ORIGINAL ARTICLE

A comparative study of disease activity scores in early rheumatoid arthritis with and without fibromyalgia in Aswan university hospital

Loay Aglan[1], Nihal Fathi[2,] Alaa Hazem[1], Fatma Elnoby[2]

[1]Department of Rheumatology, physical medicine, and rehabilitation, Faculty of Medicine, Aswan university

[2]Department of Rheumatology, physical medicine, and rehabilitation, Faculty of Medicine, Assiut university

ABSTRACT

Keywords: A comparative study, disease activity scores, early rheumatoid arthritis with, without fibromyalgia.

*Corresponding author:

Alaa Allah Mohamed Hazem

Email: kendafawaz51@gmail.com

Phone: 01148348144

Background: Fibromyalgia (FM) often coexists with RA, The prevalence of FM in the general population is 2.7-5.1% and in RA it reaches a prevalence of up to 20%, It is characterized by chronic, widespread musculoskeletal pain, fatigue, sleep disturbance physical and psychological impairment, Concern has been raised regarding the validity of RA disease activity scores in patients with coexistent RA and FM, making a "treat-to target" strategy questionable in these patients. **Aim:** The aim of this study was to evaluate disease activity scores in patients with rheumatoid arthritis (RA) with and without secondary fibromyalgia. **Patients and Methods:** This study is comparative cross-sectional study of 100 patients seen to rheumatology outpatient clinic in Aswan university hospital. The study included two groups of patients with early RA with and without fibromyalgia. **Results:** The frequency of FM in RA patients was 35% (92% female, 8% male). In RA patient with FM, the TJC and DAS median value were significantly higher than in patient without FM (P< 0.001) , Median values of disease activity scores in RA patient with FM were higher than in patient Without FM (P< 0.034). **Conclusion:** Simplified disease activity index (SDAI) Score was significantly higher in RA patients with FM than those without FM, disease activity score (DAS) and clinical disease activity index (CDAI) were higher in FM cases but not reaching statistical significance. The current study also revealed that tender point count was positively correlated DAS and the number of tender joints.

INTRODUCTION

Fibromyalgia (FM) often coexists with RA (**1**). The prevalence of FM in the general population is 2.7-5.1% and in RA it reaches a prevalence of up to 20% (**2**)**.** It is characterized by chronic, widespread musculoskeletal pain, fatigue, sleep disturbance physical and psychological impairment, Concern has been raised regarding the validity of RA disease activity scores in patients with coexistent RA and FM, making a "treat-to target" strategy questionable in these patients (**3**). Cross-sectional studies have shown that FM patients have higher DAS28, higher TJC, worse self-reported global health (GH), and worse functional impairment (**4**).

Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by inflammatory arthritis and extra-articular involvement. It is a chronic inflammatory disorder of unknown etiology that primarily involves synovial joints. It typically starts in small peripheral joints, is often symmetric, and progresses to involve proximal joints if left untreated**. (5)**.

Joint inflammation over time leads to the destruction of the joint with cartilage and bone erosion. RA with symptom duration of fewer than six months is defined as early RA, and when the symptoms have been present for more than six months, it is defined as established RA **(5)**.

The aim of this study was to evaluate disease activity scores in patients with rheumatoid arthritis (RA) with and without secondary fibromyalgia.

PATIENTS AND METHODS:

This study is comparative cross-sectional study of 100 patients seen to rheumatology outpatient clinic in Aswan university hospital. The study included two groups of patients with early RA with and without fibromyalgia.

Inclusion criteria:

Patients aged 18–70 year, early rheumatoid arthritis with 2ry fibromyalgia and early rheumatoid arthritis without 2ry fibromyalgia.

Exclusion criteria: Rheumatoid Patients were taking disease-modifying drugs (DMARDS) previously; rheumatoid Patients were taking steroids previously, Primary fibromyalgia, other auto-immune diseases and other psychiatric disorders.

Method:

Department of Rheumatology in Aswan university hospital, for a period of 6 months, Patients above 16 years of age, of either gender, we will study two groups of rheumatoid arthritis patients, one with and the other without fibromyalgia.

Clinical and laboratory assessment:

- C-reactive protein (CRP).
- Erythrocyte sedimentation rate (ESR).
- Presence of rheumatoid factor (RF) and anti-citrullinated cyclic peptides antibodies (ACPA).
- The number of tender joints (TJC) and swollen joints (SJC) out of 28.

All investigation need to reach a final diagnosis

Imaging: X-rays on bilateral hand, PA view

Statistics: Data was collected using Microsoft Excel program, Continuous data was presented as mean +/-s.d or median (interquartile range), while categorical variables was reported as number of patients with (proportion of patients with) the certain characteristic. The results were represented in tables and graphs. Statistical analysis was performed using statistical program for social science "SPSS V21.0, SPSS Inc., Chicago, IL, USA". Student t-test was used for comparison between two normally distributed quantitative data while Mann-Whitney U-test was used for comparison between two non-normally distributed data. For comparing categorical data, Chi-square($X2$) or Fischer exact test was used. Spearman's rank correlation coefficient was applied for correlation analysis. Intra individual comparisons were performed using either Student's t -test or Wilcoxon signed-rank test for paired samples. P value >0.05 considered non-significant, P value < 0.05 considered significant and P value < 0.01 considered highly significant.

RESULTS

The study included 100 patients with rheumatoid arthritis, the whole patients divided into 2 groups, **group 1** >> 65 patient rheumatoid arthritis without fibromyalgia and **group 2** >> 35 patients rheumatoid arthritis with fibromyalgia. The mean age of patients in this study is 45 years old. Female

patients are more than male patients with a ratio of 9:1, and the average duration of rheumatoid arthritis is 12 months (**Table 1**)

Table 1: Demographic data for the study group

		Mean / N	SD / %	Median (IQR)	Range
Group	Without fibromyalgia	65	65.0%		
	With fibromyalgia	35	35.0%		
Age		45.36	11.36	46 (37 - 56)	(23 - 62)
Sex	Male	8	8.0%		
	Female	92	92.0%		
Marital status	Single	4	4.0%		
	Married	91	91.0%		
	Widow	5	5.0%		
Disease duration		12.02	5.84	11 (7 - 17)	(2 - 23)

Regarding lab finding within the whole group, Mean **Hemoglobin** range between (7.7-and 13.8),Mean **WBCs** range between (4.8 and 12.4), Rheumatoid **factor** is positive in all patients, **ESR** is ranged between (10 and 100), **CRP** is positive in 80 % of patient. And **Anti ccp** is positive in 90 % of patient (**Table 2**)

Table 2: Lab investigations for the study group

		Mean / N	SD / %	Median (IQR)	Range
Hb		10.49	1.75	10.7 (8.95 - 11.85)	(7.7 - 13.8)
WBCs		9.69	1.73	9.7 (8.35 - 11.1)	(4.8 - 12.4)
RF	Negative	0	0.0%		
	Positive	100	100.0%		
ESR		46.56	19.23	44.9 (30.8 - 62.65)	(10 - 100)
CRP	Negative	20	20.0%		
	Positive	80	80.0%		
Anti CCP	Negative	10	10.0%		
	Positive	90	90.0%		

Regarding Hand x-ray finding within the whole group , **Joint narrowing** is found in 59% of patients ,**Soft tissue swelling** is found in 75% of patients, **Marginal bone erosion** is found in 35% of patient , **Bone Cyst** is found in 5 % of patient.(**Table 3**)

Table 3: Hand X-ray findings for the study group

		N	%
Joint narrowing	No	41	41.0%
	Yes	59	59.0%
Soft tissue	No	25	25.0%
	Yes	75	75.0%

swelling			
Marginal erosion	No	65	65.0%
	Yes	35	35.0%
Cyst	No	43	43.0%
	Yes	57	57.0%

Number of tender joint of rheumatoid patients is range between zero and 28 with mean 8.75 and number of tender point of fibromyalgia patients is range between zero and 18 with mean 7.66.**(Table 4)**
Table 4: number of tender joints and tender point within rheumatoid arthritis patients with fibromyalgia

	Mean	SD	Median (IQR)	Range
Number of tender joints	8.57	5.54	8 (4 - 13)	(0 - 20)
Tender point of FM	7.66	4.66	8 (4 - 10)	(0 - 18)

This study included 100 patient of Rheumatoid arthritis whish divided into two groups , first group is rheumatoid arthritis   without fibromyalgia which represent 65 % of patients, and second group is rheumatoid arthritis with fibromyalgia which represent 35 % of patients.
According to Age of two groups included in study, Mean age of first group is 45.2 years old, and mean age of second group is 45.4 years old. According to the gender of two groups,   in first group female patients more than male patient as 62:3, and in second group female patients more than male patients as 30:5. According to Disease duration of two groups, average of disease duration in first group is 5 months and average of Disease duration in second group is 6 months.
 Regarding to **hand x-ray finding** of two group in this study, **Joint narrowing**, first group represent in 37 patients and in second group represent in 22 patients, **Soft tissue swelling,** first group represent in 48 of patients and in second group represent in 27 of patients**, Marginal bone erosion,** in first group represent in 19 of patients, and in second group represent in 16 of patients, **bone Cyst,** in first group represent in 33 of patients, and in second group represent in 24 of patient.**(Table 5)**
Table 5: Hand X-ray findings between two studied groups

		Group		Chi-Square test	
		Without fibromyalgia (N= 65)	With fibromyalgia (N= 35)		
		N (%)	N (%)	p-Value	Sig.
Joint narrowing	No	28 (43.08%)	13 (37.14%)	0.565	NS
	Yes	37 (56.92%)	22 (62.86%)		
Soft tissue swelling	No	17 (26.15%)	8 (22.86%)	0.717	NS
	Yes	48 (73.85%)	27 (77.14%)		
Marginal erosion	No	46 (70.77%)	19 (54.29%)	0.099	NS
	Yes	19 (29.23%)	16 (45.71%)		
Cyst	No	32 (49.23%)	11 (31.43%)	0.086	NS
	Yes	33 (50.77%)	24 (68.57%)		

Disease activity score (DAS), in first group (DAS) mean is 4.3 and in second group DAS mean is 4.7, **Clinical disease activity index (CDAI) score,** in first group **CDAI** mean is 19.3 and in second group CDAI mean is 19.3, **Simplified disease activity index (SDAI) score,** in first group SDAI mean is 20.6 and in second group SDAI mean is 28.8. **Table 6**

Table 7: Disease activity scores between two studied groups

		Group		Test of significance	
		Without fibromyalgia (N= 65)	With fibromyalgia (N= 35)		
		Mean ± SD (Median (IQR)) N (%)	Mean ± SD (Median (IQR)) N (%)	p-Value	Sig.
Disease activity score (DAS)		4.37 ± 1.63	4.73 ± 1.38	0.152$^{(M)}$	NS
		4.1 (3 - 5.3)	4.8 (3.4 - 5.9)		
Categories	Remission	8 (12.31%)	3 (8.57%)	0.117$^{(F)}$	NS
	Low disease activity	11 (16.92%)	1 (2.86%)		
	Moderate disease activity	27 (41.54%)	15 (42.86%)		
	High disease activity	19 (29.23%)	16 (45.71%)		
Clinical disease activity index (CDAI) score		19.33 ± 13.9	24.57 ± 16.05	0.175$^{(M)}$	NS
		15.5 (7.7 - 27.3)	18.5 (11.9 - 38.9)		
Categories	Remission	6 (9.23%)	1 (2.86%)	0.239$^{(F)}$	NS
	Low disease activity	12 (18.46%)	3 (8.57%)		
	Moderate disease activity	28 (43.08%)	16 (45.71%)		
	High disease activity	19 (29.23%)	15 (42.86%)		
Simplified disease activity index (SDAI) score		20.62 ± 15.67	28.83 ± 18.81	0.034$^{(M)}$	S
		17.5 (7.9 - 27.3)	23.7 (13.3 - 46.4)		
Categories	Remission	6 (9.23%)	1 (2.86%)	0.403$^{(F)}$	NS
	Low disease activity	14 (21.54%)	6 (17.14%)		
	Moderate disease activity	27 (41.54%)	13 (37.14%)		
	High disease activity	18 (27.69%)	15 (42.86%)		

$^{(M)}$ Mann-Whitney test of significance.
$^{(F)}$ Fisher's Exact test of significance.

DISCUSSION

This comparative cross-sectional study was conducted in the rheumatology outpatient clinic in Aswan university hospital. This study was conducted on 100 patients with early rheumatoid arthritis with (n=35) and without (n=56) secondary fibromyalgia.

Regarding the demographic data for the study group, it was found that the mean age was 45.36 ±11.36 years with the majority of females, the majority were married (91%), and mean disease duration was 12.02±5.84 years. The study comprised 65% without fibromyalgia (FM) and 35% with FM.

Comparison of the RA patients with and without FM showed that there was no significant difference between the studied groups as regard age, sex, marital status, and disease duration.

In agreement with the current study **Durmaz & Ilhanli, (6)** enrolled 381 RA patients included 322 (84.5%) females and 59 (15.5%) males. The mean (SD) age of the patients was 59.2 (9.6) years and the median disease duration was 9 (0.25-35) years. Ninety-eight (25.7%) of the RA patients had FM, including 89 females (90.8%). The study revealed that there was no significant difference between RA with and without FM groups as regard age, sex, and disease duration.

Regarding lab investigations for the study group, we found that the mean Hb was 10.49±1.75, mean WBC was 9.69±1.73 and mean ESR was 46.56±19.23, all patients were RF positive and 80% were positive CRP. Comparison of the RA patients with and without FM, showed that there was no significant difference between the studied groups as regard Hb, WBC, ESR and CRP.

In agreement with the current study **Durmaz & Ilhanli, (6)** revealed that there was no significant difference between the studied groups as regard CRP. Also, **Lee et al., (7)** revealed that there was no significant difference between the studied groups as regard CRP and RF positivity.

The current study revealed that there was no significant difference between the studied groups as regard hand X-ray findings including joint narrow, soft tissue swelling, marginal erosion and cyst.

In agreement with our results **Chakr et al., (8)** revealed that there was no significant difference between the studied groups as regard erosion on radiograph.

Regarding the correlation between tender point of FM and DAS and number of tender joints within patients' group who had R.A with fibromyalgia, the current study showed that there was significantly positive correlation between tender point of FM and both disease activity score (DAS) and number of tender joints.

Fibromyalgia was diagnosed using 19 tender point examination (**9**). The study by **Chakr et al., (8)** revealed that the number of tender points was 14.0 (12.0–16.5) among RA patients with FM and 4.0 (2.0–6.0) in RA patients without FM with significant difference.

However, no studies in literature have directly assessed the relation between tender point count and disease activity score or with number of tender points. Our results were supported by **Azzam et al., (10)** who revealed that there was significant association between the presence of FM in RA cases with number of tender joints and DAS-score.

CONCLUSION

Simplified disease activity index (SDAI) Score was significantly higher in RA patients with FM than those without FM, disease activity score (DAS) and clinical disease activity index (CDAI) were higher in FM cases but not reaching statistical significance. The current study also revealed that tender point count was positively correlated DAS and the number of tinder joints.

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