Peripheral arthropathy among patients with inflammatory bowel disease in Sulaimani

Raouf Rahim Mirza[1], Sabriya A Rafiq[2], Adnan A Humadi[3]

ABSTRACT

Background: **Arthropathies are a major clinical problem in patients with inflammatory bowel disease (IBD). Often it is difficult to control the articular symptoms with the anti-inflammatory strategies used for IBD. Recently, interest in the multidisciplinary approach to patients with IBD and arthropathy has been increasing, early recognition and proper management of arthropathy is mandatory.**

Objectives: **To find out the frequency of peripheral arthropathy and pattern of joint involvement in inflammatory bowel diseases.**

Patients and Methods: **Forty-eight patients with a definite diagnosis of inflammatory bowel disease (IBD) (41 ulcerative colitis and 7 crohn's disease) have been assessed for peripheral joint involvement and enthesopathy. Patients clinically assessed for bowel conditions, peripheral arthritis, enthesitis and pattern of joint involvement (monoarticular, pauciarticular or polyarticular). Blood test for full blood count, ESR, CRP, RF, Serum electrolytes and serum albumin done for the assessment of disease activity. Radiological assessment of the symptomatic peripheral joints was done by conventional x-ray.**

Results: **Five (10.4%) cases had peripheral arthritis, 4(80%) were pauciarticular, arthralgia and enthesopathy accounted in 10(20.8%) and 2(4.2%) cases respectively. Peripheral arthritis was more among female patients 4(21.05%) with P-value (0.051). All patients with peripheral arthritis were in active state of inflammatory bowel disease. Patients with ulcerative colitis who had extensive colonic involvement were more likely to develop peripheral arthritis with frequency of 2(50%) for left side colitis, 1(25%) for extensive colitis and 1(25%) for pan colitis, While crohn's disease with colonic localization was more likely to develop peripheral arthritis 1(100%) for ileocolitis.**

Conclusion: **The commonest musculoskeletal manifestations of IBD were arthralgia, followed by arthritis and the least was enthesopathy. The most common pattern of peripheral arthritis was pauciarticular and mostly involved the lower limb joints.**

It was more common in female patients and occurred independent to the duration of inflammatory bowel disease.

Keywords: peripheral arthritis (PA), chronic inflammatory bowel diseases (IBD).

إعتلال المفاصل الطرفية بين المرضى الذين يعانون من مرض الأمعاء الالتهابي في السليمانية

الخلفية: اعتلالات المفاصل هي مشكلة سريرية كبيرة في المرضى الذين يعانون من مرض الامعاء الالتهابي وغالبا ما يكون من الصعب السيطرة على الأعراض المفصلية بأستعمال الاستراتيجيات المضادة للالتهابات لمرض الأمعاء الالتهابي ففي الآونة الأخيرة، إزداد الاهتمام في النهج متعدد التخصصات مع المرضى الذين يعانون مرض الأمعاء الالتهابي وإعتلال المفاصل. ان الكشف المبكر والمعالجة الصحيحة لاعتلال المفاصل اصبح الزامي.

الأهداف: لمعرفة معدل حدوث إعتلال المفاصل الطرفية ونمط شمول المفاصل في أمراض الأمعاء الالتهابية.

المرضى وطريقة اجراء الدراسة: تم تقييم ثمانية وأربعون مريضا الذين يعانون من تشخيص مؤكد لأمراض الامعاء الالتهابية (٤١ التهاب القولون التقرحي ومرض كرون ٧) من حيث شمول المفاصل الطرفية واعتلال مرتكز العظم. وتم تقييم سريريا للمرضى من حيث حالة الامعاء والتهاب المفاصل الظرفية والتهاب الارتكاز ونمط شمول المفاصل (أحادي المفصل، قليل المفاصل) وتم اختبار الدم لحساب عدد الكريات و ESR، CRP، RF، وكهربائيات الدم وألالبومين في مصل الدم لتقييم نشاط المرض. وقد تم التقييم الشعاعي في المفاصل الطرفية ذات الأعراض بواسطة الأشعة التقليدية.

Division of rheumatology, Department of Medicine, Faculty of Medical Sciences, University of Sulaimani.
Corrsponding email raofmerza@yahoo.com
Rheumatology unit, Sulaimani General Hospital

النتائج: خمس حالات (١٠.٤٪) لديها التهاب الاعصاب المحيطية من بينها أربع (٨٠٪) كان عندها الآم المفاصل معدودة و إعتلال مرتكز العظم في ١٠(٢٠,٨%) و ٢(٤,٢%) على التوالي. وكان التهاب المفاصل المحيطية أكثر عند الاناث ٤ (٢١,٥%) (قيمة الاحتمال **0.051**). وكان كل المرضى المصابين بالتهاب المفاصل المحيطية في الحالة الفعالة لمرض التهاب الامعاء الالتهابية. وان مرضى التهاب القولون التقرحي الذين يشمل مرضهم أجزاء كبيرة من القولون هم الاكثر عرضة لالتهاب المفاصل المحيطي وبمعدل ٢(٥٠%) لالتهاب القولون الايسر وواحد (٢٥%) لالتهاب القولون الواسع، وواحد (٢٥%) لالتهاب القولون الشامل. أما مرض كرون المتركز في القولون فيكون الميل الاكثر لظهور التهاب المفاصل المحيطي، واحد (١٠٠%) لالتهاب القولون والدقيق.

الاستنتاج: ان المظاهر العضلية الهيكلية لمرض الامعاء الالتهاب هي الام المفاصل يأتي بعدها وبدرجة أقل إعتلال مرتكز العظم. وان النوع الاكثر شيوعا" لالتهاب المفاصل المحيطية هو التهاب المفاصل القليلة والتي تشمل عادة مفاصل الاطراف السفلية. وهو أكثر حدوثا" في الاناث ويحدث بشكل مستقل عن مدة مرض الامعاء الالتهابي.

الكلمات المفتاحية: التهاب الاعصاب المحيطية، أمراض الامعاء الالتهابية المزمنة

INTRODUCTION

Ulcerative colitis and Crohn's disease are chronic inflammatory bowel disease.[1,2] The incidence of IBD varies within different geographic areas. The peak age of onset of UC and CD is between 15 and 30 years.[3] The pathogenesis of the disease is not fully understood but likely involves a genetic predisposition and a dysregulated immunologic response to the local microenvironment of luminal bacteria.[4] Ulcerative colitis (UC) may present as ulcerative proctitis, distal colitis or proctosegmoiditis, left sided colitis and pancolitis.[5] Crohn's disease may involve the entire gastrointestinal tract from mouth to perianal area.[6] Apart from intestinal symptoms, IBD is associated with a variety of extra intestinal manifestations (EIMs), with a reported prevalence varying from 6 to 36%.[7,8] These EIMs are occasionally the presenting symptom. The most common EIM in CD and UC is articular involvement but, cutaneous, ocular, hepatobiliairy and hematologic manifestations may also occur. Musculoskeletal manifestations occur in 20%-50% of patients with IBD.[9,10] The arthropathies of UC and CD have many similarities and the combinations of Peripheral and axial skeletal disease, enthesopathies, mucocutaneous, and ocular disease fit nearly into the diagnostic realism of sero-negativespondyloarthropathies (SpA) which is a heterogeneous group of disorders sharing certain common characteristics; these include predilection in young males, inflammatory back pain, insertional tendonitis (enthesopathy), and asymmetric oligoarthritis involving lower limb joints, persistent seronegativity for rheumatoid factors, familial aggregation and strong association with HLA-B27.[1,11] These disorders include ankylosing spondylitis, reactive arthritis, psoriatic arthritis & spondylitis, Enteropathic arthritis & spondylitis, Juvenile onset spondyloarthritis & undifferentiated spondyloarthritis. [13] The clinical picture of IBD-SpA characterized by axial and/or peripheral joint involvement in the absence of rheumatoid factors and of typical extra-articular findings of rheumatoid arthritis (e.g. subcutaneous nodules).[14] Axial arthropathy associated with IBD includes isolated sacroiliitis, inflammatory backache (IBP) and ankylosing spondylitis (AS), which is onset of frequently precedes that of IBD, the course is independent of the IBD course and bowel surgery does not alter the course of associated sacroiliitis or AS. [15] Peripheral arthropathies include peripheral arthritis, arthralgia, enthesitis and dactylitis. [16] Peripheral arthritis in IBD patients is mostly asymmetric and oligoarticular and is predominantly seen in CD.[17,18] It predominantly affects the large lower limb joints (knees, ankles, hips) but wrists and small

joints of the hands and feet can also be involved.[19] The arthritis is typically nonerosive, occurring in intermittent attacks lasting up to 6 weeks.[18] Dactylitis and enthesitis reiterate the close relationship to the Spondylarthropathieses. The activity of the Peripheral arthritis generally correlates well with the degree of active bowel inflammation, particularly in UC; Indeed, colectomy performed for control of UC can be associated with a complete remission, the same is not true for surgical interventions for CD.[20] IBD associated with peripheral arthritis is diagnosed clinically based on exclusion of other specific forms of arthritis.[21,22]

PATIENTS AND METHODS

Forty-eight patients with a definite diagnosis of inflammatory bowel disease (IBD) [forty-one patients with ulcerative colitis (UC) and seven patients with Crohn's disease (CD)] were included in this cross-sectional study. Patients collected from the Gastroenterology and Hepatology center of Sulaimani Teaching Hospital in Kurdistan region from January to July 2010 have evaluated for peripheral joint involvement. All the cases with IBD were diagnosed and confirmed by clinical examination, endoscopic, histopathological and radiological investigations. Patients on medications causing colitis, infectious colitis and other cases of colitis were excluded from the study. History was taken with special attention to the number of bowel motions, whether the stool mixed with blood or not, abdominal pain, fever, weight loss and duration of the disease. Rhemotological history include joint pain and its duration, joint swelling, the pattern of articular involvement (monoarticular, pauciarticular or polyarticular), morning stiffness, restriction of joint movements, localized pain at iliac crest, tibial tuberosity, ischial tuberosity and heel region was taken. Patients examined to identify the joint involvement and those with recorded joint swelling or effusion were classified as having arthritis; patients without evidence of swelling or effusion were classified as having arthralgia. Detection of Enthesopathy was done clinically by detection of local tenderness at the site of pathology. Axial skeletal involvements were excluded from the study. Blood and serological tests done, full blood count, ESR, CRP, rheumatoid serum factor (RF), electrolytes and serum albumin to evaluate the IBD activity. Tissue typing of HLA-B27 not done (unavailable). Radiological assessment of the symptomatic peripheral joints performed by conventional x-ray. A verbal consent was taken from all patients for being included in the study. The collected data were arranged and analyzed by using (SPSS version 16), P-value of < 0.05 was considered as significant from the statistic point of view.

RESULTS

Forty eight patients with IBD 29(60.4%) male and 19(39.6%) female enrolled in the study, 41(85.42%) had UC and 7(14.58%)CD. Patient's age ranged between 16-67 years with the mean of 38.1 and standard deviation (SD) 13.3 years, the IBD duration ranged from more than a month to 26 years with the mean of 4 years and SD 5.4. Regarding the activity of IBD and frequency of disease distribution among the studied sample, 37(77.08%) were in the active state and 11(22.92%) in the inactive state, [4(57.1%), 2(28.6%) and 1(14.3%)] of UC patients had colitis, ileocolitis and ileitis respectively, and large number of cases of UC had left side colitis with a frequency of [7(17.1%), 13(31.7%), 14(34.1%), 5(12.2%) and 2(4.9%)] for proctitis, proctosigmoiditis, left side colitis, extensive colitis and pancolitis respectively. While the frequency distribution of peripheral arthropathies among the studied sample explored that a high percentage of cases had arthralgia with a frequency of [10(20.8%), 5(10.4%) and 2(4.2%)] for arthralgia, arthritis and enthesopathy respectively (figure-1).

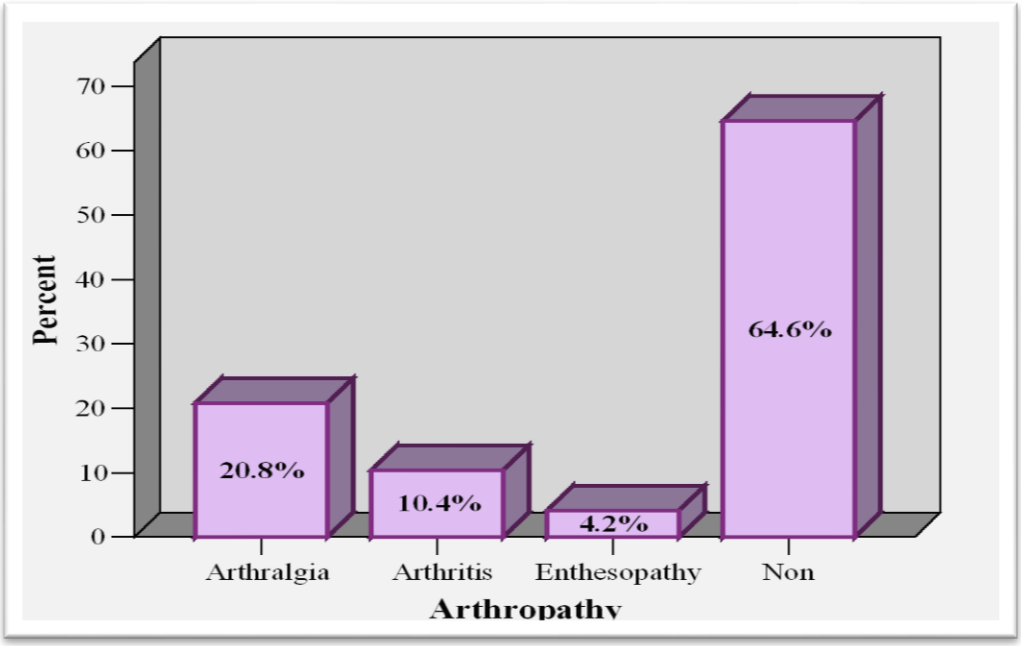

Fig 1. Shows the frequency distribution of peripheral arthropathies among IBD patients.

Conventional x-ray performed in five patients, no signs of destructions or erosions were found. The association between peripheral arthritis (PA) and gender is shown in (Table-1) and it reveals that PAIBD was more common among female patients with frequency of 4(21.05%) for females and 1(3.45%) for males with P-value of (0.051).

Table 1. Association between PA and gender.

Gender	Arthritis		Total No. (%)	P-value
	Positive No. (%)	Negative No. (%)		
Male Female	1 (3.45) 4 21.05)	28 (96.55) 15 (78.95)	29 (100) 19 (100)	0.051

The frequency distribution of the types of joint involvement, Pattern of arthritis and the onset of arthritis is shown if (Table-2), it reveals that the knee joints were the most commonly involved joints 5(100%) cases, the pattern of arthritis was most commonly pauciarticular with a frequency of 4(80%) cases, and the onset of arthritis was most commonly post-date the onset of IBD with a frequency of 4(80%) cases. The calculation is made according to musculo-skeletal involvement in IBD cases.

Table 2. Types of joint involvement, pattern of arthritis and the onset of PA among the studied sample

Variables	Frequency	%
Joint involvement		
Knee joint	5	100
Ankle joint	3	20
Wrist joint	1	20
Elbow joint	1	20
Small joints of hand and feet	1	
Pattern of arthritis		
Pauciarticular	4	80
Polyarticular	1	20
Onset of arthritis		
Pre-onset of IBO	1	20
Post-onset of IBO	4	80

The association between PA and the duration of IBD in (Table-3), it reveals that the mean duration of patients with PA was 7.0 years [(SD) 4.2 years], while those without arthritis was 3.7 years [(SD) 5.5 years] with P-value of (0.201).

Table 3. Association between PA and the duration of IBD.

Arthritis	Duration of IBD years Mean ± STD. Deviation	P-value
Yes	7 ± 4.2	0.201
No	3.7 ± 5.5	

The association between PA and the IBD activity status is shown in (Table-4); it reveals that all of those patients who had PA were in the active state of IBD with P-value of (0.198)

Table 4. Association between PA and the IBD activity status.

Ibd activity status	Arthritis		Total No. (%)	P-value
	Yes No. (%)	No. No. (%)		
Active	5(13.5)	32 (86.5)	37 (100)	0.198
Inactive	0	11 (100.0)	11 (100)	

The association between PA and the extent of IBD (UC and CD) is shown in (Table-5) and it reveals that among cases of UC those who had pan colitis were more likely to develop PA with a frequency of 1(50%) followed by extensive colitis 1(20%) and left side colitis 2(14.29%), while patient with proctitis and proctosigmoiditis were not likely to develop PA. Among cases of CD those who had ileocolitis were more likely to develop PA 1(50%).

Table 5. Association between PA and the extent of UC and CD.

Disease activity	Arthritis		Total (%)	P-value
	No No. (%)	Yes No. (%)		
Extent of UC				
Proctitis	7 (00.0)	0 (0.0)	7 (100.0)	
Proctosigmoiditis	13 (100.0)	0 (0.0)	13 (100.0)	
Left side colitis	12 (85.71)	2 (14.29)	14 (100.0)	0.149
Extensive colitis	4 (80.0)	1 (20.0)	5 (100.0)	
Pancolitis	1 (50.0)	1 (50.0)	2 (100.0)	
Extent of CD				
Ileitis	1 (100.0)	0 (0.0)	1 (100.0)	
Ileocolitis	1 (50.0)	1 (50.0)	2 (100.0)	
Colitis	4 (100.0)	0 (0.0)	4 (1000)	0.223

DISCUSSION

Inflammatory bowel disease (IBD) comprises the clinical entities of ulcerative colitis and Crohn's disease; these are chronic and idiopathic inflammatory diseases of the gastrointestinal tract that share common symptoms such as diarrhea, abdominal pain, fever, and weight loss.[23] Musculoskeletal manifestations are relatively common andare well-defined extra-intestinal manifestations of inflammatory bowel diseases (IBD). There is little data regarding the frequencies of IBD and extra-intestinal manifestations from Central and East Europe and Middle Eastern countries, chronic IBD can affect joints, skin, eyes, bile ducts, and various other organs; The most frequent rheumatologic manifestations are peripheral arthritis and axial arthropathies. [24] The present study focuses on the frequency of peripheral arthropathy among patients with IBD, its articular distributions and its relation to the activity and to the extent of IBD. In this study we found that 5(10.4%) of 48 patients with diagnosis of IBD had PA this is close to the results concluded by de Vlam K, et al. [25] who found that peripheral arthritis in IBD occurred in 10%. Ten(20.8%) of our patients had arthralgia this figure is higher than that recorded by de Vlam K et al. [25] who found that arthralgia occurred in 16% & its lower than that recorded by Palm O, et al. [26] who found arthralgia to be in 30% of their cases, this variation might be explained on the bases of ethnic, environmental or other causes. Enthesopathy is a recognized feature of seronegativeSpA, 2(4.2%) of our patients had it, while de Vlam K.[25] reported a higher frequency of enthesitis (7%). The results indicate that arthritis was more common in CD than in UC with the frequency of 1(14.3%) in CD and 4(9.76%) in UC. Orchard Et al reported that PA was more common in CD than in UC, but the figure was lower than that reported by our study with a frequency of 10% in CD and 6% in UC. Palm et al.[26] also concluded that there was a trend toward a higher rate of PAIBD in CD patients than in UC with figures closer to ours with a frequency of 14% for CD and 11% for UC, but neither of these studies reached a statistically significant level. IlhamiYulesel et al.[27] claimed female preponderance when PA occur in IBD with difference to be statistically significant, this is consistent with our results but the differences in ours didn't reach statistical significant level p-value (0.051), this might be due to low number of female patients. Regarding the pattern of joint involvement four of the patients had pauciarticular arthritis and only one patient had polyarticular joint involvement and all of the patients had knee joints involvement with or without other joints. The frequency of joint involvement in our study was [knees five cases, ankles three cases, wrists

one case, elbows one case and small joints of hands and feet one case], these are consistent with the finding of Palm O, et al.[26] who claimed that lower limb joints are more frequently involved and pauciarticular pattern more than polyarticular, but the figures was lower than ours [knees (55%), ankles (35%), and small joints of fingers and toes in (18%)], symmetrical polyarthritis (35%) and pauciarticular pattern in (65%), this might be due to higher number of patients included in their study (521 patients). Haslock I et al. [28] also found that the knee was the most commonly involved joint, followed by the Ankle, less commonly involved are the hips, shoulders, wrists, and elbows and occasionally the hands and feet are affected. Palm O et al. [26] results revealed no signs of joint destruction or erosions on x-ray; this is consistent with our findings. We found that arthritis occurred independent on the duration of IBD, similar finding observed by Wright V, et al. [29] who found that initial presentation of arthritis is likely to occur in patients who have bowel disease of less than 6 months duration as it is to occur in patients who have disease duration of more than 10 years. Regrding the onset of PA, we found that 1(20%) case developed PA 2 years before the development of IBD while in 4(80%) cases the arthritis occurred after the development of IBD and this is close to what have been concluded by IlhamiYulesel et al. [27] who found that peripheral arthritis started before the onset of IBD in (12.1%) of the cases. Palm O, et al.[26] also found that PA preceded IBD inonly 18% of their patients while others developed it after the onset of bowel disease. Although all our cases with PA were in active state for the IBD but the relation did not reach statistically significant level p-value (0.198), a similar conclusion made by R. D'Inca, et al. [30] who could not confirm an association between the Peripheral arthropathy and flare up of IBD. We reported one case who developed symmetrical polyarthritis after total proctocolectomy following inflammation of reconstructed ileal pouch (pouchitis), similarly Lomuller JL, et al. [31] and Axon JM, et al.[32] had found that arthritis developed at the same time as ilealpouchitis after total proctocolectomy for UC activity. Regarding the association between the extent of gastrointestinal inflammation and the development of PA there were a conflicting results, as early study done by Wright V, et al. [29] found an association between the incidence of PA and the extent of bowel inflammation in UC. However a study done by Veloso, et al. [8] did not confirm such association. In our study we found that patients with UC those who had left side colitis, extensive colitis and pan colitis were more likely to develop PA in frequencies of [2(14.29%), 1(20.0%) and 1(50.0%)] for left side colitis, extensive colitis and pan colitis respectively, while no patients with PA was recorded among those who had proctitis or proctosigmoiditis, and out of seven patients with CD, only one patient with colonic localization of the disease developed PA (ileocolitis). This is consistent with the study done by Reinisc et al. [33] who revealed that 95% of CD with PA had colonic involvement. This indicates that the extensive UC and the colonic localization of CD might predispose to the development of PA among susceptible patients.

CONCLUSIONS & RECOMMENDATIONS

Peripheral arthropathies are common musculoskeletal manifestations among IBD patients. P.A occurred in considerable number of IBD patients, more commonly pauciarticular and mostly involved the lower limb joints. It may predate the onset of inflammatory bowel disease but mostly occurred after the onset of inflammatory bowel disease. PA was more common among female patients, occurred independent on the duration of IBD, present in the active stage of IBD, Extensive UC and the colonic localization of CD might be a predisposing factor for developing PA. Our

study highlights the need for further studies about the peripheral arthritis in IBD patients to look for the lifetime risks of PAIBD, preferably those designed as prospective population-based surveys, It may worth that Gastroenterologist refer IBD cases to the Rheumatologist for assessment of any rheumatological manifestation.

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