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Assessment of Bone Mineral Density and Risk of Fracture in Patients with Recent Ulcerative Colitis

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ABSTRACT

Background: Ulcerative colitis (UC) is a chronic, idiopathic inflammatory disease that affects the colon, commonly associated with systemic manifestations, and musculoskeletal disorders.

Objectives: We aimed to study the musculoskeletal disorders in patients with recent ulcerative colitis (UC) compared to old cases of UC, and compared to healthy controls.

Subjects and methods: 50 patients with UC and 50 healthy controls were included in case control study. They were assessed by clinical examination, laboratory investigations as well as radiological assessment.

Results: The musculoskeletal disorders in cases with recent ulcerative colitis were significantly higher than that in old cases regarding morning stiffness, inflammatory low back pain, knee pain, and joint swelling, with a significant lower metabolic bone disease (MBD) in lumbar spine and femur neck in patients versus controls. Additionally, cases had significantly higher FRAX scores compared to controls.

Conclusion: Our study suggests the higher rate of musculoskeletal disorders in newly diagnosed patients with ulcerative colitis compared to old cases, and that UC patients have low BMD and higher FRAX score in comparison to controls. Therefore, caution and continuous monitoring of these patients is mandatory, and treatment must be started as soon as possible for newly diagnosed cases to avoid musculoskeletal complications as well as sudden fractures.

Keywords: Ulcerative colitis, Bone mineral density, Risk of fracture, Musculoskeletal disorders.

INTRODUCTION

Ulcerative colitis (UC) is an inflammatory disease that affects the colon, most commonly affecting adults in the middle aged. It is characterized by relapsing and remitting course **(1).**

Musculoskeletal disorders are the most common extraintestinal manifestations of ulcerative colitis that affect peripheral and axial joints. Axial involvement is linked to intestinal inflammatory activity **(2)**. It has been demonstrated that a number of humoral and cell-mediated immunopathophysiological mechanisms link gastrointestinal and synovial inflammation. Patients with UC may experience peripheral arthritis, arthralgia, enthesitis, and dactylitis, or axial arthropathy, which includes inflammatory back pain, isolated sacroiliitis, and ankylosing spondylitis. Additionally, people with IBD are often affected by metabolic bone illnesses including osteoporosis **(3)**. Osteoporosis is a systemic metabolic bone disease that is a cause of morbidity and mortality. It is common in cases of UC. Metabolic bone disease (MBD) imparts a significant morbidity if pathologic fractures were to occur. Several risk factors may contribute to the increased risk of MBD in UC patients **(4,5).**

We aimed to study the musculoskeletal disorders in recent cases of ulcerative colitis compared to old cases, and compared to healthy controls.

SUBJECTS AND METHODS

This study was conducted on 100 participants including 50 patients with ulcerative colitis (cases group) and 50 healthy subjects of matched age and sex as (control group), they were collected from Rheumatology and Rehabilitation Outpatient Clinic.

Exclusion criteria: Patients below 18 years or above 60 years, other immunological, metabolic, or endocrinal diseases, and GIT disorder other than UC.

All participants were subjected to socio-demographic data recording, general examination, and local joint assessment of both peripheral and axial joints, laboratory measurement of acute phase reactants, CBC, liver, and kidney function tests, serum calcium (total, and ionized), vitamin D, assessment of UC disease duration, activity, medications, and assessing the BMD, risk of fracture by DEXA scan, and FRAX score.

Ethical approval:

The Ethics Committee of the Menoufia Faculty of Medicine has given its approval to this project. Each participant completed a permission form when all information was received. Throughout its implementation, the study complied with the Helsinki Declaration.

Statistical analysis: SPSS, version 26.0 was utilized on an IBM compatible computer to analyze the data. Mean± SD was used to represent quantitative data, which were compared by Student t-test. While; numbers (N) and percentages (%) were used to represent the qualitative data, which were compared by X^2-test. P value of <0.05 was considered significant.

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RESULTS

Table (1) shows demographic data among participants. The patients mean age was 35.4 ± 7.2 years and the mean BMI was 26.9 ± 6.5. Regarding medical treatments, sulfasalazine was used in half of patients, followed by azathioprine in 40% of patients. No significant difference between cases and control groups was found regarding age, sex, and BMI.

Table (1): Socio-demographic, and clinical data among the studied groups.

Parameters	**Cases group** (N = 50) *M ± SD or N (%)*	**Control group** (N = 50) *M ± SD or N (%)*	***Test value***	***P value***
Age (years)	35.4 ± 7.2	31.7 ± 4.2	1.14‡	0.034
Sex:				
Male Female	23 (46%) 27 (54%)	26 (52%) 24 (48%)	1.56	0.22
Body mass index BMI (kg/m^2)	26.9 ± 6.5	28.8 ± 5.9	1.2‡	0.34
Treatments:**				
Sulfasalazine	25 (50%)	Not applicable	Not applicable	Not applicable
Mesalazine	4 (8%)			
Azathioprine	20 (40%)			
Adalimumab	10 (20%)			
Infliximab	3 (6%)			
Ustekinumab	2 (4%)			

‡Two−samples T−test. *Chi−squared test. **Some patients received combined treatments.

Table (2) shows statistically significant difference between cases and control groups regarding hemoglobin, platelet, vitamin D, and serum calcium (total and ionized).

Table (2): The studied groups' laboratory parameters.

Parameters	**Cases group** (N = 50) *M ± SD*	**Control group** (N = 50) *M ± SD*	***Test value****	***P value***
ESR (mm/h)	39.1±9.61	10.3±2.41	9.04	<0.001
CRP (mg/dL)	16.1±3.88	2.4±0.60	2.23	0.001
CBC:				
HB (g/dL)	10.2 ± 1.3	12.5 ± 0.5	1.23	0.001
TLC (10^9/L)	6±1.32	5.9±1.21	0.382	0.45
PLT (10^9/L)	219 ± 45	299 ± 43	2.13	0.001
Liver enzymes:				
AST (U/L)	17.1±4.10	12.6±2.97	0.342	0.723
ALT (U/L)	20.7±4.99	19.3±4.81	0.234	0.543
KFTs:				
Serum Urea (mg/dL)	22.6± 4.5	19.4 ± 4.80	0.123	0.654
Serum Creatinine (mg/dL)	0.83 ± 0.11	0.71 ± 0.12	1.346	0.097
Total Ca^{++} (mg/dL)	8.1 ± 1.0	9.6 ± 0.64	0.564	0.033
Ionized Ca^{++} (mg/dL)	2.1 ± 0.34	3.5 ± 0.69	1.432	0.032
Vitamin D (ng/mL)	15.2±3.69	31.5±7.8	1.241	<0.001

*Two−samples T−test, ESR: erythrocyte sedimentation rate, CRP: C−reactive protein, CBC: complete blood count, HB: hemoglobin, TLC: total leucocytic count, PLT: platelet count, AST: aspartate aminotransferase, ALT: alanine transaminase. ALP: alkaline phosphatase

Table (3) shows Joint manifestations among the studied groups, as recent cases of UC had high rates of morning stiffness, inflammatory low back pain, knee pain, and joint swelling, compared to old UC cases, and the rate of musculoskeletal disorders was positively associated with UC disease activity in relation to MAYO score.

Table (3): Joint manifestations among groups of the present study.

Parameters	Early diagnosed UC (Group I) (N = 20) M ± SD or N (%)	Established UC cases(Group II) (N = 15) M ± SD or N (%)	*Test value*	*P value*
Morning stiffness (min)	59.3 ± 11.5	48.9 ± 12.8	0.98*	0.024
Joint pain:				
ILBP VAS	2.9±3.1	4.7±3.8	1.928‡	0.157
Knee pain (VAS)	3.7±3.2	3.45±3	0.218‡	0.805
Ankle pain (VAS)	2.47±2.74	2.15±3	0.051‡	0.95
Joint Swelling:				
Knee	4 (20%)	2 (13.3%)	0.6*	0.741
Ankle	3 (15%)	4 (26.7%)	1.85*	0.241
Joint tenderness:				
Sacroiliac	6 (30%)	7 (46.7%)	7.57*	0.191
Hip	3 (15%)	8 (53.3%)	5.26*	0.262
Knee	8 (40%)	9 (60%)	6.82*	0.146
Ankle	9 (60%)	4 (20%)	12.58*	0.014

‡One-way ANOVA. *Chi−squared test. ILBP: inflammatory low−back pain, LEI: Lead enthesitis index, LDI: Lead dactylitis index.

Table (4) shows bone mineral density (BMD) using DEXA scan, and reveals that BMD was significantly lower in lumbar spine and femur neck, in UC patients versus controls. Additionally, cases had significantly higher FRAX scores compared to controls.

Table (4): The studied groups Bone mineral density (BMD).

Parameters	Cases (N = 50) M ± SD	Controls (N = 50) M ± SD	*Test value**	*P value*
DEXA scan (Z score)				
Lumbar spine	-2.13 ± .09	-0.73 ± 1.11	5.432	<0.001
Femur neck	-1.98 ± 1.11	-0.35 ± 1.23	4.321	<0.001
Radius	-1.22 ± 1.32	-0.76 ± 0.85	-2.452	0.255
FRAX score (major)	1.56 ± 0.93	1.33 ± 0.9	4.223	0.001
FRAX score (hip)	0.43 ± 0.25	0.22 ± 0.12	3.231	0.005

*Two−samples T−test, DEXA: dual X−ray absorptiometry, FRAX: fracture risk assessment tool.

DISCUSSION

Musculoskeletal disorders are the most common extraintestinal manifestations of ulcerative colitis that affect peripheral and axial joints. Axial involvement is linked to intestinal inflammatory activity [(2)].

Our study aimed to study the musculoskeletal disorders in patients with recent ulcerative colitis (UC) compared to old cases of UC, and compared to healthy controls.

The present study revealed significant reduction of the complete blood count parameters regarding hemoglobin and platelet in UC cases with a significant decrement of serum vitamin D, and calcium (total, ionized) compared to controls.

In consistent with our results, several studies reported the significant decrement of platelet and hemoglobin levels in UC cases [(6-8)]. Similarly, **Mosli and Saadah [(9)], Jemaa *et al.* [(10)] and Sharifi *et al.* [(11)]** reported the significant differences between UC cases and controls regarding, serum vitamin D and calcium with significant decrement of bone density indices.

The current study documented a significant decrement of BMD in femoral neck as well as the lumbar spine measured by DEXA scan, with a significant increment of FRAX scores in UC patients versus controls (P<0.001). This was in agreement with **Sharma *et al.*** [(5)] who reported, the significant decrement of BMD that was measured by DEXA at the spine as well as the hip in UC patients compared to controls**.**

Also, **Zhou *et al.*** [(12)] study included the analysis of 13 cross-sectional research that involved 1154 participants in a meta-analysis, which revealed a strong negative relationship between bone mineral density and ulcerative colitis in steroid-free patients. Additionally, other subgroup analyses also revealed a strong relationship.

Another study reported that the prevalence of osteopenia was 69/150 (46%) and osteoporosis was

identified in 15/150 (10%) patients with UC at baseline [11]. Also, **Sharifi *et al.*** [11] reported that based on the femoral T-score index, 74.3%of patients with UC had normal femoral density, while 23.8% were osteopenic and 2% had osteoporosis. Similarly, it was reported that, FRAX scores had statistically significant higher values in the UC patients with ($P<0.05$) [12].

Our results showed a higher rate of musculoskeletal disorders in recent cases of UC compared to old cases regarding morning stiffness, inflammatory low back pain, knee pain, and joint swelling and the rate of musculoskeletal disorders was positively associated with UC disease activity in relation to MAYO score, that could be explained as old UC cases were on medications that controls disease activity with subsequent improvement of extra intestinal manifestations, including the musculoskeletal disorders, also, the inflammatory process responsible for the pathogenesis of UC plays an important role in causing musculoskeletal disorders, the rate of which increases with increasing indicators of ulcerative colitis disease activity.

This is in agreement with **Sheth *et al.*** [2] who reported that peripheral and axial arthritis similar to spondyloarthropathy, as well as enthesitis and dactylitis, are among the most frequent extra-intestinal manifestations of ulcerative colitis, and that the rate of these disorders increases with increasing ulcerative colitis disease activity, as well as in uncontrolled cases (either new cases that were not on medications, or patients who received insufficient treatment).
Similarly, **Feagins *et al.*** [13] **and Wolfe *et al.*** [14] reported a strong association between UC with arthralgia, and peripheral arthritis, especially asymmetric arthritis. They also documented that the incidence of their occurrences is commonly associated with UC flares.

Similarly, **Calin *et al.*** [15] documented that the most common musculoskeletal disorder among UC patients is the inflammatory back pain that improved with activity and increases on rest, with morning stiffness that manifests newly diagnosed untreated cases and increased with increment of ulcerative colitis activity.

CONCLUSION

Our study suggests the higher rate of musculoskeletal disorders in recent cases with ulcerative colitis compared to old cases, and that UC patients have low BMD and higher FRAX score compared to controls. Therefore, caution and continuous monitoring of these patients is mandatory, and treatment must be started as soon as possible for newly diagnosed cases to avoid musculoskeletal complications as well as sudden fractures.

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