

## Fibromyalgia Syndrome in 104 Iraqi Patients with Inflammatory Bowel Disease

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### ABSTRACT:

#### BACKGROUND:

Fibromyalgia syndrome (FMS) is a common rheumatologic syndrome with multiple systemic manifestations & associated with many diseases.

#### OBJECTIVE:

To assess fibromyalgia syndrome in inflammatory bowel disease.

#### PATIENTS AND METHODS:

One hundred four Iraqi patients with inflammatory bowel disease were studied and compared with another (112) healthy individuals matched for age and sex as a control group. Full history was taken and complete clinical examination was done for all individuals in both groups. Fibromyalgia syndrome was diagnosed in all patients on base of the American College of Rheumatology (ACR) 1990 Criteria for the classification of FMS. Inflammatory bowel disease was detected by colonoscopy & tissue biopsy.

#### RESULTS:

There was a significant increase in the frequency of FMS among individuals with IBD (24 %) compared to healthy control group (5.4%) ((P-value =0.0001, Odd ratio=0.18, 95% CI=0.07-0.46).

#### CONCLUSION:

FMS occurs with increased frequency in IBD.

**KEY WORDS:** inflammatory bowel disease, fibromyalgia syndrome, fibromyalgia in inflammatory bowel disease

### INTRODUCTION:

Fibromyalgia (FM) is a debilitating and frustrating syndrome characterized by a chronic widespread pain and tenderness with prevalence rate of 4.9% in the general population <sup>(1)</sup>. Although its pathogenesis and treatment remain unclear <sup>(2)</sup>, fibromyalgia has been linked to the occurrence of various forms of physical trauma <sup>(3)</sup>, infectious disorders <sup>(4)</sup>, emotional trauma <sup>(5)</sup>, and genetic factors <sup>(6)</sup>.

There appears to be considerable overlap between FM and depression with many patients carrying both diagnoses <sup>(7)</sup>; and the medications used for the treatment of depression are frequently implemented in the management of FM <sup>(8)</sup>.

The inflammatory bowel diseases (IBD), Crohn's disease (CD) and ulcerative colitis (UC) are inflammatory diseases affecting the gastrointestinal tract and are often associated with several extraintestinal manifestations. Approximately 25% of patients with IBD have combinations of several extracolonic manifestations <sup>(9)</sup>. Musculoskeletal symptoms are described in 6%–46% of IBD patients and they are considered the most common extraintestinal manifestations in IBD <sup>(10)</sup>. Skeletal pain is a very common symptom in IBD patients and its origin cannot be easily identified in all cases <sup>(11)</sup>.

The prevalence of FM in patients with chronic diseases appears to be significantly high <sup>(11)</sup>, so it is possible to find a relationship between FMS and IBD.

The aim of the study is to assess the relationship between FMS and IBD.

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### PATIENTS AND METHODS:

A cross-sectional study was carried out at Baghdad Teaching Hospital / Gastroenterology Unit, Medical Department; and Outpatient Clinic of the Gastroenterology & Hepatology Hospital from January 2009 till May 2010. One hundred four patients had IBD. Our patients were diagnosed by gastroenterologists on base on full history, complete clinical examination, & colonoscopy with confirmatory histology seen on colonic biopsy. The severity & activity of IBD were assessed using: Truelove & Witts Severity Index<sup>(12)</sup>; Simple Clinical Colitis Activity Index<sup>(13)</sup>, and Simple Index of Crohn's Activity<sup>(14)</sup>. Another 112 healthy individuals matched for age and sex were collected from relatives and accompanying persons of patients attending to Rheumatology Unit & Medical Department were studied as a control group. The American College of Rheumatology 1990 Classification Criteria for fibromyalgia which include a history of chronic widespread pain involving all four quadrants of the body and the axial skeleton, plus the presence of 11 of 18 tender points on physical examination were applied to all the patients and controls.<sup>(15)</sup>

Patients were excluded from the study if they had conditions mimic FMS like: autoimmune disorders, neurological disorders, endocrine disorders, hepatitis C, malignancy, & osteomalacia<sup>(16)</sup>

A signed consent was taken from all individuals studied. Ethical approval was obtained from the Ethics Committee of Baghdad University, College of Medicine, Medical Department.

Statistical analysis was done using statistical package for social science software (SPSS16) for Windows. Association between different categorical variables was measured using Chi-square test or Fisher's exact test where appropriate. Difference between continuous variables was measured using t-test. Multiple logistic regression analysis was done to find the predictors of FMS in IBD. P-values<0.05 were considered significant.

### RESULTS:

The 104 patients with IBD (57 males & 47 females) compared with 112 healthy individuals (49 males & 63 females) as a control group (P-value= 0.134). The mean age was (36.60±12.21) years for the IBD patients group, and (38.31 ±12.57) years for the control group (P-

value=0.314) indicating no statistical significant difference between both groups (Table 1).

The frequency of FMS in 104 patients with IBD was 24% compared to 5.4% in 112 healthy individuals (P-value =0.0001, Odd ratio=0.18, 95% CI=0.07-0.46) indicating a statistical significant difference between both groups as shown in Table 2.

The frequency of FMS was more in Crohns disease (25%) compared with ulcerative colitis (23.9%) but no statistical significant difference between the two (P-value=1, Odd ratio=1.06, 95%CI= 0.31-3.65) as shown in Table 3.

There was a very high statistical significant difference between frequency of FMS symptoms (wide spread pain, headache, fatigue, sleep disturbances, & depression) in 104 patients with IBD & 112 controls (p= 0.0000001, p= 0.0000002, p= 0.0000001, p= 0.0000001, p= 0.0000002) respectively as shown in Table 4.

Also, there was a statistical significant difference between frequency of FMS symptoms (anxiety, numbness, & irritable bowel syndrome) in 104 patients with IBD & 112 controls (p=0.03, p=0.02, p=0.03) respectively as shown in Table 4.

Multiple logistic regression analysis reveals that there is negative relationship between the independent variables: sex (male gender compared to female) [B=-2.18, p=0.03,OR=0.11(95% CI=0.02-0.83)],severity of IBD[B=-4.59, p=0.02, OR=0.01(0-0.49)], family history of fibromyalgia or rheumatic diseases [B=-7.35, p=0.00004, OR=0.001(95%CI=0=0.02)]; and the dependent variable (FMS) as shown in Table 5.

Also there is no significant relationship between the independent variables: age [B=0.32, p=0.47, OR=1.03 (95%CI=0.95-1.13)], duration of disease [B=0.07, p=0.29, OR=1.07 (95%CI=0.94-1.22)], types of IBD [B=-0.008, p=0.10, OR=0.99 (95%CI=0.05-18.200)], activity of IBD[B=-0.14,p=0.89, OR=0.87(95%CI=0.12-6.15)], drugs [steroids(B=1.38,p=0.23, OR=3.97(95%CI=0.41-38.08); sulfasalazine(B=-1.56, p=0.16,OR=0.21(95% CI=0.02 -1.87); azathioprine (B=1.37, p=0.38, OR=3.95 (95%CI=0.18-84.77) ; and the dependent variable (FMS) as shown in Table 5.

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**Table1: Demographic characteristics of 104 patients with IBD and 112 healthy controls**

Variables	Patients n=104	Controls n=112	P-value
Age (mean) ( years)	36.60±12.21	38.31±12.57	0.314 <sup>ns</sup>
Gender			
Male n (%)	57(53.8)	49(46.2)	0.134 <sup>ns</sup>
Female n (%)	47(42.7)	63(57.3)	

IBD, inflammatory boel disease; n., number; %, percentile; ns, P-value is not significant

**Table 2: Frequency of FMS in 104 patients with IBD and 112controls**

Group	FMS		P-value	OR (95%CI)
	Present n. (%)	Absent n.(%)		
Patients n=104	25(24)	79(76)	0.0001**	0.18 (0.07-0.46)
Controls n=112	6(5.4)	106(94.6)		

FMS, fibromyalgia syndrome; \*\* P-value is highly significant. ;OR, odd ratio; CI, confidence interval; FMS, fibromyalgia syndrome

**Table 3: Frequency of FMS according to the type of 104 patients with IBD**

Variables	FMS		P-value	OR( 95%CI)
	Present n.(%)	Absent n.(%)		
Ulcerative colitis n=88	21(23.9)	67(76.1)	1	1.06 (0.31-3.65)
Crohns disease n=16	4(25)	12(75)		

n, number; %, percentile

**Table 4: Frequency of FMS symptoms in 104 patients with IBD compared to 112 healthy controls**

Variables	IBD n=104	Controls n=112	P-value	OR( 95%CI)
Diffuse pain n(%)	27(93.1)	2(6.9)	0.0000001**	0.05(0.01-0.23)
Fatigue n(%)	27(93.1)	2(6.9)	0.0000001**	0.05(0.01-0.23)
Headache n(%)	26(92.9)	2(7.1)	0.0000002 **	0.05(0.13-0.24)
Sleep disturbances n(%)	27(93.1)	2(6.9)	0.0000001**	0.05(0.01-0.23)
Depression n(%)	26(92.9)	2(7.1)	0.0000002**	0.05(0.13-0.24)
Anxiety n(%)	9(81.8)	2(18.2)	0.03 *	0.19(0.04-0.91)
Numbness n(%)	7(87.5)	1(12.5)	0.02 *	0.13(0.02-1.03)
IBS n(%)	5(100)	0(0)	0.03*	0.47(0.41-0.54)

\*\* P-value is highly significant; \*,P-value is significant; n., number; %, percentile

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**Table 5: Multivariable logistic regression analysis of predictors for FMS in 104 IBD patients**

Variables	B	P-value	OR (95% CI)
Age	0.32	0.47	1.03(0.95-1.13)
Sex:male (compared to female)	-2.18	0.03*	0.11(0.02-0.83)
Duration (years)	0.07	0.29	1.07(0.94-1.22)
Type of IBD	-.008	0.10	0.99(0.05-18.20)
Severity of IBD	-4.59	0.02*	0.01(0-0.49)
Activity of IBD	-0.14	0.89	0.87(0.12-6.15)
FHx	-7.35	0.00004**	0.001(0-0.02)
Drugs			
Steroids	1.38	0.23	3.97(0.41-38.08)
SSZ	-1.56	0.16	0.21(0.02-1.87)
Azathioprine	1.37	0.38	3.95(0.18-84.77)

B, regression coefficient; \* p-value is significant; \*\* p-value is highly significant; OR, odd ratio; CI, confidence interval. FHx, family history; SSZ, sulfasalazine; -; negative relationship between independent variable( predictor) and dependent variable( fibromyalgia syndrome)

### DISCUSSION:

In the present study we found a significant association between FMS and IBD.

Multiple factors may explain this association including chronicity of IBD, genetic factors, & environmental factors.<sup>(11,17,18)</sup>

In the present study, the frequency of FMS among patients with IBD was 24 %, compared to that of healthy individuals (5.4%) (P-value =0.0001, Odd ratio=0.18, 95% CI=0.07-0.46) which does indicate a significant association between the two conditions. This finding is comparable to another study done by Buskila D et al (30%)<sup>(17)</sup>. Such finding may indicate a role of stress related factors of chronic disease in etiopathogenesis of FMS. The stress and pain accompanying IBD might be putative triggering agents for development of FMS. Also, the frequency of FMS was more in Crohns disease compared with ulcerative colitis. This agreed with previous studies done by Bourikas LA & Papadakis KA<sup>(11)</sup>, and Buskila D et al<sup>(17)</sup>; but it is in contrast with another study done by Palm O et al in which frequency of FMS in ulcerative colitis was 3.7% compared to FMS in Cronhs disease which was 3%<sup>(18)</sup>, this might be explained by variations in social, cultural, and educational backgrounds of patients studied, but more likely, differences in study design appears to be the main reason for differences in estimated prevalence rates. Our study was based on patients attending a hospital unit, while in Palm O et al, the study based on patients recruited from general population. The frequency of symptoms of FMS was significantly more in patients with IBD than frequency of FMS symptoms in controls. This

finding goes with previous study done by Buskila D et al<sup>(17)</sup>.

In the present study; male sex, family history of FMS or rheumatic diseases, & severity of IBD are predictors with significant negative relationship to FMS in patients with IBD.

In the present study, there was no statistical significant association between FMS; and: age, duration, type, activity, and medication used in treatment of IBD. This might be explained by the small limited sample studied.

The diagnosis, assessment, & follow up of FMS relies on self reported syndrome, commonly pain and tenderness is subjective reflecting many factors like, ethnicity, age, sex, social back ground, underlying concomitant chronic disease and psychological stress<sup>(19)</sup>. This is also true regarding management, there is no specific treatment for FMS<sup>(20)</sup>, management will encompass multiple strategies, including education, stress management and aerobic exercise to help the patients cope with their symptoms and improve their quality of life<sup>(21)</sup> The occurrence of FMS has certain clinical implications. The clinical features may in some patients imitate increased IBD activity and thus be misinterpreted as a disease relapse. Such mistake may occasionally result in increased administration of drugs<sup>(22)</sup>. Clinicians should be aware of the frequent occurrence of gastroenterological symptoms in FMS. According to some authors, as many as 70% of patients with FMS may exhibit symptoms consistent with irritable bowel

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syndrome<sup>(23)</sup>, so it is important to be aware of coexistence in some patients.

A number of limitations of the current study must be pointed out. We did not perform a detailed assessment of depression, anxiety, or coping among patients who developed tenderness and other symptoms of FMS. More detailed analyses of these parameters would better characterize these aspects and would assist in the evaluation of the association between IBD and the development of FM symptoms. The relatively small size of the study sample must be noted. Despite these limitations, our findings call attention to important relationship between FMS & IBD.

We recommend assessing patients with IBD for FMS to prevent misdiagnosis and ensure correct treatment.

### CONCLUSION :

FMS occurs with increased frequency (24 %) in patients with IBD.

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