

# Fibromyalgia Complicating Disease Management in Rheumatoid Arthritis

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## ABSTRACT

**Objective:** To evaluate frequency of fibromyalgia in rheumatoid arthritis and its effect on disease activity score.

**Study Design:** Cross-sectional study.

**Place and Duration of Study:** The Indus Hospital, Karachi, from December 2010 to May 2011.

**Methodology:** All adult patients of either gender diagnosed as rheumatoid arthritis on the basis of clinical, laboratory and X-ray criteria were included in the study. The sample data was separated into two groups depending on presence or absence of fibromyalgia and 28 joint disease activity score (DAS-28) value was evaluated.

**Results:** There were 31 (25.83%) patients with rheumatoid arthritis and fibromyalgia (RAFM) out of the total 120. The median (IQR) age of patients was 40 (32 - 51) years. All were females. The overall female frequency was 79 (88.8%). The median (IQR) DAS-28 score in RA group was 4.9 (3.66 - 5.71), while the median (IQR) DAS-28 score in RAFM was 7.04 (6.62 - 7.64) [ $p < 0.0001$ ]. The number of patient getting combination therapy of DMARD in RAFM group was 61.3% while in RA group was 42.7%.

**Conclusion:** DAS-28 was found to be significantly higher in RAFM patients probably because of higher perception of pain.

**Key Words:** Rheumatoid arthritis. Fibromyalgia. DAS-28 (disease activity score).

## INTRODUCTION

Rheumatoid arthritis (RA) is a common inflammatory joint disease with a prevalence rate of 1% with women affected 3 - 5 times more than men and more common in smokers.<sup>1</sup> There is a genetic concordance amongst monozygotic twins of 15 - 20%.<sup>2,3</sup> The disease can be as limited as affecting only small joints of hand with little, if any, deformity to the extent of debilitating disease. The standard treatment of rheumatoid arthritis is with non-biologic Disease Modifying Anti-Rheumatic Drugs (DMARD), with an increasing trend towards biologic agents noted recently, anti-inflammatory drugs and analgesics are also used<sup>4,5</sup> DMARDs can be given as a single agent or as combination therapy.<sup>6</sup>

RA can also involve extra articular sites and can also be associated with non-inflammatory articular diseases. One of such diseases is fibromyalgia (FM) which makes the true assessment of severity of rheumatoid arthritis difficult. The system evolved to measure the disease activity of rheumatoid arthritis is Disease Activity Score (DAS).<sup>7,8</sup> Treatment of rheumatoid arthritis is usually based on disease activity score which is calculated by the number of tender and inflamed joints, patient general

health by a 100 mm visual analogue scale of pain<sup>9</sup> and erythrocyte sedimentation rate. In the presence of FM, the disease activity score and hence the DMARDs therapy becomes arguable. The frequency of FM in general population is around 2% while previous studies have mentioned the frequency of 'fibromyalgia with rheumatoid arthritis (RAFM)' between 10 - 20%.<sup>10-12</sup> It has also been shown in studies that patients who are affected by RA with FM have higher clinical disease activity, poor outcome and inferior quality of life as compared to other patients with rheumatoid.<sup>13</sup>

The prevalence of RA in Pakistani population is the same as in other part of the world.<sup>14</sup> However, no Pakistani study could be found to show the frequency of FM in this population as well as how FM affects the disease activity score.

The objective of this study was to evaluate frequency of FM in RA and its effect on disease activity score.

## METHODOLOGY

It was a cross-sectional study conducted in the Outpatient Rheumatology Clinic of The Indus Hospital, Karachi, from December 2010 to May 2011.

Inclusion criteria for eligibility were all adults 18 years and above of either gender who were diagnosed with RA on the basis of clinical, laboratory and X-ray criteria. Any patient with thyroid dysfunction and Vitamin-D deficiency ascertained through laboratory investigations were excluded. Patients with other known rheumatological diseases were also excluded. Prior to commencing

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study, ethical approval was obtained from the IRD (Interactive Research and Development) Institutional Review Board. Similarly, informed consent was obtained from the participants before including them in the current study project.

The criteria used to diagnose RA was adapted from American College of Rheumatology in which at least four of the following should be present : (a) morning stiffness, (b) arthritis of three or more joint areas, (c) arthritis of hand joints, (d) symmetric arthritis, (e) rheumatoid nodules, (f) serum rheumatoid factor, (g) radiographic changes. Additionally, a patient was diagnosed with fibromyalgia if any two of the following conditions were met: (i) the presence of widespread pain for more than three months and (ii) pain, not just tenderness that can be elicited by manual pressure at 11 or more defined tender points.<sup>15</sup>

All patients giving informed consent were interviewed and examined by principal researcher. Information was collected on the patient's age, gender, socioeconomic status, number and type of joints involved, duration of disease and limitation of physical activity,<sup>16</sup> and assessment of pain on a pre-coded proforma. Blood samples were taken for blood chemistries and thyroid function test were done as routine tests performed in the hospital laboratory. The disease activity score was calculated by number of tender and swollen joints involved, visual analogue scale and ESR.

All the data was entered and analyzed in Statistical Package for Social Sciences (SPSS) version 17. Shapiro Wilk's test was applied to check the normality of quantitative variables like age, number of medications; rheumatology consults over past year, disease activity score, number of tender and swollen joints, visual

analogue scale and ESR. Median (IQR) was computed for all the quantitative variables mentioned before depending on the normality assumption. Means and medians of the aforementioned quantitative variables were compared among FM groups i.e. RA with FM and RA only, using Mann-Whitney test. Frequency and percentages were calculated for qualitative variables, gender, duration of disease and functional status. Chi-square or Fisher's exact test was applied to check association among FM groups and aforementioned qualitative variables. P-values less than 0.05 were considered significant.

The normality of each and every quantitative variable (not string or qualitative variable) was checked separately and tested through Shapiro Wilk's test. Means and medians of the aforementioned quantitative variables were compared among FM groups i.e. RA with FM and RA only, using Mann-Whitney test.

## RESULTS

Total number of patients studied was 120. Out of them, the number of patients with RA was 89 (74.2%) while the number of patients with RAFM was 31 (25.8%). The median (IQR) age of patients was 40 (32-51). There was no statistically significant difference in median age between RA and RAFM patients (38 vs. 40;  $p = 0.721$ ; Table I).

All patients in the RAFM group were females ( $n=31$ ) in comparison to 88.8% in the RA only group ( $n=79$ ). There were statistically significant differences in DAS-28 score between RA and RAFM groups. The median DAS-28 score in RA group was 4.9 in comparison to 7.04 in RAFM group ( $p < 0.001$ ). Individual components of DAS score are mentioned in Table II.

**Table I:** Descriptives of study population of rheumatoid arthritis (RA) and rheumatoid arthritis with fibromyalgia (RAFM).

Characteristics	RA with fibromyalgia n=31	RA only n=89	p-value	Normality test
Age (years)				
Median (IQR)	38 (35-45)	40 (30 - 52)	0.721	0.005 <sup>†</sup>
Total number of medications; median IQR	3 (3 - 4)	3 (2 - 4)	0.05	0.000 <sup>††</sup>
Number of rheumatology consults over past year; median (IQR)	4 (2 - 6)	3 (1 - 5)	0.042 <sup>*</sup>	0.000 <sup>††</sup>
Gender; n (%)				
Male	0 (0.00)	10 (11.2)	0.062 <sup>**</sup>	-
Female	31 (100)	79 (88.8)		
Duration of disease; n (%)				
< 5 years	25 (80.6)	59 (66.3)	0.276 <sup>**</sup>	-
5 - 10 years	5 (16.1)	21 (23.6)		
> 10 years	1 (3.2)	9 (10.1)		
Functional status; n (%)				
Class 1	0 (0.00)	31 (34.8)	0.000 <sup>**</sup>	-
Class 2	0 (0.00)	40 (44.9)		
Class 3	31 (100)	15 (16.9)		
Class 4	0 (0.00)	3 (3.4)		

<sup>†</sup>  $p < 0.05$ ; <sup>††</sup>  $p < 0.0001$ ; shows that particular variable is non-normal (Shapiro Wilk's test)

<sup>\*</sup>  $p$ -value  $< 0.05$  and <sup>\*\*</sup>  $p$ -value  $< 0.0001$ , calculated by Mann-Whitney U-test

<sup>\*\*</sup>  $p$ -value  $< 0.001$ , calculated by chi-square test

IQR = Inter Quartile Range i.e. 25th percentile - 75th percentile

**Table II:** DAS and its components - comparison of rheumatoid arthritis (RA) and rheumatoid arthritis with fibromyalgia (RAFM), median (IQR).

Characteristics	RA with fibromyalgia n=31	RA only n=89	p-value	Normality test
Disease activity score; median (IQR)	7.04 (6.62 - 7.64)	4.9 (3.66 - 5.71)	0.000**	0.008†
Total number of tender joints; median (IQR)	24 (24 - 28)	5 (2 - 12.5)	0.000**	0.000††
Number of swollen joints; median (IQR)	9 (2 - 18)	3 (1 - 7)	0.006*	0.000††
Visual analogue scale; median (IQR)	80 (70 - 80)	20 (10 - 30)	0.000**	0.000††
ESR; median (IQR)	37 (26 - 48)	40 (22 - 60)	0.876	0.000††

†  $p < 0.05$ ; ††  $p < 0.0001$ ; shows that particular variable is non-normal (Shapiro Wilk's test)

\*  $p$ -value  $< 0.05$  and \*\*  $p$ -value  $< 0.0001$ , calculated by Mann-Whitney U-test test

IQR = Inter Quartile Range i.e. 25th percentile - 75th percentile.

Combination of DMARD i.e. more than one disease modifying drug used to treat the disease was also evaluated. The number of patient getting combination therapy of DMARD in RAFM group was  $n=19$  (61.3%) while in RA group was  $n=38$  (42.7%).

## DISCUSSION

The result of this study show that almost one-quarter of the patients had RA with FM while other studies have shown it to be between 10% and 20%.<sup>17,18</sup> The higher frequency in this study need more research in this regard. It is a complex and challenging task to assess the disease activity in rheumatoid arthritis patients.<sup>13</sup> This is the first study of this type in Pakistan. It has shown the problem associated with using DAS-28 score to tailor DMARD therapy. DAS-28 is currently considered as determinant for assessment of patients with RA and has authority in the indication or alteration of treatment; therefore, it must take into consideration the presence of FM as a feature that leads to an overestimation of this index.

Although the DAS-28 is significantly different in two groups, the ESR has no significant difference. ESR being one of the inflammatory markers signifies that the anti-inflammatory therapy could be injudiciously given if we consider DAS-28 as marker of disease activity. DAS-28 has both subjective and objective assessments in which Visual Analogue Scale (VAS) is totally patient dependent. The presence of significant difference in VAS and absence of significant difference in ESR shows the limitation of DAS-28 score in that it may not be an objective assessment of DAS. One of the interesting findings in a study was the presence of less erosion in RAFM patients despite of more DAS-28 score.<sup>18</sup> This was probably because of more complaints of pain and consequently more use of DMARD in this group. The effectiveness of this study is that a clinician should be aware of high prevalence of RAFM (26% in this study) and should look for other causes of pain in RA patient.

One of the important findings of this study is the effect of FM on quality of life of patients. All the patients in RAFM group had functional class 3 while RA group had only 20% patients in functional class 3 and 4. It is observed that patients with RA who have concomitant FM have a

poor functional capacity. The number of tender joints in RAFM group was also significantly more than RA group. This all contributing to the quality of life of RAFM patients and increasing their agony and hence pain threshold. The treatment plan for RAFM group should be tailored according to the severity of each problem, a detailed knowledge of treatment history, course of disease and complications of RA. Another interesting finding is significant difference between number of swollen joints, indicating the presence of more inflammation of synovial in RAFM patients. This finding was also present in other studies.<sup>19</sup>

As The Indus Hospital is free of cost, more poor and middle class patients tend to visit the facility but the standard of care is same for all hence socioeconomic status of the patients did not differ in the study groups. The duration of more than 10 years of disease was 3% in RAFM group and about 10% in RA group. Studies have shown a relation of duration of disease to the aggressive use of DMARDs.<sup>20</sup> This point needs further evaluation in the local population.

The use of combination therapy, although not reaching the significant level, at least showed a trend toward RAFM group. Studies have shown a less erosive pattern on X-ray in RAFM group, the reason could be using more aggressive therapy.<sup>18</sup> Further studies in our part of the world are needed to further evaluate this issue as well.

None of the patients were on biological treatment due to the cost. Most of these patients belong to poor or middle class group and are not affording to bear the cost of this treatment. Others studies also had similar limitation and reason for not using this mode of treatment.<sup>21</sup>

## CONCLUSION

In this study, near one-quarter of RA patients also had FM which is higher than reported elsewhere. In the absence of any significant differences in ESR count, the assessment of DAS-28 in this population was largely based on subjective criteria of pain perception. Thus, DAS-28 should be applied with caution in the presence of FM and alternative criteria that are pertinent in the local population should be evaluated.

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