The impact of concomitant fibromyalgia on visual analogue scales of pain, fatigue and function in patients with various rheumatic disorders

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ABSTRACT

Objective. *To evaluate the impact of concomitant fibromyalgia on the rating of pain, fatigue, and dysfunction, in patients with various rheumatic disorders.*

Methods. *A cross-sectional study was carried out in a hospital-based rheumatology unit. Standard clinical and laboratory data were obtained and all patients completed questionnaires on pain, fatigue, and daily function. The rate of concomitant fibromyalgia was estimated using the 1990 American College of Rheumatology (ACR) classification criteria for fibromyalgia and the analysis concentrated on visual analogue scales (VAS).*

Results. *Six hundred and eighteen visits of 383 patients with inflammatory as well as non-inflammatory rheumatic disorders were analysed. Concomitant fibromyalgia was noted in 74 patients (23% of the cohort). Patients with rheumatic diseases and concomitant fibromyalgia had significantly higher mean VAS scores for pain, fatigue, and function (79±17, 81±18, 80±18 respectively) as compared to patients who had no features of fibromyalgia (47±28, 50±29, 44±30, respectively; all p-values <0.001). The scores reported by patients with rheumatic diseases and concomitant fibromyalgia were similar to the scores obtained from patients with primary FM.*

Conclusion. *Concomitant FM is common both among patients with inflammatory and patients with non inflammatory rheumatic disorders. Concomitant FM has a remarkable impact on the severity of symptoms and, moreover, patients with concomitant FM exhibit extreme and significantly distinct levels of pain and fatigue which is as severe as that reported by patients with primary FM. It seems that fibromyalgic features dominate and become the main cause of morbidity in rheumatological patients with concomitant FM.*

Introduction

Fibromyalgia (FM) often accompanies other rheumatic disorders. Although FM is present in about 2-5% of the general population, it has been reported to coexist in 25% of patients with rheumatoid arthritis (RA), 30% of patients with systemic lupus erythematosus (SLE) and 50% of patients with primary Sjögren's syndrome (pSS) (1). It is well established that patients with active inflammatory disease and coexisting FM may report greater symptom intensity than patients without concomitant FM (2-5), nevertheless, there are only limited reports on the actual prevalence and magnitude of this phenomenon in general rheumatology clinical practice. We have carried out a cross-sectional study in a hospital-based rheumatology unit, in which visual analogue scales for pain, fatigue and function in patients with rheumatic disorders were evaluated (6). The aim of the present study is to evaluate the impact of concomitant fibromyalgia on the rating of pain, fatigue and dysfunction in patients with various rheumatic disorders.

Pain, fatigue and functional disability are mutual key outcomes applying to most rheumatic disorders. Pain has long been evaluated successfully using the visual analogue scale (VAS), both in clinical trials and as clinical standard of care (7). The use of VAS scale for the evaluation of fatigue and function has been suggested as well. Wolfe et al. used the VAS scale to evaluate fatigue in 7760 patients with RA and showed that it performed as well as or better than the other longer questionnaires generally used (8). A preliminary evaluation of the VAS function scale has indicated that it may be suitable for use both in the clinical setting and in research (9). We chose to use concomitant VAS of pain, fatigue and function for our clinical outcome assessment

because these measures apply to all rheumatic disorders. It is also short, simple, reliable, sensitive to change and user-friendly in the clinic environment and less linguistic-dependent.

Fibromyalgia is characterised by chronic widespread musculoskeletal pain (WSP) and tenderness. The 1990 American College of Rheumatology (ACR) classification criteria for FM syndrome are based upon these two components. In clinical practice, the most common presenting complaint of a patient with FM is "pain all over", and tenderness is determined by a tender point examination (TPs). Yunus has coined the concept of "incomplete FM syndrome" (rheumatology clinic patients with only one component; either WSP or TPs), and suggested that these patients, considering the whole clinical picture, may be diagnosed with FM, albeit generally mild (10). We chose to use this concept for our clinical assessment to identify patients with secondary fibromyalgia.

Material and methods

This cross-sectional study was carried out in the rheumatology clinic of Asaf-Harofeh Medical Center, Israel between January and December 2006. The methods of this study have been described (6). Briefly, inclusion criteria of this study included adult patients aged ≥18 years attending the rheumatology clinic. Patients were diagnosed with various rheumatic disorders according to clinical, laboratory and radiographic findings and received current standard level of care. In the beginning of each visit, before clinical examination, patients completed a self-administered questionnaire (in Hebrew, Arabic, or Russian), which included questions about demographics, patient history, presence and duration of morning stiffness, fatigue and daily activity. Pain, fatigue and functional disability during the week prior to the visit were assessed using three VAS scales. The VAS was a 10cm line double anchored and indexed from one end - no pain or fatigue or functional disability to the other end - worst possible pain or fa-tigue or functional disability. During clinical examination, in addition to the standard rheumatologic evaluation, the rheumatologist completed a report which included the chief complaint, pattern of articular involvement, pres-ence or absence history of widespread pain (WSP), swollen and tender joint counts, tender points (TPs), laboratory markers of inflammation, diagnosis, the physician's global assessment of overall disease activity (MD global) on a visual analogue scale (VAS), medica-tions and comorbidities. Case report forms were collected, the quality of data was confirmed and a final elec-tronic database was created.

Statistical analysis.

The data were analysed using BMDP (ref: BMDP Statistical Software (1993), chief editor: W.J. Dixon, University of California Press, Los Angeles. Descriptive statistics included the mean value and standard deviation of the continuous variables, and the percentages and proportions of the categorical variables. We used Analysis of Variance (ANOVA) with Bonferroni's correction for multiple comparisons to compare the continuous variables by diagnoses. Pearson's Chi-square test was applied to compare discrete variables. We computed correlation coefficients using Pearson's correlation. A p-value of ≤0.05 was considered significant.

Results

During 2006, a total of 1754 patient-visits were recorded at the rheumatology clinic. In 875 of the 1754 patient-visits, patients agreed to participate and completed the self-assessment forms. Of these, data of 257 patient-visits were excluded due to diagnostic uncertainty, lack of information or poor patients' self-administered forms. Statistical analyses were performed on 618 patient-visits of 383 patients.

Patients with concomitant fibromyalgia

Three hundred and eighty three patients were included in the analysis. Ninety-two patients had rheumatoid arthritis (RA), 21 patients had systemic lupus erythematosus (SLE), 51 patients had spondyloarthritis (SpA), 48 patients had other inflammatory rheumatic disorders (IRD) (Sjögren's syndrome, systemic sclerosis, polymyositis, vasculitis, adult onset Still's disease, etc.), 13 patients had gout, 16 patients had polymyalgia rheumatica (PMR), 57 patients had other non-inflammatory rheumatic disorders (NIRD) (joint hypermobility, overuse syndromes, low back pain, arthralgias, etc.), 41 patients had osteoarthritis (OA), and 44 patients had primary fibromyalgia (FM).

Our analysis concentrated on patients with concomitant features of FM. The proportions of patients with concomitant Fibromyalgia are shown in Table I. Overall, secondary fibromyalgia was noted in 74 patients (23% of the cohort) including: 24 patients with RA (26%), 6 patients with SLE (28%), 4 patients with SpA (8%), 14 patients with IRD (29%), 0 patients with gout, 1 patient with PMR (6%), 14 patients with NIRD (24%), 11 patients with OA (26%). Coexisting FM was less prevalent in patients with SpA and PMR, than in patients with RA, SLE, other inflamma-

Table I. The proportion of patients with concomitant fibromyalgia.

	RA	SLE	SpA	IRD	PMR	NIRD	OA	Total
No of Patients (n)	92	21	51	48	16	57	41	326
Group 1 (n)	68	15	47	34	15	43	30	252
Group 2 (n)	10	3	4	7	0	14	4	42
Group 3 (n)	14	3	0	7	1	0	7	32
Proportion of patients with concomitant fibromyalgia (%) (either complete or incomplete)	26%	28.5%	7.8%	29.1%	6.2%	24.5%	26.8%	23%

n: number of patients.
Group 1: Patients with rheumatic diseases without features of FM.
Group 2: Patients with rheumatic diseases and concomitant incomplete FM (patients with either widespread pain (WSP) or tender points (TPs).
Group 3: Patients with rheumatic diseases and concomitant complete FM (patients with both WSP and TPs).

tory rheumatic disorders, OA and other non-inflammatory rheumatic disorders. The demographic characteristics of the group of patients with concomitant FM are shown in Table II. Patients with concomitant FM differed from patients without FM in two variables: gender and years of education. Concomitant FM patients were mostly females (95%) and had less years of education. There were no significant differences between the two groups in age, disease duration, and marital status.

VAS scores of pain, fatigue and function

We compared VAS scores for pain, fatigue and function among four groups of patients (Table III): 1. Patients with any underlying rheumatic disorder without coexisting FM; 2. Patients with any underlying rheumatic disorders with secondary incomplete complete FM; 3. Patients with any underlying rheumatic disorders with secondary complete FM; and 4. Patients with primary FM. Using univariate analysis we found that patients with rheumatic diseases and coexisting fibromyalgia had significantly higher mean VAS scores for pain, fatigue, and function (79±17, 81±18, 80±18 respectively) as compared to patients who had no features of fibromyalgia (47±28, 50±29, 44±30 respectively; all *p*-values <0.001). The VAS scores showed an increase between patients with rheumatic diseases with no features of FM, and patients with incomplete coexisting FM (patients with either widespread pain (WSP) or tender points (TPs), and again between patients with incomplete coexisting FM and patients with complete coexisting FM (patients with both WSP and TPs). The highest scores were obtained from patients with primary FM. Patients with primary FM had significantly higher mean VAS of fatigue (91±12) than patients with coexisting FM (81±18; *p*-value = 0.002). Patients with secondary FM had a significantly higher VAS scores for pain, fatigue and function, as compared to patients without features of FM ($p<0.001$).

We also compared VAS scores for pain, fatigue and function between patients with and without concomitant FM in various rheumatic disorders including: RA, IRD, OA, and NIRD (Table IV). In all groups, patients with secondary FM had a significantly higher VAS scores for pain, fatigue and function, as compared to patients without features of FM (all *p*-values <0.05).

Table II. Demographic characteristics of patients with concomitant fibromyalgia.

Demographic characteristics	Patients with concomitant FM	Patients without concomitant FM	*p* value
No of patients	74	265	
Age years, mean ±SD	49.8 ± 18	52.3 ± 16	0.29
Gender Female (%)	70 (95%)	172 (65%)	<0.001
Education years, mean	11.2 ± 2.8	12.6 ± 2.6	<0.001
Marital status married (%)	47 (64%)	170 (64%)	0.42
Disease duration years, mean	5.5 ± 6.9	5.1 ± 6.9	0.99

Table III. VAS of pain, fatigue, and function in patients with rheumatic disorders without concomitant fibromyalgia, patients with rheumatic disorders with concomitant complete or incomplete fibromyalgia and patients with primary fibromyalgia.

	Group 1	Group 2	Group 3	Group 4
VAS Pain, meam ± SD	48 ± 29*	70 ± 21	80 ± 18	87 ± 16
VAS Fatigue, meam ± SD	50 ± 30*	70 ± 24	81 ± 19	91 ± 12**
VAS Function, meam ± SD	44 ± 31*	71 ± 24	80 ± 18	86 ± 18

Group 1: Patients with rheumatic diseases without features of FM [265 patients, 439 patient-visits].
Group 2: Patients with rheumatic diseases and secondary incomplete FM (patients with either widespread pain (WSP) or tender points (TPs)) [42 patients; 65 patient-visits].
Group 3: Patients with rheumatic diseases and secondary FM (patients with both WSP and TPs) [32 patients; 50 patient-visits].
Group 4: Patients with primary FM [44 patients; 64 patient-visits].
*Significantly lower in group 1 compared to groups 2-4 ($p<0.001$).
**Significantly higher in groups 4 compared to group 3 ($p<0.001$).

Table IV. VAS of pain, fatigue, and function in patients with various rheumatic disorders with and without secondary fibromyalgia.

	VAS PAIN		VAS FATIGUE		VAS FUNCTION	
	Patients without FM	Patients with FM	Patients without FM	Patients with FM	Patients without FM	Patients with FM
RA	46 ± 28	*81 ± 17	50 ± 31	*79 ± 21	42 ± 31	*81 ± 18
IRD	50 ± 28	*70 ± 24	47 ± 28	*72 ± 26	48 ± 28	*70 ± 25
OA	62 ± 22	*77 ± 20	57 ± 24	*73 ± 22	60 ± 24	*80 ± 18
NIRD	62 ± 22	*77 ± 11	65 ± 26	*82 ± 14	55 ± 29	*72 ± 17

RA-: Patients with rheumatoid arthritis [175 patient-visits]. IRD-: Patients with inflammatory rheumatic disorders [84 patient-visits]. OA -: Patients with osteoarthritis [53 patient-visits]. NIRD-: Patients with non-inflammatory rheumatic disorders [58 patient-visits].
*Significantly higher in patients with FM compared to patients without FM ($p<0.05$).

Discussion

It has been estimated that concomitant FM is present in about one fifth of patients with RA and even more frequently in SLE (11). In this cross-sectional study conducted in a hospital based rheumatology clinic we identified concomitant FM in 23% of the study population. According to our results concomitant FM is common in patients with any underlying chronic musculoskeletal disorder (excluding patients with primary FM).

Interestingly, the prevalence of concomitant FM was the same among patients with autoimmune and inflammatory diseases, osteoarthritis and other non-inflammatory disorders. This finding is consistent with the theory of central sensitisation of pain suggesting that chronic widespread pain may result from any long-lasting pain condi-

tion in the musculoskeletal system (11). Although the literature mainly emphasizes the high prevalence of concomitant FM in autoimmune inflammatory rheumatic diseases (12-15), there is only limited data on concomitant FM in other rheumatic conditions. There is emerging evidence that coexisting FM has a significant impact on symptoms severity and response to therapy in patients with OA (16) and in patients with other conditions such as chronic lateral epicondylitis (17).

In the present study patients with concomitant FM reported higher scores for pain, fatigue and dysfunction as compared to patients without coexisting FM. The coexistence of FM had a remarkable impact on symptoms intensity, as VAS scores were increased by about 60% on average (Table III), and nearly doubled in patients with RA (Table IV). The same effect of concomitant FM on VAS scores of pain and fatigue in RA patient was observed by Pollard *et al*. (3) and by Lage-Hansen *et al*. (4). Moreover, our patients with concomitant FM exhibited extreme and significantly distinct levels of pain and fatigue which were as severe as those reported by patients with primary FM.

Rheumatoid arthritis with co-existing fibromyalgic features has been termed "fibromyalgic RA" (18). Its importance has been highlighted by Wolfe and colleagues who described its characteristic high levels of pain, fatigue and disability (19). In the light of the results of the present study, it may be appropriate to use the term "fibromyalgic rheumatism", to describe rheumatological patients with any underlying rheumatic disorder and coexisting fibromyalgic features, because the fibromyalgic features seem to dominate and to become the main cause of morbidity.

Most patients with secondary FM were females (95%). This is not surprising as the parameters which were used to characterise patients with FM were based on the 1990 American college of rheumatology (ACR) criteria including history of diffuse pain and tender point tenderness. It is well established that women are ten times more likely than men to experience tender point tenderness.

Concomitant FM was less prevalent in the groups of patients with PMR and SpA. It is well known that prednisone therapy in patients with PMR usually results in rapid and dramatic improvement of the musculoskeletal aching and stiffness. This therapeutic effect is probably appreciable in the results of our survey, as PMR patients were less exposed to prolonged musculoskeletal pain. The relatively short duration of pain in these patients may have prevented the development of secondary fibromyalgia. Concomitant FM was also less prevalent in the group of patients with SpA. This may reflect the significantly lower Female/Male ratio in this group (1:1), as compared to the all other groups. On the other hand, this may suggest a different underlying cause of fatigue and widespread pain in this disorder.

The role of central pain processing mechanisms, such as loss of descending analgesic activity and central pain augmentation, has been well documented in primary FM. There is emerging evidence that central nervous system pain mechanisms may also play a role in the generation and maintenance of chronic pain in RA and OA (20). For the rheumatologist, this issue is highly relevant as it affects treatment decisions, particularly in the era of the emerging treat to target concept. First, disease activity scores may become disproportionately high in patients with centralised pain. Second, when a patient with any rheumatic disorder develops evidence of centralisation of pain, it is likely that treatments considered effective for acute and peripheral pain will be less effective (21). Third, non-pharmacologic therapies, which can be helpful for patients with primary FM may be difficult to use in secondary FM because of the underlying disorder.

Our study has several limitations. Since the study was conducted in a single hospital clinic, the data obtained could be affected by the study population. In addition, the VAS scores that were used for fatigue and functional disability assessment are less validated than multi-item outcome measures.

In summary, concomitant FM was common in this cohort of rheumatological patients and was similarly prevalent among patients with inflammatory and non-inflammatory rheumatic disorders. Concomitant FM had a remarkable impact on symptoms severity and, moreover, patients with concomitant FM exhibited extreme and significantly distinct level of pain and fatigue which were as severe as that reported by patients with primary FM. It seems that fibromyalgic features dominate and become the main cause of morbidity in rheumatological patients with concomitant FM. Further studies are necessary to determine whether these patients may benefit from treatment that targets central pain mechanisms.

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