

## Fibromyalgia in Egyptian Rheumatoid Arthritis Patients and patients with Depression

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### ABSTRACT

**Background:** Fibromyalgia (FM) is a chronic musculoskeletal disorder resulting in chronic widespread pain. Although it is currently believed to be the result of a central nervous system malfunction that increases pain transmission and perception. Patients with fibromyalgia frequently experience psychiatric problems. **Objectives:** Is to estimate the presence of fibromyalgia among Egyptian patients with rheumatoid arthritis (RA) and those with chronic depression. **Patients and methods:** This study was done on 277 patients; 176 patients with rheumatoid arthritis (group I), and 101 patients with chronic depression (group II). The patients were selected from Al-Zahraa University Hospital, Al-Azhar University. All patients were subjected to thorough clinical examination, laboratory investigation, calculation of disease activity score, modified Beck scale for depression. **Results:** Among RA patients FM diagnosis was established in 21.02% patients and 20.45% were females. Their mean age; 48.43 ( $\pm 6.85$ ) years that was significantly higher than RA patients only (29.48 $\pm$ 8.59) years. Among (group II) patients, FM diagnosis was established in 40 (39.60%) female patients and 3(2.97%) male patients. Our results showed that depressive symptoms were more common in RA patients with fibromyalgia. DAS28 score was significantly higher in RA patients with FM mainly due to subjective component (number of tender joints and patient global assessment). **Conclusion:** Fibromyalgia may coexist with autoimmune inflammatory disorder like RA, commoner in older age, females and it worsens the disease activity. However, it is more common in patients with chronic depression. [Egypt J Rheumatology & Clinical Immunology, 2014; 2(1): 97-103]

**Key Words:** Fibromyalgia, rheumatoid arthritis, depression.

### INTRODUCTION

Fibromyalgia syndrome (FMS) is a clinically well-defined chronic condition of unknown etiology characterized by chronic widespread pain that often co-exists with sleep disturbances, cognitive dysfunction and fatigue. Patients often report high disability levels and poor quality of life.<sup>1</sup> The estimated overall prevalence of FMS was 2.9% in the general population of European countries.<sup>2</sup>

Lacking a specific laboratory test, diagnosis is established by a history of the key symptoms and the exclusion of somatic diseases that could explain the key symptoms.<sup>3</sup> For the clinical classification; the American College of Rheumatology (ACR) 1990 classification<sup>4</sup>, the ACR 2010 preliminary diagnostic criteria<sup>3</sup> and the modified ACR 2010 preliminary diagnostic criteria (survey criteria) can be used.<sup>1</sup>

Depression is a common comorbid condition in FMS and a major contributor to poor quality of life and disability. However, depression can be difficult to assess in patients with FM due to overlapping symptoms between the two conditions.<sup>5</sup>

FM is often associated with other autoimmune diseases that act as confounding and aggravating factor, such as primary Sjögrens' syndrome (pSS), systemic lupus erythematosus (SLE), and rheumatoid arthritis (RA).

The aim of this work was to estimate the presence of fibromyalgia among Egyptian patients with rheumatoid arthritis and among patients with chronic depression.

### PATIENT AND METHODS

This study was done on 277 patients; 176 patients with rheumatoid arthritis (group I) and 101 patients with chronic depression (group II). Two hundred and forty six (88.81%) patients were female and 31(11.19%) patients were male. Their ages ranged from 18 to 65 years with mean ( $\pm$ SD) age of 36.920

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(±11.6) years. The patients were selected from Al-Zahraa University Hospital, Al-Azhar University.

**Inclusion criteria:** Age range from 18-70 year, both sexes included, RA patients should fulfill ACR criteria for RA classification (1987) and gave an informed consent.

**Exclusion criteria:** included other causes of chronic widespread pain such as clinical or laboratory evidence of other autoimmune inflammatory diseases, thyroid or parathyroid gland disorder, chronic liver or kidney diseases, metastatic cancer, multiple myeloma or infection at the evaluation visit.

**Group 1:** Patients with definite RA (according to ACR criteria (1987)). They included 176 patients, 161(90.1%) were females and 15(9.9%) were males. Their ages ranged from 18 to 65 year with a mean (±SD) of 33.46 (±11.3) years. The disease duration ranged from 1 to 25 year with mean (±SD) of 6.58 (±5.33) years (Table 1).

**Group II:** They were 101 patients suffering from chronic depression. Their age ranged from 20 to 64 year with a mean (±SD) of 32.43 (±10.24) year; 85 (84.16%) were females and 16 (15.84%) were males. The duration of depression ranged from 1 to 18 year with mean (± SD) of 3.02 (±2.68) years (Table 1).

All patients were subjected to the following:

- 1- Full medical history and clinical examination.
- 2- Depressive symptoms were assessed using the modified Beck scale (BDI).<sup>6</sup> It contains 30points; each point contains three items and gives score from zero to three degree according to severity of the symptoms. Results of the tests: The score is classified into the following: Zero up to 4 = Normal. 5 up to 7 = Mild depression. 8 up to 15 = Moderate depression. 16 and above = severe depression.
- 3- LFESSQ: This is a screening questionnaire used to evaluate patients with wide spread pain.<sup>7</sup> A positive screen was defined as either:
  - a- Meeting the pain criteria alone (LFESSQ-4).
  - b- Meeting both the pain and the fatigue criteria (LFESSQ-6).
- 4- Clinical examination for detection of specific tender points. Calculation of disease activity score (DAS28) to evaluate disease activity for RA patients;  $DAS\ 28 = 0.56\sqrt{t28} + 0.28\sqrt{sw28} + 0.7\ln(ESR) + 0.014GA$  (tender joints, – swollen joints) in RA patients.
- 5- Laboratory investigations including:
  - I. Biochemical tests: using Hitachi 911auto-analyzer included: Fasting blood sugar (FBS), kidney function, liver enzymes and function tests, serum calcium, and serum electrolytes.

II. Complete blood count and urinalysis.

III- Inflammatory markers including: ESR and CRP to assess disease activity.

IV. Immunological tests: Performed for detection of RF

V. Thyroid stimulating hormone (TSH) level.

6- Imaging studies including: Plain X-ray chest, pelvi-abdominal ultrasonography.

### Statistical Methods

Statistical analysis was done using (Statistical Package for Social Science) SPSS software version 11.5 and Microsoft excel 2003. Group data were reported using means± (SD) and ranges. Two-tailed Student's t-test was also used to compare quantitative data. Level of significance (P value) ≤ 0.05 is considered significant.

## RESULTS

Female patients were 246 (88.80%) and 31 (11.19%) patients were males. Those patients were divided into group I (RA patients) and group II (patients with depression). There was no significant difference in age, duration of the primary illness, gender ratio and marital status between the two groups, (p>0.05) (Table 1).

The frequency of FM among rheumatoid arthritis patients was 37(21.02%) patients, and among patients with chronic depression were 43 (42.57%) patients (Table 2).

There was no significant difference in Hb, RBC, WBC and platelet count, blood urea, serum creatinine, Na, K, Ca, and FBS between the two groups, (p>0.05). As regard liver function tests (AST, ALT, serum albumin and serum bilirubin) also there was no significant difference between the two studied groups, (p>0.05).

As regard inflammatory markers (ESR and CRP): they were highly significantly increased in patients group I than group II, (p< 0.05) (Table 3).

Among 176 patients with RA (group I), 37(21.02%) patients fulfilled the ACR criteria 1990 for the diagnosis of FM, they were 36 (97.30%) female patients and 1(2.70%) male. Women were more predominant. The mean age and duration of the primary illness were higher in the group of RA and FM (Table 4).

Patients with RA and FM had a longer duration of morning stiffness, as 32 (86.4%) patients had morning stiffness more than 1 hour, and only 5 (13.51%) patients had morning stiffness less than 1 hour (Table 5).

The most common clinical symptoms of FM among patients with RA with FM were increased significantly than those in RA patients without FM (Figure 1).

As regard DAS28 score: High disease activity was more prevalent in RA patients group with FM. Mean ( $\pm$ SD) DAS score of RA with FM was 5.75 ( $\pm$ 0.31) that was significantly higher than that of RA patients 4.01 ( $\pm$ 0.6). This group did not have any patients in remission or low disease activity (Table 6).

Although there were no significant differences in the ESR and the swollen joint count, there were significant differences in the subjective components of the DAS28 (tender joints and Patient global assessment for disease status) (Figure 2).

The score of BDI was significantly higher among patients of RA and comorbid FM than that among patients with RA only (Figure 3).

Among 101 patients with chronic depression (group II), 43(42.57%) patients fulfilled the ACR1990 criteria for the diagnosis of FM. They were 40 (39.60%) female patients, and 3(2.97%) male patients, women were more predominant in the group with depression and FM. The mean age was higher in the group with depression and FM. There was no significant difference in duration of the primary illness

between patients with co-morbid FM and those with depression only,  $p > 0.05$  (Table 7).

The most common clinical symptoms of FM among patients (group II) were significantly higher among patients with co-morbid FM than those with chronic depression only (figure 4).

As regard LFISSQ among patients with rheumatoid arthritis, 139 (78%) patients screened positive for LFISSQ-4 (widespread pain), and 102(57.9%) patients screened positive for LFISSQ-6 (widespread pain and fatigue). 37(21%) patients were confirmed FM cases according to the ACR criteria1990. Thus the PPV for LFISSQ-4 was 26.6% and for LFISSQ-6 was 36.2%. As regard LFISSQ among patients with chronic depression,95(94%) patients screened positive for LFISSQ-4, and 86(85.14%) patients screened positive for LFISSQ-6, 43(42.57%) patients were confirmed FM cases according to the ACR criteria. Thus the PPV for LFISSQ-4 was 45.2% and for LFISSQ-6 was 50% (Table 8).

**Table 1.** The age, gender, duration of diseases of both RA and chronic depression patient groups.

		(group I) 176	(group II) 101	P-value
Gender	Male	15 (9.9%)	16 (15.84%)	0.11
	Female	161 (90.1%)	85 (84.16%)	
Age (mean $\pm$ SD) years		33.46 $\pm$ 11.3	32.43 $\pm$ 10.24	0.08
Disease duration (mean $\pm$ SD) years		6.58 $\pm$ 5.33	3.02 $\pm$ 2.68	0.08

**Table 2.** The frequency of FM among patients with RA (group I) and patients with chronic depression (group II).

	Group (I) (n 176)		Group (II) (n 101)	
	Number	%	Number	%
FM	37	21.02	43	42.57

**Table 3.** Inflammatory markers (ESR, CRP) in RA patients and patient with chronic depression.

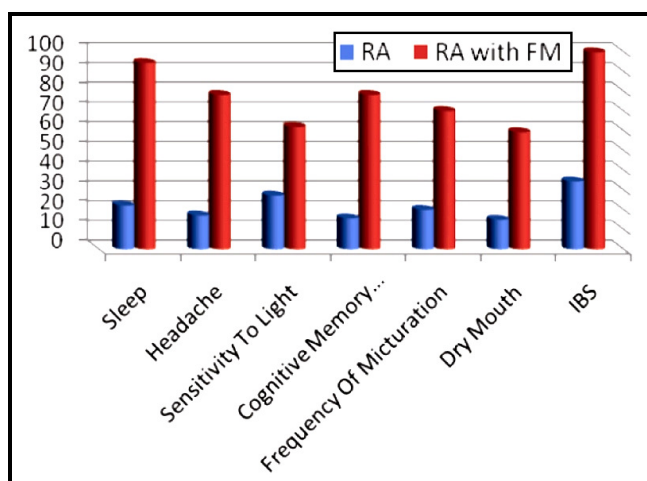
	RA (group I) n 176	Depression (group II) n 101	P-value
ESR (mean $\pm$ SD)	27.26 $\pm$ 5.44	12.02 $\pm$ 3.01	0.004
+ve CRP(n, %)	121(68.75%)	12 (11.88%)	0.003

**Table 4.** Mean age, disease duration and gender distribution in RA patients with and without FM.

	Age (year)	Duration of Illness (year)	Gender	
	Mean $\pm$ SD	Mean $\pm$ SD	Female	Male
RA without FM	29.48 $\pm$ 8.9	5.01 $\pm$ 3.99	127 (91.37%)	12 (8.63%)
RA with FM	48.43 $\pm$ 6.5	12.49 $\pm$ 5.63	36 (97.30%)	1 (2.70%)
P-value	< 0.01	< 0.01	> 0.05	$\geq$ 0.05

**Table 5.** Morning stiffness duration in RA patients with or without FM.

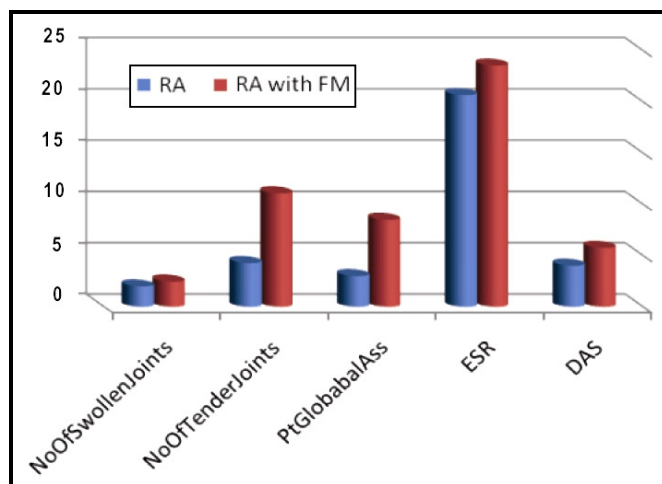
	Stiffness < 1 h	Stiffness > 1 h
RA without FM (n)	138 (99.28%)	1 (0.72%)
RA with FM (n)	5 (13.51%)	32 (86.49%)
P-value	< 0.01	< 0.01



**Figure 1.** Distribution of The main clinical symptoms of FM in RA patients (group I) with or without FM.

**Table 6.** The DAS28 score in RA patients with or without FM.

DAS Score	DAS (mean±SD)	0 - 2.6 (remission)	2.7 - 3.2 (low activity)	3.3 - 5.1 (mod. activity)	> 5.2 (high activity)	P-value
RA without FM	4.01±0.6	2 (1.44%)	35 (25.18%)	100 (71.94%)	2 (1.44%)	< 0.01
RA with FM	5.75±0.3	0	0	2 (5.41%)	35 (94.59%)	



**Figure 2.** The DAS score and its different variables in RA patients with or without FM (group I).

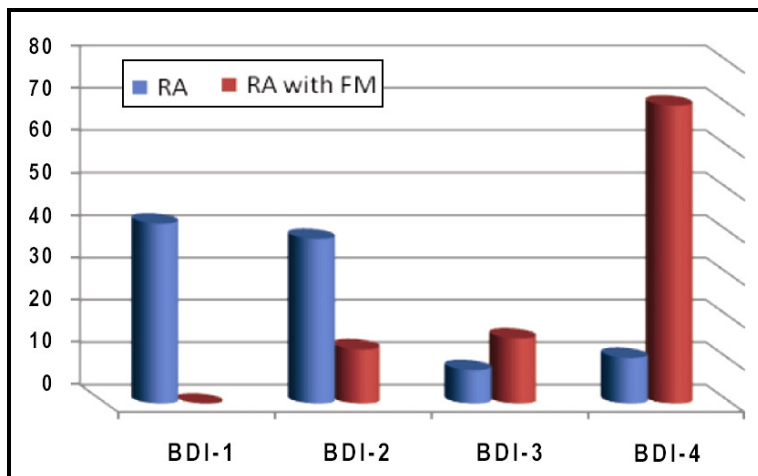


Figure 3. The BDI score in RA patients with or without FM (group I).

Table 7. Mean age, disease duration and sex distribution in chronic depression patients with and without FM.

	Age	Duration of Illness	Gender	
	Mean±SD	Mean±SD	Males	Females
(group II) without FM	30.43±9.19	2.9±2.27	7 (12.07)	51 (87.93)
(group II) with FM	35.14±11.1	3.21±3.19	3 (6.98)	40 (93.02)
P-value	< 0.05	> 0.05	< 0.05	

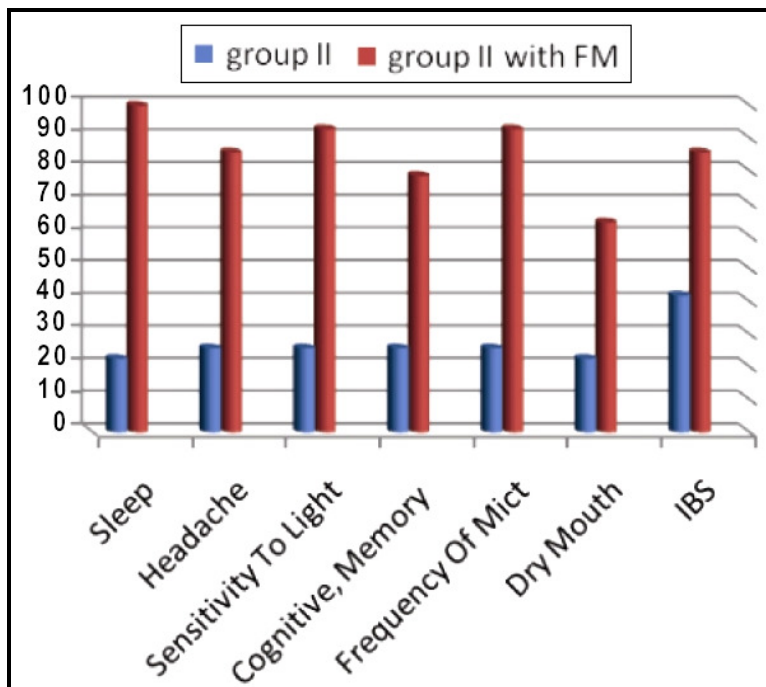


Figure 4. The main clinical symptoms of FM in 101 chronic depression patients with or without FM (group II).

**Table 8.** Positive screens for LFESSQ-4 and LFE SSQ-6 and FM cases among patients with rheumatoid arthritis and Patients with chronic depression.

	Positive screens for LFESSQ-4	Positive screens for LFESSQ-6	FM cases	Positive predictive value of LFESSQ-4	Positive predictive value of LFESSQ-6
Rheumatoid arthritis (N 176)	139(78%)	102(57.9%)	37(21%)	26.6%	36.2%
Depression (N 101)	95(94%)	86(85.14%)	43(42.57%)	45.2%	50%

## DISCUSSION

Fibromyalgia (FM) is currently defined as chronic wide spread pain (CWP) with allodynia or hyperalgesia to pressure pain, and is classified as one of the largest group of soft-tissue pain syndromes.<sup>8</sup> Its pathogenesis is not entirely understood, although it is currently believed to be the result of a central nervous system (CNS) malfunction that increases pain transmission and perception.<sup>9</sup> FM can coexist with immune-inflammatory diseases, many rheumatic and non-rheumatic diseases can easily be misdiagnosed as FM. There are no instrumental tests to confirm the diagnosis, but many of the differential diagnoses can be excluded by means of an extensive clinical examination and medical history.<sup>9</sup> Patients with fibromyalgia frequently experience psychiatric problems. Clinical investigators suggest that depressive and anxiety disorders are strongly aggregated in fibromyalgia.<sup>10</sup> FM is the most frequent co morbid condition with prevalence figures of 20–80% in patients with chronic depression.<sup>11</sup>

In this study, among RA patients FM diagnosis based on ACR criteria 1990 was established in 21.02% of patients, and it was more prevalent in female patients. This was previously reported by Toms et al.<sup>12</sup> and Pollard et al.<sup>13</sup> also found that 17% of rheumatoid arthritis patients met the ACR classification criteria for FM. However a lower frequency (13.4%) of FM among RA patients was reported by-Ranzolin et al.<sup>14</sup>

In the present study, patients with RA and FM were older and had longer disease duration than those patients without FM. This was previously reported by Vilaseca and Otero.<sup>15</sup> This study confirmed the results of Pollard et al.<sup>13</sup> as they reported no significant difference as regard marital and employment status among patients with RA and FM than patients without FM.

The present study showed RA patients with FM had prolonged morning stiffness than RA patient. This is similar to results that found by Ranzolin et al.<sup>14</sup> Associated fatigue and sleep disturbance can prolong the morning stiffness sensation typical of RA in patients with comorbid FM.

The results of this study showed an important influence of the coexistence of FM on the DAS28 value. Thus, patients with RA with FM had a higher DAS28 score. However, this difference was due to a worse score in the patient global assessment of the disease and the tender joints count. It was found that most patients with FM with RA had  $DAS28 \geq 5.1$ .<sup>16</sup>

This study found that the LFESSQ-6 had a higher PPV than that for LFESSQ-4 in detecting the frequency of FM in RA patients and also patients with depression.

The present study showed a higher frequency of FM among patients with chronic depression, FM diagnosis based on ACR criteria was established in 40 (39.60%) female patients and 3(2.97%) male patients. Also, Senna et al.<sup>17</sup> found higher rates of FM among patients with chronic depression and concluded that psychological distress is a significant risk factor for FM.

## Conclusion

The relationship between FM and systemic rheumatic diseases, especially rheumatoid arthritis is increasingly recognized. FM is common in patients with RA, however it is commoner in patients with depression and it may be the cause of many of their symptoms and much of their disability. FM worsens disease activity and should be suspected in cases of RA patients with high DAS28 score.

[Disclosure: Authors report no conflict of interest]

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