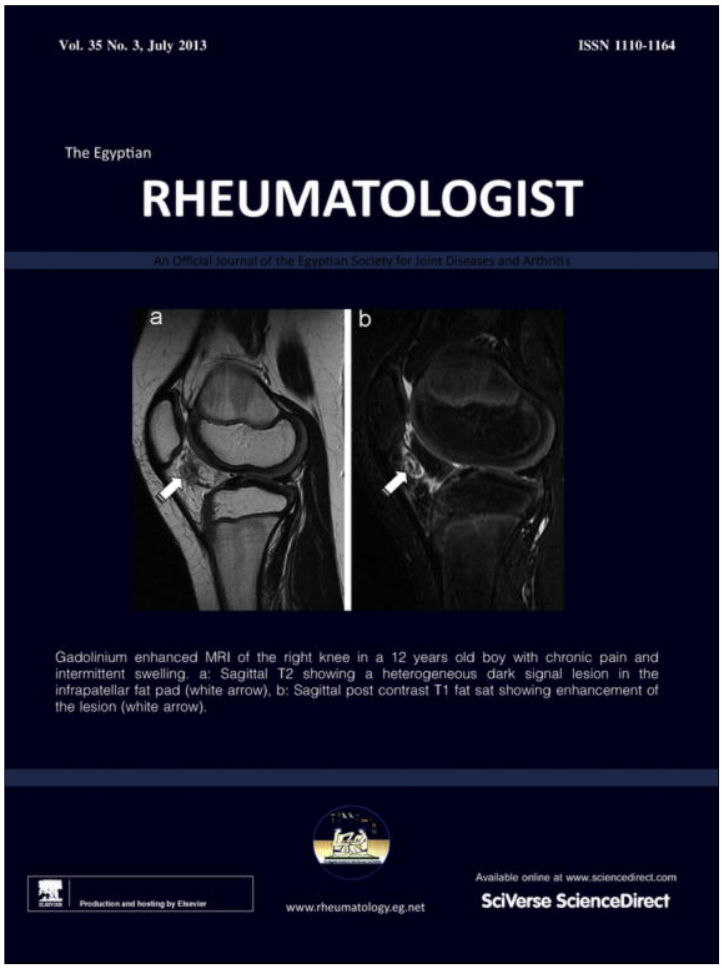
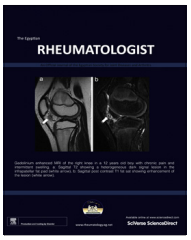


The Egyptian Rheumatologist (2013) **35**, 115–119

Egyptian Society for Joint Diseases and Arthritis

The Egyptian Rheumatologist

www.rheumatology.eg.net
www.sciencedirect.com



ORIGINAL ARTICLE

The impact of fibromyalgia on disease assessment in rheumatoid arthritis patients

Zeinab Nawito, Hanaa M. Rady *, Lobna A. Maged

Rheumatology and Rehabilitation Department, Faculty of Medicine, Cairo University, Egypt

Received 7 March 2013; accepted 7 March 2013
Available online 15 April 2013

KEYWORDS

Fibromyalgia;
Rheumatoid arthritis;
DAS 28;
CDAI;
MHAQ

Abstract *Aim of work:* To explore the influence of the presence of concomitant fibromyalgia (FM) on the evaluation of disease activity score assessing 28 joints (DAS28), clinical disease activity index (CDAI) and modified health assessment questionnaire (MHAQ) in Egyptian patients with rheumatoid arthritis (RA).

Patients and methods: This study included 50 female RA patients; out of which 25 had concomitant FM (RAF group), the other 25 RA patients who served as controls did not have concomitant FM (RA group). All patients were subjected to an assessment of disease activity using the DAS 28 and the CDAI and assessment of functional outcome using MHAQ score.

Results: The mean DAS 28 was significantly higher in RAF than RA patients (5.6 ± 1.1 versus 4.5 ± 1.3, $P = 0.009$). Also, the mean CDAI score was significantly higher in the RAF group (mean 23.3 ± 12.1 versus 13.7 ± 11.0, $P = 0.002$). The difference was attributed to significantly higher subjective items such as Tender joint count (TJC) and patient's global assessment of general health (VAS-GH) in the RAF group. Mean MHAQ score was also higher in the RAF group (0.7 ± 0.6 versus 0.31 ± 0.4, $P = 0.006$).

Conclusion: FM is related to worse scores on the DAS28, CDAI and MHAQ in patients with RA. The presence of FM may have major implications in the interpretation of the DAS28 and CDAI scores because it is related to higher scores independently of objective evidence of RA activity.

* Corresponding author. Address: P.O. Box 109, Cairo 11559, Egypt. Tel.: +20 1005268101.
E-mail address: radyhanaa@hotmail.com (H.M. Rady).

Peer review under responsibility of Egyptian Society for Joint Diseases and Arthritis.

Production and hosting by Elsevier

1. Introduction

Fibromyalgia (FM) is a chronic, musculoskeletal, non inflammatory pain disorder. Patients frequently suffer from sleep disturbances, headaches, anxiety, morning stiffness, and a poor sense of well-being. It is characterized by the presence of at least 11 tender points, as well as widespread bilateral pain for at least 3 months [1]. FM occurs in 1–4% of the normal population, but has a much higher prevalence in rheumatic dis-

1110-1164 © 2013 Production and hosting by Elsevier B.V. on behalf of Egyptian Society for Joint Diseases and Arthritis.
http://dx.doi.org/10.1016/j.ejr.2013.03.003

eases [2]. In patients with rheumatoid arthritis (RA), concomitant FM has been reported in 10–20% of cases and may represent an additional factor that worsens pain, physical, social and emotional limitations in these patients [3,4].

Disease remission is now considered a realistic goal for many RA patients. Measures of outcome such as composite indices of disease activity and questionnaires for functional status, facilitate clinical decision making to achieve this goal, and studies in RA show that treating to target improves outcomes [5,6]. However, previous studies [7–10] found that patients with RA and concomitant FM (RAF) have worse scores on Disease Activity Score in 28 joints (DAS28) and Health Assessment Questionnaire (HAQ), independent of objective evidence of RA activity which could lead to an unjustified increase of the burden of treatment with risk of adverse events and higher cost in this subset of RA patients. Thus this study was conducted to evaluate the impact of fibromyalgia on two composite indices of disease activity: DAS 28 and clinical disease activity index (CDAI) as well as on functional outcome using Modified Health Assessment Questionnaire (MHAQ) score among a cohort of Egyptian RA patients.

2. Patients and methods

Out of 150 consecutive RA patients screened at the outpatient clinic of the Rheumatology and Rehabilitation Department, Faculty of Medicine, Cairo University who fulfilled the 2010 ACR criteria for diagnosis of RA [11], fifty were recruited to the study. Twenty-five patients who concomitantly fulfilled the ACR criteria for diagnosis of FM [12] were selected as the first group (RAF). They were all females. Another 25 female RA patients of matching age served as the control group (RA). They did not have concomitant FM with a tender point count (TPC) using manual point survey of <6 points. The cut off of $\geqslant 6$ TPC better discriminates patients with FM from those without FM in clinical practice [13]. Excluded from our study were RA patients with other causes of widespread pain as endocrinopathies, end stage liver or kidney disease, major psychiatric disorders or metabolic bone disease. All patients gave their informed consent and the study was approved by the local ethics committee.

All studied patients were subjected to full history taking, thorough clinical examination and routine laboratory investigations. Plain radiographs were done for hands and wrists. Assessment of disease activity was done using two scores: the DAS 28 [14] with its components, tender (TJC) and swollen joint counts (SJC), visual analog scale for patient's global assessment of general health (VAS-GH scored 0–100 mm), and erythrocyte sedimentation rate (ESR in mm/first hour), as well as the CDAI score which is based on the simple summation of the count of swollen and tender joint count of 28 joints along with VAS-GH and physician global assessment (VAS-PH) [15]. Assessment of functional outcome was done using MHAQ score [16]. Types and doses of medications were recorded for each patient group.

Statistical analysis: Data were analyzed using the computer program, SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 15 for Microsoft Windows. Data were described in terms of mean ± standard deviation (±SD), frequencies (number of cases) and percentages when appropriate. Comparison of quantitative variables between the study groups was done using Mann Whitney U test for independent samples. For comparing categorical data, Chi square (χ^2) test was performed. Exact test was used instead when the expected frequency was <5. A probability value (P value) <0.05 was considered statistically significant.

3. Results

The demographic and clinical characteristics of patients with and without FM shown in Table 1 were not significantly different. Regarding somatic symptoms of fibromyalgia, all except morning stiffness, dysmenorrhea and irritable bowel syndrome were significantly higher in the RAF group as shown in Table 2.

On comparing disease activity scores in the studied population, we found that mean DAS 28 was significantly higher in the RAF compared to the non-fibromyalgia group (5.6 ± 1.1.16 versus 4.5 ± 1.3, $P = 0.009$). Also, mean CDAI score was significantly higher in the RAF group (23.3 ± 12.1 versus 13.7 ± 11.0, $P = 0.002$).This significant statistical difference was related to the subjective components of DAS28 and CDAI (TJC and VAS -GH) while no significant difference was found in SJC, ESR or VAS-PH as shown in Table 3. The TJC and SJC were positively correlated in the non-fibromyalgia group ($P = 0.001$). However in RAF group they were poorly correlated ($P = 0.993$) (Figs. 1 and 2).The distribution of our RA patients among different disease activity grades of both DAS28 and CDAI is demonstrated in Table 4.

Regarding MHAQ score, its mean in the RAF group was significantly higher than in the non-fibromyalgia group (0.7 ± 0.6 versus 0.31 ± 0.4, $P = 0.006$).

As shown in Table 5, the number of patients receiving steroids as well as their mean steroid cumulative dose were higher in the RAF group but the difference reached statistical significance for the dose only ($P = 0.005$). On the other hand, the number of patients using methotrexate was higher in the non-fibromyalgia group while leflunomide was used by more patients in the RAF group and the difference was statistically significant as regards patients' number ($P = 0.005$ and 0.008 respectively) but no significant difference was found in drug doses. The number of patients using chloroquine and its dose was comparable in both groups ($P = 0.157$).

4. Discussion

In the present study, all recruited patients were females. Previous studies have shown a higher prevalence of RAF among women [3,4,8,10]. As we chose to have both patient groups comparable in age, sex and disease duration, it was not possible to study these factors as risk factors. Although the BMI of RAF patients studied was higher than RA patients the difference was statistically insignificant. In the studies of Coury and colleagues [7] and Dhir and colleagues [2] the BMI of RAF population was significantly higher than the BMI of the RA population.

Morning stiffness which is a hallmark of rheumatoid arthritis is also considered one of the somatic symptoms of fibromyalgia. In our study, both the prevalence and duration of morning stiffness were higher in the RAF group but the difference was statistically insignificant. Morning stiffness duration was significantly longer in RAF patients in the studies of Cou-

Table 1 Demographic and clinical data of studied rheumatoid arthritis patients.

	Patients		*P* value
	RAF (no = 25)	RA (no = 25)	
Age (years)	42.6 ± 10.2	45.3 ± 11.5	0.34
BMI	31.2 ± 5.7	29.3 ± 5.9	0.14
Disease duration (years)	9.5 ± 6.5	7.5 ± 7.1	0.15
Morning Stiffness duration (min)	18 ± 21.9	12.4 ± 20.6	0.2
Extraarticular features: no (%)	4 (16%)	4 (16%)	1.00
Deformities: no (%)	10 (40%)	7 (28%)	0.37
Rheumatoid factor positivity: no (%)	19 (76%)	19 (76%)	1.00
Erosive changes in X-ray: no (%)	14 (56%)	16 (66.7%)	0.44

RAF: rheumatoid arthritis with concomitant fibromyalgia, RA: rheumatoid arthritis, BMI: body mass index. Results are presented as mean ± SD and no (%).

Table 2 Somatic manifestations of studied rheumatoid arthritis patients.

Somatic manifestations percentage (%)	Patients		*P* value
	RAF (25)	RA (25)	
Widespread pain	100	28	< 0.001
Sleep disturbance	68	32	0.011
Fatigue	92	52	0.002
Morning stiffness	56	36	0.156
Headache	56	24	0.021
Depression	88	40	< 0.001
Anxiety	72	40	< 0.001
Parasthesia	76	32	0.002
Cognitive symptoms	56	16	0.003
Dysmenorrhea	20	20	1
Irritable bowel syndrome	16	4	0.157

RAF: rheumatoid arthritis with concomitant fibromyalgia, RA: rheumatoid arthritis.

Table 3 Disease activity assessment scores and their individual components in studied rheumatoid arthritis patients.

Disease activity components	Patients		*P*-Value
	RAF (25)	RA (25)	
Tender joint count	12.3 ± 9.1	4.5 ± 4.2	0.01
Swollen joint count	2.8 ± 3.2	3 ± 4.1	0.96
ESR (mm/h)	38.2 ± 16.8	41.8 ± 22.5	0.53
Patient VAS (mm)	64 ± 23.6	46.8 ± 25.9	0.019
Physician VAS (mm)	18.8 ± 16.6	16.6 ± 16.7	0.345
DAS 28	5.6 ± 1.1	4.5 ± 1.3	0.009
CDAI	23.3 ± 12.1	13.7 ± 11.0	0.002
MHAQ	0.7 ± 0.6	0.31 ± 0.4	0.006

RAF: rheumatoid arthritis with concomitant fibromyalgia, RA: rheumatoid arthritis. ESR: erythrocyte sedimentation rate, VAS: visual analog scale, DAS28: disease activity score in 28 joints, CDAI: clinical disease activity index, MHAQ: modified health assessment questionnaire.

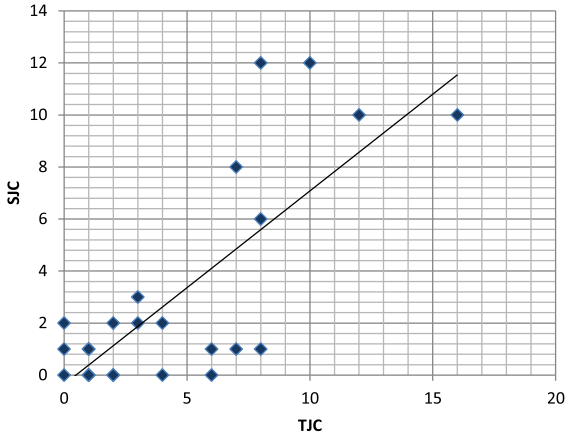


Figure 1 Correlation between tender joint count (TJC) and swollen joint count (SJC) in non fibromyalgic rheumatoid arthritis (RA) patients.

ry and colleagues [7] and Ranzolin and colleagues [8]. Prolonged morning stiffness in RAF patients was explained by pain, fatigue, and sleep disturbance.

The mean DAS 28 in the present study was significantly higher in the RAF group. The difference was attributed to the subjective measures of the score: the tender joint count and VAS-GH which were significantly higher in the fibromyalgic group. The objective measures on the other hand: swollen joint count and ESR were found to be comparable (statistically insignificant difference) in both groups. Similar results were reported by Ton and colleagues [9], Ranzolin and colleagues [8] and Vilaseca and Oteroin [17]. In our study as well as that conducted by Dhir and colleagues [2] the TJC and SJC were significantly positively correlated in the RA group while in the RAF

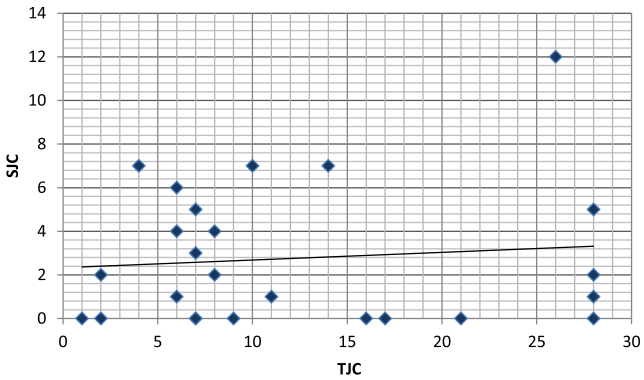


Figure 2 Correlation between tender joint count (TJC) and swollen joint count (SJC) in fibromyalgic rheumatoid arthritis (RAF) patients.

Table 4 Classification of disease activity in studied RA patients according to the disease activity indices (DAS 28 and CDAI).

Disease activity		Patients	
		RAF (25)	RA (25)
DAS28			
High	(DAS28 > 5.1).	16 (64%)	7 (28%)
Moderate	(3.2 < DAS28 ⩾ 5.1)	9 (36%)	14 (56%)
Low	(DAS28 ⩽ 3.2)	0 (0%)	3 (12%)
Remission	(DAS < 2.6)	0 (0%)	1 (4%)
CDAI			
High	(CDAI > 22)	10 (40%)	6 (24%)
Moderate	(10 < CDAI ⩽ 22)	12 (48%)	8 (32%)
Low	(2.8 < CDAI ⩽ 10)	3 (12%)	10 (40%)
Remission	(CDAI ⩽ 2.8)	0 (0%)	1 (4%)

RAF: rheumatoid arthritis with concomitant fibromyalgia, RA: rheumatoid arthritis.DAS28: disease activity score in 28 joints, CDAI: clinical disease activity index.

group they were poorly correlated. But in their study, both the TJC and SJC were significantly higher in the RAF group. Coury and associates [7] also reported higher SJC in RAF patients using the ACR joint count including 66 joints which were partially due to a higher swollen metatarsophalangeal joint count in patients with RAF. This count is known to be difficult to assess, especially in obese patients, who were more numerous in their RAF group, as shown by BMI.

Regarding the mean CDAI score in the present study, it was found to be significantly higher in the RAF group. Like DAS 28, the difference was attributed to the higher subjective measures of the score: the tender joint count and VAS-GH while the swollen joint count and VAS-PH were comparable. The use of CDAI in our study was considered as an alternative to DAS28 in assessment of RAF patients owing to the hypothesis that unlike DAS28 where TJC receives double the weighing received by SJC, in CDAI both items are weighed equally. However, it showed no advantage over DAS28 in avoiding overestimation of disease activity in RAF. This could be explained by the fact that in the CDAI, VAS-GH receives a higher weight than in DAS28. On the other hand, it does not include an acute phase reactant, one of the objective measures of disease assessment used in DAS28. This agrees with the study of Pollard and colleagues [18].

Functional assessment of patients was performed in the present study using the MHAQ score. Our results revealed that its mean in the RAF group was significantly higher than the RA group. These results came in accordance with previous studies [2,4,7,8] which reported a worse functional outcome assessed using HAQ -DI. Proposed explanation was that FM per se has been described as being related to a worse functional outcome similar to that observed in RA.

Regarding the treatment of our studied patients, the number of patients receiving steroids and the cumulative steroid dose were both higher in the RAF group with a significant statistical difference regarding steroid cumulative dose. These results are in accordance with those of Ranzolin and colleagues [8]. This may reflect a response to the higher disease activity indices reported in RAF patients. However, Dhir and colleagues [2] found no difference when it came to steroids as regards the number of patients using them and dosage.

Hence as proved in our study and other studies, DAS28 as well as the CDAI overestimate disease activity in RAF patients. Therefore, the possibility that FM affects the interpretation of this score may have important implications. In routine clinical practice, misclassification of disease activity may lead to an unnecessary change in the therapy of RA. It may affect the selection of patients in clinical trials, because a high DAS28 score is frequently used as one of the inclusion criteria. The interpretation of results may also be affected, considering that FM symptoms are not expected to respond to therapeutics directed toward RA.

5. Conflict of Interest

None.

Table 5 Comparison of types and doses of medications received by studied rheumatoid arthritis patients.

		Steroids (gm/ intake)	MTX (mg/week)	Leflunomide (mg/day)	Chloroquine (mg/day)
RAF	No (%)	15 (60%)	13 (52%)	11 (44%)	4 (16%)
	Dose	5.4 ± 11.7	20.2 ± 4.4	20 ± 0.0	250 ± 0.0
RA	No (%)	9 (36%)	22 (88%)	2 (8%)	1 (4%)
	Dose	2.0 ± 0.4	19.4 ± 4.2	20 ± 0.0	250 ± 0.0
P	No	0.089	0.005	0.008	1
Value	Dose	0.005	0.544	0.157	1

RAF: rheumatoid arthritis with concomitant fibromyalgia, RA: rheumatoid arthritis. MTX: methotrexate.

References

[1] Rosenzweig TM, Thomas TM. An update on fibromyalgia syndrome: the multimodal therapeutic approach. AJL 2009;3:226–37.

[2] Dhir V, Lawrence A, Aggarwal A, Misra R. Fibromyalgia is common and adversely affects pain and fatigue perception in North Indian patients with rheumatoid arthritis. J Rheumatol 2009;36:2443–8.

[3] Wolfe F, Cathey MA, Kleinheksel SM. Fibrositis (fibromyalgia) in rheumatoid arthritis. J Rheumatol 1984;36:340–7.

[4] Wolfe F, Michaud K. Severe rheumatoid arthritis (RA), worse outcomes, comorbid illness, and sociodemographic disadvantage characterize RA patients with fibromyalgia. J Rheumatol 2004;31:695–700.

[5] Smolen JS, Aletaha D, Bijlsma JW, Breedveld FC, Boumpas D, Burmester G, et al. Treating rheumatoid arthritis to target: recommendations of an international task force. Ann Rheum Dis 2010;69:631–7.

[6] Grigor C, Capell H, Stirling A, McMahon AD, Lock P, Vallance R, et al. Effect of a treatment strategy of tight control for rheumatoid arthritis (the TICORA study): a single-blind randomized controlled trial. Lancet 2004;364:263–9.

[7] Coury F, Rossat A, Tebib A, Letroublon MC, Gagnard A, Fantino B, et al. Rheumatoid arthritis and fibromyalgia: a frequent unrelated association complicating disease management. J Rheumatol 2009;36:58–62.

[8] Ranzolin A, Brenol JC, Bredemeier M, Guarienti J, Rizzatti M, Feldman D, et al. Association of concomitant fibromyalgia with worse disease activity score in 28 joints, health assessment questionnaire, and short form 36 scores in patients with rheumatoid arthritis. Arthritis Rheum 2009;61:794–800.

[9] Ton E, Bakker MF, Verstappen S, Borg T, van Albada I, Schenk Y, et al. Look beyond the DAS28: tender points influence the DAS28 in patients with rheumatoid arthritis. J Rheumatol 2012;39:22–7.

[10] Naranjo A, Ojeda S, Francisco F, Erausquin C, Rúa-Figueroa I, Rodríguez-Lozano C. Fibromyalgia in patients with rheumatoid arthritis is associated with higher scores of disability. Ann Rheum Dis 2002;61:660–1.

[11] Aletaha D, Neogi T, Silman AJ, Funovits J, Felson DT, et al. 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Ann Rheum Dis 2010;69:1580–8.

[12] Wolfe F, Smythe HA, Yunus MB, Bennett RM, Bombardier C, et al. The American College of Rheumatology 1990 criteria for the classification of fibromyalgia. Arthritis Rheum 1990;2:160–72.

[13] Katz RS, Wolfe F, Michaud K. Fibromyalgia diagnosis: a comparison of clinical, survey, and American College of Rheumatology criteria. Arthritis Rheum 2006;54:169–76.

[14] Prevoo ML, Van 't Hof MA, Kuper HH, van Leeuwen MA, van de Putte LB, et al. Modified disease activity scores that include twenty-eight–joint counts: development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. Arthritis Rheum 1995;38:44–8.

[15] Aletaha D, Smolen J. The simplified disease activity index (SDAI) and the clinical disease activity index (CDAI): a review of their usefulness and validity in rheumatoid arthritis. Clin Exp Rheumatol 2005;23(5 Suppl. 39):S100–8.

[16] Pincus T, Summey JA, Soraci Jr SA, Wallston KA, Hummon NP. Assessment of patient satisfaction in activities of daily living using a modified stanford health assessment questionnaire. Arthritis Rheum 1983;26:1346–53.

[17] Vilaseca DR, Otero CH. Effect of the coexistence of fibromyalgia in the DAS28 index in women with rheumatoid arthritis. Rheumatol Clin 2008;4:96–9.

[18] Pollard L, Kingsley G, Choy E, Scott D. Fibromyalgic rheumatoid arthritis and disease assessment. Rheumatol 2010;49:924–8.