

Role of Musculoskeletal Ultrasonography in Screening of Subclinical and Degree of Joint Affection in Patients with Inflammatory Bowel Diseases

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ABSTRACT

Background: Chronic inflammatory illnesses with unknown causes known as inflammatory bowel diseases (IBD) involve ulcerative colitis (UC), Crohn's disease (CD), as well as atypical colitis.

Objective: This study aimed to detect the role of musculoskeletal ultrasound in screening of subclinical involvement and degree of joint affection in hand and wrist joints in IBD patients with and without musculoskeletal manifestations.

Subjects and methods: This was Cross-sectional research performed on seventy-five subjects, involving fifty cases that had been previously diagnosed with IBD through colonoscopy, and biopsy examined histopathologically at Tanta University Hospitals. They were compared with 25 healthy individuals during the period from December 2022 to January 2024. **Results:** This study detected synovitis in 33 subjects (44%), including 20 patients with UC, 6 patients with CD, and 7 in the control group. All cases of synovitis were without a power Doppler signal, except for two patients in the UC group who exhibited a grade one Doppler signal. In terms of the number of affected joints, synovitis was detected in 68 joints. The most commonly affected joint with synovitis was the left second metacarpophalangeal (MCP) joint, followed by the left and right wrists.

Conclusion: Musculoskeletal ultrasound (MSUS) can detect mild to moderate joint involvement in IBD patients, indicating its value as an accessible imaging tool for assessing joint involvement. It is recommended to include MSUS in IBD patient evaluations, especially those with elevated inflammatory markers, as it provides additional information.

Keywords: Musculoskeletal ultrasonography, Joint affection, IBD.

INTRODUCTION

Chronic inflammatory illnesses with unknown causes known as IBD include ulcerative colitis (UC), Crohn's disease (CD), as well as atypical colitis like lymphocytic and collagenous colitis⁽¹⁾. The two primary kinds are CD and UC that differ in a number of ways, such as where and how much inflammation is present, and which populations of mucosal cells are engaged in the immune response⁽²⁾. Patients with IBD who have musculoskeletal involvement should be especially worried since it impairs their quality of life and makes them more disabled⁽³⁾. In both CD as well as UC, the frequency of musculoskeletal manifestations is between 20-50%, while it is generally believed that this number is overestimated due to the temporary nature of some oligoarticular patterns or the utilize of continuous corticosteroid treatment⁽⁴⁾.

Musculoskeletal ultrasonography was extensively utilized in the treatment of rheumatic diseases, demonstrating to be an accurate and reproducible instrument in both inflammatory and non-inflammatory diseases. The European League Against Rheumatism (EULAR) additionally recognized the importance of this instrument, recommending ultrasound as one of the imaging techniques that may be utilized to assist in the clinical treatment of a variety of disorders⁽⁵⁾. Ultrasonography (US) is a technique used to identify inflammatory lesions in the peripheral joint and periarticular structures, including enthesitis, synovitis, bursitis, and tenosynovitis. US is being utilized more frequently by rheumatologists and radiologists to diagnose disorders associated with IBD⁽⁶⁾.

The research aimed to detect the role of musculoskeletal ultrasound in screening of subclinical involvement and degree of joint affection in hand and

wrist joints in IBD patients with and without musculoskeletal manifestations.

PATIENTS AND METHODS

This was cross-sectional research performed on seventy-five subjects, involving fifty cases that had been previously diagnosed with IBD through colonoscopy, and biopsy examined histopathologically at Tanta University Hospitals. They were compared with 25 healthy individuals during the period from December 2022 to January 2024.

The participants were categorized into 3 groups: **Group I** involved 39 cases with ulcerative colitis, **group II** involved 11 cases with Crohn's disease and **group III** involved 25 healthy volunteers (control) matched age and gender.

Inclusion Criteria: Patients previously diagnosed with IBD through colonoscopy and histopathological examination of biopsy at Tanta University Hospitals.

Exclusion Criteria: Patient < 18 or > 80 years old, patients with chronic forms of arthritis (Rheumatoid, gouty arthritis), patients with severe trauma or previous joint surgery, patients refused consent and patients with other diseases such as hepatitis, renal, collagen, DM, excluded from the study.

All cases were subjected to the following: Sociodemographic data (name, sex, and age), clinical assessment of both IBD and rheumatologic manifestations: Inflammatory bowel disease assessment included history of type of IBD, disease duration, number of flares, biological drug history and assessment of disease activity using the CD Activity Index and the UC Mayo Index⁽⁷⁾.

• **Rheumatological evaluation:** Included physical examination of any tenderness or swelling in examined joints.

• **Laboratory investigations:** ESR (Erythrocyte sedimentation rate), CRP (C-reactive protein), CBC (Complete blood count), FBS (Fasting blood sugar) and HbA1c (Haemoglobin A1c), blood urea, serum creatinine, SGOT, SGPT, faecal calprotectin and ELISA for rheumatoid factor.

• **Musculoskeletal ultrasonography with Power Doppler (PD):** The ultrasound examination has been performed at the musculoskeletal ultrasonography unit of the Internal Medicine Department's Rheumatology unit to eliminate inter-operator variability. Cases and controls underwent bilateral musculoskeletal Ultrasonographic examinations, with hand and wrist PD evaluations performed simultaneously.

Type and name of Ultrasound machine: The device used in hand and wrist joints examination was ALPINION Model E-CUBE 5 (made in Korea) with frequency of probe 12.

Patient positions and techniques: Ultrasonographic exams were done using a multiplanar scanning technique and in line with the EULAR guidelines for musculoskeletal US in rheumatology. To properly assess synovial vascularization, an appropriate quantity of warm gel was used for each MSUS evaluation, and compression with the probe was avoided.

Wrist examination: Positioning of the patient: Sitting position: A dynamic investigation that involves active flexion/extension of the fingers, with the hand positioned on top of the thigh or on an examining table. **Standard scans:** Dorsal longitudinal scan (Radial), dorsal longitudinal scan (Median), dorsal longitudinal scan (Ulnar), dorsal transverse scan (Radial), dorsal transverse scan (Ulnar), Volar transverse scan and Volar longitudinal scan. **Hand Examination: Positioning of the patient:** as wrist examination. **Standard scans for metacarpophalangeal joints (MCPs):** Dorsal longitudinal scan, dorsal transverse scan, palmar longitudinal scan, palmar transverse scan and lateral longitudinal scan (II & V joints). **Standard scans for proximal interphalangeal joints (PIPs):** Dorsal longitudinal scan, dorsal transverse scan, palmar longitudinal scan, palmar transverse scan, lateral longitudinal scan and medial longitudinal scan, thenar longitudinal scan, thenar transverse scan, hypothenar longitudinal scan and hypothenar transverse scan. The subsequent joints were bilaterally scanned, wrist joint (Radiocarpel, intercarpal & carpometacarpal). Metatarsophalangeal (MCP) and proximal interphalangeal (PIP) joints and total joints were examined bilaterally for each patient (22 joints). Total joints were examined bilaterally for total subjects (1650 joints).

Outcome measures in rheumatology (OMERACT) definitions of ultrasonographic pathologies ⁽⁹⁾: Synovial hypertrophy (SH), effusion, bone erosion, enthesopathy, tenosynovitis, OA osteophytes, OA hyaline cartilage damage, gout double contour, gout tophus, CPPD fibrocartilage and CPPD synovial fluid.

Synovial vascularization has been evaluated with PD estimation: Each joint was assessed separately and classified for SH and intra-articular PD utilising the Szkudlarek grading method, a semi-quantitative grading method ⁽¹⁰⁾, which grades each parameter individually as follows: **Synovial hypertrophy: Grade 0:** No synovial thickening, **grade 1:** Minimal synovial thickening (filling the angle within the periarticular bones, with no bulging over the line connecting the tops of the bones), **grade 2:** Synovial thickening bulging over the line connecting the tops of the periarticular bones with no extension along the bone diaphysis and **grade 3:** Synovial thickening bulging over the line connecting the tops of the periarticular bones with extension to a minimum one of the bone diaphysis ⁽¹⁰⁾. **Power Doppler: grade 0:** no flow in the synovium, **grade 1:** single vessel signal, **grade 2:** vessel signals in less than half of the synovium, and **grade 3:** vessel signals in more than half of the synovium ⁽¹⁰⁾.

Ethical consideration: The current research was carried out according to the Helsinki Declaration. The Ethics Committee of Tanta Faculty of Medicine accepted the research protocol (Code no36176/12/22). Written informed consent was obtained from each patient. The research outcomes were exclusively utilised for scientific purposes and weren't utilised for any other purposes. Complete aseptic techniques and sterilisation were utilised to reduce the risk of infection through blood sampling or musculoskeletal ultrasound. **Unexpected risks of the work: No Unexpected risks of the work.**

Statistical analysis:

A test of normality has been performed to numerical data. The mean \pm SD, median, and interquartile range were used to statistically define normally distributed data in comparison with data that wasn't normally distributed. Categorical data were expressed as percentages and numbers. Comparison of normally distributed data was performed utilizing one way ANOVA test and pairwise comparison was done using Bonferroni test. Comparison of non-normally distributed data was done using Kruskal Wallis test. Comparing categorical data has been performed using Chi square, Montecarlo and Fisher exact test. Statistically significant two-sided p values were determined to be ≤ 0.05 . IBM SPSS (Statistical Package for the Social Science; IBM Corp, Armonk, NY, USA) version 25 for Microsoft Windows was utilised to perform all statistical calculations.

RESULTS

Sociodemographic characteristics of the studied groups: Group I included 25 females and 14 males, aged 23-55 years with a median age (IQR) of 33 ± 17 years. Group II involved 8 females and 3 males, aged 23-35 years with a median age (IQR) of 26 ± 7 years. Group III included 11 females and 14 males, aged 22-34 years with a median age (IQR) of 29 ± 6 years. The analysis revealed a significant difference in age between the study groups (Table 1).

Table (1): Sociodemographic data of the studied groups

Studied variables		Group I UC (a)	Group II CD (b)	Group III Control (c)	Total	P value	
Age (Years)	Min-Max	23-55	23-35	22-34	23-57	0.002*(1)	
	Median(IQR)	33(17)	26(7)	29(6)	31(14)		
Pairwise comparison		P1=0.011* P2>0.999 P3=0.017*					
Sex	Male	N	14	3	14	0.166(2)	
		%	35.9%	27.3%	56.0%		41.3%
	Female	N	25	8	11		44
		%	64.1%	72.7%	44.0%		58.7%

Regarding MSUS finding (synovitis) in studied groups, in group I data showed that 20 (51.3%) patients had synovitis, with 16 patients categorized as grade 1 and four cases as grade 2. In group II data showed that 6 (54.5%) patients had synovitis, all classified as grade 1. In group III data showed that 7 (28%) patients had synovitis, all classified as grade 1 (Table 2).

Table (2): MSUS finding (synovitis) in studied groups

Studied variables		Group I UC	Group II CD	Group III control	Total	P value	
Synovitis	No	N	19	5	18	0.140(1)	
		%	48.7%	45.5%	72.0%		56.0%
	Yes	N	20	6	7		33
		%	51.3%	54.5%	28.0%		44.0%
Grade	1	N	16	6	7	0.688(2)	
		%	80.0%	100.0%	100		87.8%
	2	N	4	0	0		4
		%	20.0%	0.0%	0.0%		12.2%
Power Doppler	No	N	37	11	25	0.646	
		%	94.9%	100.0%	100.0%		97.3%
	Yes	N	2	0	0		2
		%	5.1%	0.0%	0.0%		2.7%

- 13 patients didn't receive biological treatment and at the same time didn't have synovitis by MSUS, which represented 39.4% of all patients who didn't receive biological treatment.
- 11 patients received biological treatment and didn't have synovitis by MSUS, which represented 64.7% of all the patients who received biological treatment.
- 20 patients didn't receive biological treatment and had synovitis by MSUS, which represented 60.0% of all the patients who didn't receive biological treatment.
- 6 patients who received biological treatment had synovitis by MSUS, which represented 35.3% of all patients who received biological treatment (Table 3).

Table (3): Association between synovitis and receiving biological therapy

Studied variables		Biological treatment		Total	P value	
		No	Yes			
Synovitis	No	N	13	11	24	0.080(1)
		%	39.4%	64.7%	48.0%	
	Yes	N	20	6	26	
		%	60.6%	35.3%	52.0%	
Grade	1	N	16	6	22	0.542(2)
		%	80.0%	100.0%	84.6%	
	2	N	4	0	4	
		%	20.0%	0.0%	15.4%	
Power Doppler	No	N	31	17	48	0.542
		%	93.9%	100.0%	96.0%	
	Yes	N	2	0	2	
		%	6.1%	0.0%	4.0%	

In group I, the most affected joints were the LT 2nd MCP in nine joints, followed by the LT wrist in seven joints, LT 3rd MCP and RT wrist in six joints, RT 2nd MCP in five joints, RT 3rd MCP in four joints, and 2nd & 3rd PIP in three joints. In group II, the most affected joints were the LT 2nd MCP in five joints, followed by the LT 3rd MCP and RT wrist in three joints. In group III, the most affected joints were the LT 2nd MCP and RT 2nd MCP, each affecting two joints (Table 4).

Table (4): Distribution of the affected joints among the studied groups

Affected joint	Group I UC		Group II CD		Group III Control		Total	
	N	%	N	%	N	%	N	%
Left wrist	7	16.3	2	12.5	1	11.11	10	14.7
Right wrist	6	13.9	3	18.75	1	11.11	10	14.7
Left second MCP	9	20.9	5	31.25	2	22.22	16	23.5
Left third MCP	6	13.9	3	18.75	0	0	9	13.24
Right second MCP	5	11.6	1	6.25	2	22.22	8	11.76
Right third MCP	4	9.3	1	6.25	0	0	5	7.35
Left second and third PIP	3	7	0	0	0	0	3	4.4
Right first MCP	1	2.3	0	0	0	0	1	1.47
Right first PIP	1	2.3	0	0	0	0	1	1.47
Right second PIP	0	0	0	0	1	11.11	1	1.47
Left fourth MCP	1	2.3	0	0	0	0	1	1.47
Left fifth MCP	0	0	1	6.25	0	0	1	1.47
Right fourth MCP	0	0	0	0	1	11.11	1	1.47
Right fifth MCP	0	0	0	0	1	11.11	1	1.47

There was a highly significant positive correlation between disease activity and faecal calprotectin levels ($p < 0.001$) (Table 5).

Table (5): Correlation between faecal calprotectin and disease severity

	Fecal calprotectin	
	rs	P
Disease activity	0.831	<0.001*

The kappa value that measures the agreement between two rates here was equal to 7, indicating a high degree of agreement between the sonographic diagnosis of synovitis and clinical MS symptoms. This means that there is a very strong degree of agreement between the two data. In other words, when a patient has synovitis diagnosed by sonography, they are very likely to also have clinical MS symptoms (Table 6 & figures 1 & 2)).

Table (6): Agreement among sonographic diagnosis of synovitis as well as clinical musculoskeletal manifestation

Ultrasound diagnosis		Musculoskeletal manifestation		Kappa value	P value	
		No	Yes			
Synovitis	No	N	34	7	<0.001*	
		%	85.0%			22.9%
	Yes	N	6			27
		%	15.0%			77.1%



Figure (1): Grade 2 synovitis in LT 3rd MCP in patient of Ulcerative colitis showing grade 1 Doppler signal



Figure (2): Grade 1 synovitis in LT 2nd PIP in patient with Crohn's disease

DISCUSSION

Synovitis was identified in 33 subjects (44%) in the study; 20 (51.3%) of all UC patients, 6 (54.5%) of all CD patients, and 7 (28%) in the control group. All cases of synovitis were without power Doppler, except for two patients in the UC group.

The most commonly affected joint with synovitis was the left second metacarpophalangeal (MCP) joint, followed by the left and right wrists, the left 3rd metacarpophalangeal joint, the right 2nd metacarpophalangeal joint, the right 3rd metacarpophalangeal joint, then the left 2nd and 3rd proximal interphalangeal (PIP) joints.

The study diagnosed two patients with tenosynovitis, two with bone erosion, and two with osteophytes. A significant positive association has been observed among disease severity (activity) and fecal calprotectin levels. Moreover, the sonographic diagnosis of synovitis agreed well with the presence of clinical musculoskeletal manifestations, indicating a positive correlation between synovitis diagnosed by MSUS and musculoskeletal manifestations. The study also revealed an association between patients receiving biological therapy and normal MSUS results, highlighting the role of biological therapy in treating peripheral arthropathy in IBD patients. The levels of ESR, CRP, and fecal calprotectin tests were higher in the group of cases diagnosed with synovitis by MSUS compared to the group of cases with no synovitis.

The study included 39 patients with UC and 11 patients with CD, showing a higher prevalence of UC than CD. This outcome agrees with **Elbadry et al.** (11) research that investigated the epidemiology of IBD in Egypt with 1104 patients. The study reported that 81%

of the patients had UC, while 19% had CD. Similarly, **Hsiao et al.** (12) in Taiwan, involved 11 UC and 7 CD patients:

The results of musculoskeletal ultrasound findings were compared with other studies, such as **Wolheim** (13), who extensively covered peripheral arthropathy associated with IBD, commonly known as enteropathic arthritis. He revealed that in type 2 peripheral arthropathy, the metacarpophalangeal joints (MCP) were most frequently involved, with MCP in CD being the most affected, followed by MCP in UC.

Regarding the MSUS role for identifying subclinical involvement, **Rovisco et al.** (14) evaluated the role of MSUS in detecting subclinical joint and enthesal involvement within cases with inflammatory bowel disease with no musculoskeletal symptoms using joint ultrasound. They performed ultrasounds on the 2nd and 3rd MCP joints and knees to assess joint abnormalities.

Eltoraby et al. (15) evaluated the role of high-resolution ultrasonography (HRUS) in detecting subclinical hand and wrist arthritis in IBD patients. They found that HRUS detected subclinical arthritis in 40% of patients with IBD, primarily affecting MCP and PIP joints. The most common HRUS features diagnosed in their study were joint effusion, synovial hypertrophy, as well as Power Doppler signal.

Two subjects with positive Power Doppler signals in the UC group, representing 5.1%, were found in the recent research. This prevalence was much lower than that documented by **Sakellarion et al.** (16), who found Doppler signals in 14% – 67% of cases, with no variances observed between CD and UC, based on disease activity.

Landewe et al. ⁽¹⁷⁾ evaluated the effectiveness of TNF-alpha inhibitors (anti-TNF) in treating peripheral arthropathy in IBD. The study found a significant enhancement in joint pain, swelling, and function in 64% of cases taking anti-TNF compared to 29% in the control group. Additionally, reduced inflammation markers and disease activity were observed in IBD. The significant difference in results could be due to the difference in IBD activity between the studies.

The present study had 56% of the patients with mild IBD activity, 20% in remission, and all on treatment. **Sharbatdaran et al.** ⁽¹⁸⁾ had all patients early diagnosed with severe IBD activity on endoscopy and none had started treatment yet.

Both ESR and CRP were mildly elevated in the inflammatory bowel disease groups than the control group, according to the laboratory investigations. The medians for UC, CD, and control groups were as follows: ESR (mm/hr): 26 (12), 24 (14), 9 (6) and CRP (mg/l): 6 (6), 5 (5), 2 (1).

A greatly significant positive association among disease activity and fecal calprotectin was found in the present study. This is consistent with **Zittan et al.** ⁽¹⁹⁾ who found that FC was significantly associated with the Mayo clinical score ($p < 0.0001$) and the total Mayo score ($p < 0.0001$) in UC. Furthermore, **Kostas et al.** ⁽²⁰⁾ determined that serial FC measurements were beneficial for monitoring inflammatory bowel disease cases in remission, as FCs were a dependable indicator of short-term relapse and endoscopic activity.

A relation between synovitis and high readings of ESR, CRP, and fecal calprotectin was shown in the recent research, with significant differences among the group of patients who had synovitis and those who didn't have synovitis. This is consistent with **Aydin et al.** ⁽²¹⁾ who showed a significant positive association among CRP as well as synovitis severity ($r = 0.42$, $p < 0.001$) in IBD-associated peripheral arthritis. Additionally, **Kamanli et al.** ⁽²²⁾ showed a moderate positive association among CRP and synovitis ($r = 0.43$, $p < 0.001$) confirmed in a meta-analysis. Meanwhile, **Ozgocmen et al.** ⁽²³⁾ documented a similar positive association among ESR and synovitis activity ($r = 0.45$, $p < 0.001$).

The present research found an agreement between the sonographic diagnosis of synovitis and the presence of clinical musculoskeletal manifestations. This is consistent with **Ozgocmen et al.** ⁽²³⁾ who reported a positive agreement of 80% between clinical and ultrasound findings for synovitis in IBD-associated peripheral arthritis. Additionally, a meta-analysis by **Kamanli et al.** ⁽²²⁾ confirmed a moderate to strong agreement among clinical and imaging modalities (MRI, ultrasound) in the diagnosis of synovitis in IBD.

CONCLUSION

Musculoskeletal ultrasound (MSUS) can detect mild to moderate joint involvement in IBD patients, indicating

its value as an accessible imaging tool for assessing joint involvement. It is recommended to include MSUS in IBD patient evaluations, especially those with elevated inflammatory markers, as it provides additional information.

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