall NHANES examined sample sizes: UC = 131 cases; no UC = 10,273.
[c]Estimate potentially not reliable, variance estimate not shown.

fielded and, therefore, were not included.[19,20] Furthermore, NHANES 1976-1980 lacked variables needed to estimate IBP and axSpA. Four arthritis variables were reported: interview-based medical diagnosis of arthritis (Table 1); interview-based peripheral joint pain and swelling (Table 2); physical examination-based joint pain and swelling (Table 3); and ESSG or Amor criteria-based axSpA (Table 1).

Survey design variables and sample weights were used to account for differential participant selection probabilities in the complex NHANES sample design for nationally representative estimates. The sample weights accounted for unequal subgroup selection probabilities and adjusted for nonresponse and noncoverage. The US prevalence was calculated using direct standardization. Statistical analysis was performed using SAS and SUDAAN. The IBD data age range was 20-69 years in NHANES 2009-2010 and 25-74 years in NHANES 1976-1980; standard error estimation was performed using Taylor series linearization. Prevalence differences were tested using the *t* statistic at an α value of 0.05. Minimum acceptable sample size assessment employed survey design effects, degrees of freedom, and specified proportions. Absolute and relative confidence intervals were used to assess statistical estimate reliability.[21]

RESULTS

In the 4-year NHANES 1976-1980 dataset, the rates of a history of axial pain lasting 3 or more months were significantly higher in patients with UC than in the general population (19.5% vs 7.2%, respectively; $P<.01$). Chronic, site-specific pain was significantly increased in the neck or upper back (11.2% vs 3.2%, $P=.01$) and lower back (14.5% vs 5.1%, $P<.01$) but not in the mid back. Notably, 53% of neck pain cases had isolated chronic neck pain, without other axial pain. Low rates precluded the analysis of prior history of neck or axial spine injury. On physical examination, the UC cases had significantly higher rates of pain with spinal motion (14.4% vs 7.4%, $P=.05$) and had limited spinal motion (19.3% vs 9.7%, $P=.02$). These cases also had significantly increased rates of arthritis diagnosis (41.1% vs 21.1%, $P<.01$) and Amor criteria-based axial pain (13.0% vs 4.3%, $P<.01$; Table 1).

In the smaller, 2-year NHANES 2009-2010 sample, the chronic axial pain rates were also elevated for patients with IBD

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(27.7% vs 19.1%), a 45% increase over the rates in the general population but nonsignificant, given the study sample sizes. The sample sizes precluded the statistical analysis of site-specific axial pain prevalence; however, similar to NHANES 1976-1980, the crude site-specific rates were increased in the neck or upper back and lower back (Table 1). Most of those with axial pain for 3 or more months had pain onset at an age younger than 45 years. However, those with IBD were more likely to report axial pain onset at an age of 45 years or older (40% vs 26%), more likely to have rest or sleep pain (43% vs 27%), and more likely to report pain awakening from sleep (91% vs 58%) than those without IBD. In NHANES 2009-2010, 28% of IBD cases had a prior arthritis diagnosis vs 19% in the general population (P=.11). Four IBD cases reported an AS diagnosis. The crude prevalence rates of IBP, Amor criteria-based pain, and axSpA in patients with IBD were low, and the sample sizes precluded the statistical analysis.

The UC cases from NHANES 1976-1980 had increased prevalence of peripheral arthralgias and arthritis symptoms compared with the US population (30.2% vs 19.0%, respectively, P=.02 for arthralgia; 12.2% vs 6.5%, respectively, P=.01 for arthritis; Table 2). The arthralgia rates were significantly increased at the hand wrists, elbows, hips, knees, and feet-ankle areas, most often in polyarticular and symmetric patterns, with all being statistically significant (P<.05). The sample size for self-reported peripheral arthritis (any joint pain and swelling ≥6 weeks) precluded site-specific analysis. The UC cases had increased rates of a positive physician joint examination finding (11.7% vs 8.2%, P=.02), driven by lower extremity findings (10.4% vs 6.2%, P=.08; Table 3). Pain on passive joint motion was significantly increased (9.2% vs 6.5%, P=.02), but palpable joint swelling rates were not. Heberden's node prevalence was similar in patients with IBD and the general population (12.4% vs 10.2%); few were symptomatic.

DISCUSSION

We found that the overall rates of axial pain, peripheral arthritis, and arthritis diagnosis were all significantly increased in patients with UC compared with those in the US general population. In the larger NHANES 1976-1980 sample, the chronic axial pain prevalence in patients with UC was 19.5%, whereas in the general population, it was 7.2% (P<.01); the Amor criteria-based axial pain prevalence in patients with UC was 13.0% vs 4.3% in the general population (P<.01). The rates of the medical diagnosis of arthritis were high in the UC cases, with the rates almost double than those seen in the general population.

In NHANES 2009-2010, participants with IBD had high rates of chronic axial pain; yet, few cases met the IBP or axSpA criteria. If confirmed subsequently in larger population-based studies, these findings could potentially signal that the current IBD classification criteria may not fully capture all IBP or axSpA cases. For example, the expectation that IBP and axSpa principally affect younger adults could possibly function to reduce axSpa screening rates in patients with IBD. The Assessment of Spondyloarthritis International Society criteria for axSpa specify the age of the onset of axial pain to be 45 years or younger, whereas the IBP criteria specify the age of onset to be ranging from 45 years or younger to 29 years or younger.[9,19,20] We found that IBD cases were more likely to have chronic axial pain onset at the age of 45 years or older. It is unknown whether this is simply because patients with IBD on average are older, because IBD onset is highest in middle-aged adults,[2,3] or possibly due to biological differences between IBD-related and idiopathic axSpa. It is already known that IBD-related AS is less strongly correlated with human leukocyte antigen B27 than idiopathic AS, suggesting different biological mechanisms.[22] This raises a concern that many older patients with IBD-related axSpA may be underdiagnosed and better served by developing diagnostic criteria without an age cutoff.

The distribution of site-specific IBD axial pain observed here differs from that of idiopathic IBP or axSpA because neck or upper back pain was significantly elevated in patients with UC. This finding was not seen in a previous NHANES 2009-2010 study of IBP and axSpA in persons with diagnosed psoriasis.[23] Currently, the ESSG IBP or axSpA criteria include neck pain, but the Amor pain criteria and other IBP or axSpA criteria exclude it. Additionally, half

of those with IBD who had chronic neck pain had no other axial pain, potentially further reducing axSpA screening rates.

Moreover, the UC cases had significantly increased rates of pain with the passive motion of peripheral joints but lesser rates of objective joint swelling on examination. This suggests that tenosynovitis or enthesitis play larger roles than synovitis in IBD-related peripheral joint pathology. The NHANES findings are consistent with the observation that peripheral musculoskeletal manifestations in patients with IBD are subtle and may often escape detection in the usual clinical office visit setting.

Our study has important limitations, especially including the lack of imaging data for the assessment of sacroiliac or spinal disease. However, this is not a limitation for interpreting peripheral arthritis findings, which are typically nonerosive and nondeforming in patients with IBD.[5] Our finding that peripheral joint arthralgias was common in patients with UC but that frank arthritis was not common on examination is consistent with this. Imaging would be important for excluding age-related degenerative spinal disc disease and lumbar spondylosis as study confounders—an issue that could not be addressed, given the data. However, if the lumbar spondylosis and disc disease rates in patients with IBD are the same as those in the general population, then the excess rates of axial pain and arthritis diagnosis over prevalence seen in the general population would yield the proportion directly attributable to IBD. It is relevant here that Heberden's nodes prevalence was similar in patients with IBD and the general population, and symptomatic nodes were rare. Additionally, the neck and spinal injury rates in those with UC were low and not materially different from the rates in the US population. Furthermore, NHANES has never collected data on fibromyalgia; so, any associations there could not be directly assessed. However, for perspective, the prevalence of chronic widespread pain in the US adult population was 3.6% in NHANES 1999-2004.[24]

A chief limitation is that the data analyzed here were not from a specifically designed IBD-arthritis study. Nevertheless, the NHANES survey data are important because they are national in scope and can identify IBD and IBD-arthritis cases not always represented in clinical studies. Inflammatory bowel disease may have a remitting-relapsing course, a percentage of IBD cases remain localized, and many cases are undiagnosed or not well connected to clinical care. Moreover, IBD-arthritis manifestations may occur independently of IBD clinical activity. These groups of cases are fully represented in the NHANES sampling frame. The current study limitations can be addressed in the future because NHANES has the capability for fielding comprehensive arthritis surveys, including examinations, imaging, and laboratory studies.[8] The results of this study suggest that it is feasible to field such a future study to confirm our observations and assess the US burden of IBD arthritis.

POTENTIAL COMPETING INTERESTS

Dr Weisman has received honoraria for consultations from Novartis, Astra Zeneca, and Pfizer; and has received payment for expert witness testimony for Levine vs. State Farm. Dr Stens has received support from NIH Intramural Research Grant. Dr Hou has received grants from PCORI, VA HSR&D, American Regent, NIDDK, Celgene, Abbvie, AHRQ, Crohn's and Colitis Foundation, and Pfizer. Dr Miller is a government employee of NIEHS and NIH. Dr Dillon has received support from NIH and NIEHS.

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Abbreviations and Acronyms: **AS,** ankylosing spondylitis; **axSpA,** axial spondyloarthritis; **ESSG,** European Spondyloarthropathy Study Group; **IBD,** inflammatory bowel disease; **IBP,** inflammatory back pain; **NHANES,** US National Health and Nutrition Examination Survey; **UC,** ulcerative colitis

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