From Bowel inflammation to the Bone and Joints: Rheumatologic examination in Inflammatory Bowel Disease (IBD)

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Abstract

Background: The most common complications in inflammatory Bowel Disease (IBD) are musculoskeletal manifestations that are reported in more than 50% of patients.

Objectives: In this study, we aimed to evaluate the musculoskeletal and radiologic manifestations in our IBD patients.

Methods: In this study on 96 mild-to-moderate IBD patients (76 UC, 18 CD and 2 undifferentiated IBD) with mean (SD) age of 39.28 (11.42) years, 44 (45.8%) were males and 52 were (54.2%) females. Patients were examined by an expert rheumatologist and their musculoskeletal symptoms were assessed. The musculoskeletal system was evaluated by Modified Schober test, Thoracic expansion (TE), Occiput to wall distance (OWD), and Patrick's or FABER test. Peripheral joints were also examined in all four extremities. Then patients were referred for pelvic and lumbosacral x-ray. Sacroiliitis grading was performed using the New York criteria.

Results: Inflammatory low back pain was reported in 5 (5.2%), enthesopathy in 6 (6.5%) and dactilitis in 1 (1.1%). Positive Schober test was recorded in 5 (5.2%) and Patrick test in 3 (3.1%). Forty-nine (51%) cases had normal imaging with no sacroilliitis, endplate sclerosis was seen in 33 cases (34.4%), grade 3 and grade 4 were seen in 10 cases (10.4%).

Conclusions: In the present study, 34.4% of the IBD patients had mild radiologic changes as endplate sclerosis and 95% had a normal physical examination.

Background

Inflammatory bowel disease (IBD) is a chronic inflammatory disease composed of Crohn’s disease (CD) and ulcerative colitis. The etiology of IBD remains unknown but it is believed that the interaction of genetics, environment and immune system play a major role (1). There is no curative therapy for IBD and the goal of treatment is to prevent complications and reducing the progression of inflammation (2).

Extra intestinal manifestations (EIM) are common in IBD patients, more than half of the patients at least experience one extra intestinal symptom during their life (3). The incidence of EIM varies from 6–47%. Extraintestinal manifestations of IBD can affect any system such as musculoskeletal, ocular, dermatologic, hepatobiliary and etc. But the most common complication is musculoskeletal manifestations in approximately more than 50% of patients, including axial and peripheral involvements (4–6).

Axial arthritis consists of sacroiliitis and ankylosing spondylitis (AS), which are not associated with intestinal disease activity. Ankylosing Spondylitis has been reported in 5 to 10% of IBD patients who present with back pain and dryness at night, during the morning, and after immobility. Sacroiliitis alone is a common finding (up to 20% of patients) but is asymptomatic in many patients (10–11).

Spondyloarthritis (SpA) is divided into peripheral and axial. Peripheral involvement can be divided into two types: type 1 (non-destructive) asymmetrically affects the large joints including the knee, hip, wrist, elbow, and ankle associated with bowel disease activity and mostly lasts only a few weeks with no clear radiological manifestations. But type 2 (destructive) involves the small joints symmetrically and has no clear association with IBD (7–9).

The treatment of IBD and rheumatologic musculoskeletal complications are similar to the treatment of IBD itself (using 5-ASA combinations like Sulfasalazine), but immunosuppressives are used in retractable musculoskeletal pain, although they may worsen the course of the bowel disease (12–13).

In this study, we aimed to evaluate the musculoskeletal and radiologic manifestations in IBD patients.

Method

Study population and design

In this study, 100 registered IBD patients were recruited: 4 were excluded during the study because of pregnancy, among 96 remained patients, 76 were UC, 18 Crohn's disease and 2 undifferentiated IBD. Patients were invited to the Golestan Research Center of Gastroenterology and Hepatology (GRCGH) by telephone call.

Inclusion criteria:

All IBD patients registered in the IBD bank have been reached out through the telephone, and recruited into the study if agreed to terms of the study.

Exclusion criteria:

Hospital admission at the time of study and during the last month, history of fracture or trauma after the diagnosis of IBD, pregnancy and not willing to have an x-ray were among the exclusion criteria.

Patients were examined by an expert rheumatologist and their musculoskeletal symptoms were assessed throughout the following tests to evaluate the musculoskeletal symptoms: modified Schober test, Thoracic expansion (TE), Occiput to wall distance (OWD) and Patrick's test or FABER test (14). Peripheral joints of all four extremities were also examined.

Radiological evaluation

After finishing the physical examination and completing the questionnaire throughout a face-to-face interview, patients were referred to a well-equipped imaging center to perform a pelvic and lumbosacral x-ray.

Sacroiliitis grading was performed using the New York criteria (15):

Grade 0: Normal imaging

Grade 1: some blurring of the joint margins (Suspicious)

Grade 2: Minimal sclerosis with some erosion

Grade 3: definite sclerosis on both sides of joint / severe erosions with widening of joint space with or without ankyloses

Grade 4: complete ankyloses

Radiologic reports were all seen and graded by one expert radiologist. Those patients with problems in their X-ray were referred for further managements.

Results

In this study on 96 IBD patients (76 UC, 18 CD and 2 undifferentiated IBD) with mean (SD) of 39.28 (11.42) years, there were 44 (45.8%) males and 52 (54.2%) females. Table 1 shows the demographic variables of the study population. Table 1

Table 1
Demographic and anthropometric data of the studied population of IBD

Age, Mean (SD), years	**39.28 (11.42)**
Sex, N (%)	
Male	44 (45.8)
Female	52 (54.2)
Type of IBD, N (%)	
UC	76 (79.2)
CD	18 (18.8)
Undifferentiated	2 (2.1)
Duration of the bowel disease, Median (SE)	5 (0.65)
Body Mass Index (BMI), Mean (SD), kg/m2	26.26 (4.36)
BMI group, N (%)	
Underweight (< 18.5)	1 (1)
Normal (18.5–24.9)	52 (54.2)
Overweight (25–29)	27 (28.1)
Obese (≥ 30)	16 (16.7)
Waist circumference, Mean (SD), cm	89.35 (10.40)
Abdominal circumference, Mean (SD), cm	97.4 (10.97)
Medication, N (%)	
Sulfunamides (Asacol, Mesalazine, Sulfasalazine)	78 (81.2)
Anti-TNF (Remicade, Cinnora)	18 (18.8)
Azathioprine	39 (40.6)
Prednisolone	37 (38.5)

History taking and physical examination showed inflammatory low back pain in 5 (5.2%), enthesopathy in 6 (6.5%) and dactilitis in 1 (1.1%). Rheumatologic examinations of the studied population showed positive Schober test in 5 (5.2%) and positive Patrick test in 3 (3.1%). Table 2

Table 2
Results of the rheumatologic examinations in IBD patients

Occiput to Wall Distance, Mean (SD), cm	**4.31 (1.66)**
Schober test, N (%)	5 (5.2)
Positive	91 (94.8)
Negative	
Schober index, Mean (SD), cm	6.94 (1.30)
Patrick test, N (%)	3 (3.1)
Positive	93 (96.9)
Negative	
Inflammatory Low Back Pain, N (%)	5 (5.2)
Positive	91 (94.8)
Negative	
Peripheral arthropathy, N (%)	
Upper extremities	2 (2.1)
Left	2 (2.1)
Right	
Lower extremities	2 (2.1)
Left	2 (2.1)
Right	
Dactilitis, N (%)	1 (1.1)
Enthesopathy, N (%)	6 (6.5)

Lumbosacral and pelvic X-ray reports are shown in Table 3. Forty-nine (51%) cases had normal imaging with no sacroilleitis, endplate sclerosis was seen in 33 cases (34.4%), and definite sclerosis on both sides with or without ankyloses (grade 3) and complete ankyloses (grade 4) were seen in 10 cases (10.4%).

Table 3
Radiologic manifestation in IBD patients

End plate sclerosis in Lumbosacral joint, N (%)	**33 (34.4)**
Sacroilleitis grades, N (%)	49 (51)
Grade 0 (Normal imaging)	14 (14.6)
Grade 1 (Suspicious)	23 (24)
Grade 2 (Minimal sclerosis with some erosion)	8 (8.3)
Grade 3 (definite sclerosis on both sides with or without ankyloses)	2 (2.1)
Grade 4 (complete ankyloses)	

Discussion

Our study aimed to evaluate the musculoskeletal manifestations in patients with IBD. Severity of the disease was measured on the basis of New York criteria and musculoskeletal symptoms were assessed on the basis of radiological observations and physical examination of patients. Numerous reports from researchers in different countries show a wide range of rheumatologic symptoms. For example, a study in the Netherlands stated that 2 to 46 percent of IBD patients have spondyloarthropathy (16).

In our study, patients had few obvious musculoskeletal symptoms as inflammatory low back pain in 5.2%, enthesopathy in 6.5% and dactilitis in 1.1%. This may be due to the treatment with immunosuppressive and immunomodulatory medications (17). As mentioned before, approximately 50% of IBD patients experience at least one rheumatologic manifestation in their lifetime and the mean duration of the disease was 5 years in the present study. So, some may develop rheumatologic complications in the next coming years. The longer the duration, the probability of rheumatologic manifestations would be more prominent.

In our study, 34.4% of patients had radiologic changes as end plate sclerosis, but positive physical exams were seen in less than 5% of them. This indicates that many patients have not yet reached the stage of clear radiological changes. The bowel activity index was more than 6 just in 4 cases indicating that most of our patients were in the remission phase.

A study in Italy has also reported that some patients with asymptomatic IBD have radiologic evidence of spondyloarthritis (6). Asymptomatic patients are often less treated and less likely to adhere to treatment than symptomatic patients. On the other hand, asymptomatic patients have fewer referrals to a physician, and their rheumatologic symptoms are expected to be diagnosed later.

Previous studies, such as those reported in Korea, showed that ankylosing spondylitis and rheumatoid arthritis are more common in IBD patients than other rheumatologic diseases (18).

In the present study, endplate sclerosis was seen in 34.4% and higher grade of sacroilliitis (grade 3 and 4) was reported in 10.4% of IBD cases, although they were clinically asymptomatic, probably due to the prescribed treatment.

Another study in Italy suggested that genetic factors, and even the microbiome composition of IBD patients, could make a difference in musculoskeletal manifestations (19). Therefore, the potential role of genetics in the presence of extra intestinal symptoms in patients should be considered. Further studies are needed to investigate these factors.

Conclusion

In our study, one-third of patients (34.4%) had mild radiologic changes as endplate sclerosis and 94–95% of patients had a normal physical examination. Therefore, it can be concluded that even patients who have radiologic manifestations may have normal physical examinations.

Declarations

Ethics approval and consent to participate:

This study was approved in the local ethical committee of Golestan University of Medical Sciences (IR.GOUMS.REC.1398.155). The aim of study was explained for all and those who tended to enter to study signed an informed consent. All methods were carried out in accordance with relevant guidelines and regulations.

Consent for publication:

Not applicable

Availability of data and materials:

The datasets used and analyzed during the current study but not publicly available due to limitations of ethical approval involving the patient data and anonymity but are available from the corresponding author on reasonable request.

Competing interests:

Authors declare no conflict of interests.

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Authors' contributions:

S.T, N.A and S.L. contributed in the concept and design of the study, the acquisition and interpretation of data, provided final approval of the version to publish.

S.F.M, H.S.M. F.I.A. and I.SH. contributed in data collection, drafted manuscript preparation, and provided final approval of the version to publish.

A.N. and T.A. contributed in the acquisition and interpretation of data, drafted manuscript preparation and provided final approval of the version to publish

S.B. contributed in analysis and interpretation of data, drafted critical revision of the article and provided final approval of the version to publish

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References

1. Baumgart DC, Carding SR (2007) Inflammatory bowel disease: cause and immunobiology. Lancet. 2007; 369(9573):1627-40.
2. Triantafillidis JK, Merikas E, Georgopoulos F. Current and emerging drugs for the treatment of inflammatory bowel disease. Drug Des Dev Ther. 2011; 5:185.
3. Harbord M, Annese V, Vavricka SR, Allez M, Barreiro-de Acosta M, Boberg KM, et al. The first European evidence-based consensus on extra-intestinal manifestations in inflammatory bowel disease. J Crohns Colitis. 2016; 10(3):239-54.
4. Cardoneanu A, Prelipcean CC, Danciu M, Mihai C, Dranga M, Gavrilescu O, et al. Looking beyond gut inflammation in inflammatory bowel. Rom J Morphol Embryol. 2018; 59(4):1097-105.
5. Sarbu MI, Sarbu N. Musculoskeletal clinical and imaging manifestations in inflammatory bowel diseases. Open Med. 2019; 14(1):75-84.
6. Zippi M, Corrado C, Pica R, Avallone EV, Cassieri C, De Nitto D, et al. Extraintestinal manifestations in a large series of Italian inflammatory bowel disease patients. World J Gastroenterol. 2014; 20(46):17463.
7. Arvikar SL, Fisher MC. Inflammatory bowel disease associated arthropathy. Curr Rev Musculoskelet Med. 2011; 4(3):123-31.
8. Voulgari PV. Rheumatological manifestations in inflammatory bowel disease. Ann Gastroenterol. 2011; 24(3):173.
9. Olpin JD, Sjoberg BP, Stilwill SE, Jensen LE, Rezvani M, Shaaban AM. Beyond the bowel: extraintestinal manifestations of inflammatory bowel disease. Radiographics. 2017; 37(4):1135-60.

10. zochling J, Braun J, van der Heijde D. Assessments in ankylosing spondylitis. Best Pract Res Clin Rheumatol. 2006; 20(3):521-37.
11. Assassi S, Weisman MH, Lee M, Savage L, Diekman L, Graham TA, et al. New Population-Based Reference Values for Spinal Mobility Measures Based on the 2009–2010 National Health and Nutrition Examination Survey. Arthritis Rheumatol. 2014; 66(9):2628-37.
12. Palazzi C, D'Angelo S, Gilio M, Leccese P, Padula A, Olivieri I. Pharmacological therapy of spondyloarthritis. Expert Opin Pharmacother. 2015; 16(10):1495-504.
13. Pouillon L, Bossuyt P, Peyrin-Biroulet L. Considerations, challenges and future of anti-TNF therapy in treating inflammatory bowel disease. Expert Opin Biol Ther. 2016; 16(10):1277-90.
14. Antonelli-Incalzi R, Pedone C, Cesari M, Di Iorio A, Bandinelli S, Ferrucci L. Relationship between the occiput-wall distance and physical performance in the elderly: a cross sectional study. Aging Clin Exp Res. 2007; 19(3):207-12.
15. Linden SVD, Valkenburg HA, Cats A. Evaluation of diagnostic criteria for ankylosing spondylitis. Arthritis Rheum. 1984; 27(4):361-8.
16. Bennebroek Evertsz' F, Nieuwkerk PT, Stokkers PC, Ponsioen CY, Bockting CL, Sanderman R, et al. The patient simple clinical colitis activity index (P-SCCAI) can detect ulcerative colitis (UC) disease activity in remission: a comparison of the P-SCCAI with clinician-based SCCAI and biological markers. J Crohns Colitis. 2013; 7(11):890-900.
17. Callhoff J, Sieper J, Weiß A, Zink A, Listing J. Efficacy of TNFα blockers in patients with ankylosing spondylitis and non-radiographic axial spondyloarthritis: a meta-analysis. Ann Rheum Dis. 2015; 74(6):1241-8.
18. Bae JM, Choo JY, Kim K-J, Park K-S. Association of inflammatory bowel disease with ankylosing spondylitis and rheumatoid arthritis: a nationwide population-based study. Mod Rheumatol. 2017; 27(3):435-40.
19. Bandinelli F, Manetti M, Ibba-Manneschi L. Occult spondyloarthritis in inflammatory bowel disease. Clin Rheumatol. 2016; 35(2):281-9.