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ORIGINAL ARTICLE

Fibromyalgia in patients with other rheumatic diseases: prevalence and relationship with disease activity

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Abstract Fibromyalgia (FM) is a syndrome characterized by chronic widespread pain and the presence of specific tender points. The prevalence of FM has been estimated at 2–7 % of the general global population. The presence of FM in several rheumatic diseases with a structural pathology has been reported as 11–30 %. The objectives of this study were to determine the prevalence of FM and to evaluate the possible relationship between FM existence and disease activity among rheumatic diseases. The study group included 835 patients—197 rheumatoid arthritis (RA), 67 systemic lupus erythematosus (SLE), 119 ankylosing spondylitis (AS), 238 osteoarthritis (OA), 14 familial Mediterranean fever (FMF), 53 Behçet's disease (BD), 71 gout, 25 Sjögren's syndrome (SS), 20 vasculitis, 29 polymyalgia rheumatica (PMR), and two polymyositis (PM)—with or without FM. Recorded information included age, gender, laboratory parameters, presence of fatigue, and disease activity indexes. The prevalence of FM in patients with rheumatologic diseases was found to be 6.6 % for RA, 13.4 % for SLE, 12.6 % for AS, 10.1 % for OA, 5.7 % for BD, 7.1 % for FMF, 12 % for SS, 25 % for vasculitis, 1.4 % for gout, and 6.9 % for PMR. One out of two patients with PM was diagnosed with FM. Some rheumatologic cases (AS, OA) with FM were observed mostly in female patients ($p = 0.000$). Also, there were significant correlations between disease activity indexes and Fibromyalgia Impact Questionnaire scores for most rheumatologic patients (RA, AS, OA, and BD) ($p < 0.05$; respectively, $r = 0.6$, 0.95, 0.887, and 1). Concomitant FM is a common clinical problem in rheumatologic diseases, and its recognition is important for the optimal management of these diseases. Increased pain, physical limitations, and fatigue may be interpreted as increased activity of these diseases, and a common treatment option is the prescription of higher doses of biologic agents or corticosteroids. Considerations of the FM component in the management of rheumatologic diseases increase the likelihood of the success of the treatment.

Keywords Rheumatologic diseases · Fibromyalgia · Disease activity

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Introduction

Fibromyalgia (FM) is a syndrome characterized by chronic widespread musculoskeletal pain and generalized tender points. Its prevalence has been estimated to be around 2–7 % of the general global population [1–3], and its

presence in several rheumatic diseases with a structural pathology has been reported as being 11–30 % [4–10].

Rheumatic diseases, for example, rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), ankylosing spondylitis (AS), osteoarthritis (OA), familial Mediterranean fever (FMF), Behçet's disease (BD), Sjögren's syndrome (SS), gout, vasculitis, and polymyalgia rheumatica (PMR), usually have a chronic course (affecting the musculoskeletal system), may result in systemic involvement, and are indicated by acute relapses and remissions.

Fibromyalgia is frequently associated with rheumatic diseases [5–8], and the relationship between FM and RA, SLE, and AS has been well established. However, FM has also been reported in a limited number of studies on patients with OA, SS, BD, PMR, and FMF. In addition, there are no or few published data on the influence of disease activity in concomitant FM cases. This study is the first to investigate the relationship between FM, gout, vasculitis, and PMR.

The objectives of the study were to identify the prevalence of FM among rheumatic diseases and to evaluate the possible relationship between FM presence and disease activity.

Subjects and methods

Our study group included 835 consecutive patients (197 RA, 67 SLE, 119 AS, 238 OA, 14 FMF, 53 BD, 71 gout, 25 SS, 20 vasculitis, 29 PMR, and two PM) attending the outpatient Rheumatology Clinic, Faculty of Medicine, Fatih University, with or without FM. These patients all fulfilled the relevant diagnosis criteria [11–22]. In all patients, we assessed the presence of FM according to the criteria of the American College of Rheumatology (ACR) classification, which includes two concomitant criteria: (1) chronic generalized pain in both sides of the body, both axial and peripheral, below and above the waist; (2) the presence of at least 11 of the 18 specified tender points described for FM [23]. We excluded from the study any patient known to have thyroid function disorders, infections, and any other chronic diseases.

We compiled the following data, which relate to the patients' last visit, using a computerized patient database: age, gender, presence of arthritis, Reynaud's syndrome, and fatigue, disease activity indexes, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and anti-nuclear antibody (ANA). In addition, we recorded the presence of some somatic symptoms, which often accompany FM [4–24], in patients with this disorder.

As an index of disease activity, patients completed questionnaires as follows: FM Impact Questionnaire (FIQ) for patients with concomitant FM; Disease Activity Score in 28 joints (DAS-28) for patients with RA; Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) for patients with SLE; Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) for patients with AS; Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) for patients with OA; Tel Hashomer key to severity score (THKSS) for patients with FMF; and BD Current Activity Form (BDCAF) for patients with BD as an index of disease activity [7, 9, 25–33].

Statistical analysis

We performed all statistical analyses using SPSS for Windows, version 17.0. Unless otherwise stated, results were expressed as mean ± SD. We used the Mann–Whitney U test or independent sample t test between two subject groups, and used the Pearson correlation test or Spearman correlation test, as appropriate. We used multiple regression analysis to exclude possible confounding effects of other variables in the results of each correlation analysis and considered a result of $p < 0.05$ as statistically significant.

Results

Thirteen of 197 patients with RA (6.6 %), nine of 67 patients with SLE (13.4 %), 15 of 119 patients with AS (12.6 %), 24 of 238 patients with OA (10.1 %), three of 53 patients with BD (5.7 %), and one of 14 patients with FMF (7.1 %) met the criteria for the diagnosis of FM [20]. Information regarding the age, gender ratio, laboratory parameters, and disease activity scores of patients with or without FM is presented in Table 1.

Three of 25 patients with SS (12 %) and five of 20 patients with vasculitis (25 %) fulfilled the criteria for the diagnosis of FM [20]. Information regarding the age, gender ratio, laboratory parameters, presence of Reynaud's syndrome, fatigue, and arthritis in patients with or without FM is presented in Table 2.

Among 71 patients with gout and 29 patients with PMR, one (1.4 %) and two (6.9 %), respectively, were diagnosed with FM [20]. Information on the age, gender ratio, laboratory parameters, presence of fatigue, and arthritis in patients with or without FM is shown in Table 3. Of two patients with PM, one was diagnosed with FM [20].

In the majority of the rheumatologic diseases, with the exception of SLE and FMF, disease activity scores were significantly higher in patients with FM than in patients without FM ($p < 0.001$ for RA, AS, and OA and $p < 0.05$ for BD). In addition, we primarily observed FM in female patients ($p < 0.05$ for OA and BD; $p < 0.001$ for AS), and all patients with SLE were female. In general, the mean ages were lower in the groups with FM, and this was

Table 1 Age, gender ratio, laboratory investigations, and disease activities of rheumatologic patients with(out) FM

		Age	Gender (women/men)	CRP	ESR	Disease activity scores*
RA $n = 197$	With FM	42.15 ± 8.25	13/0 (100 %)	13.8 ± 12.92	30.72 ± 16.74	5.68 ± 0.47
	Without FM	53.09 ± 13.12	145/39 (78 %)	26.76 ± 30.72	39.29 ± 28.22	4.16 ± 1.41
	p	0.003[a]	NS	NS	NS	0.000[a]
SLE $n = 67$	With FM	36.88 ± 10.72	9/0	17.96 ± 23.14	29.22 ± 17.97	7.11 ± 2.47
	Without FM	39.86 ± 14.58	58/0	33.34 ± 90.55	35.91 ± 33.26	6.5 ± 2.62
	p	NS		NS	NS	NS
AS $n = 119$	With FM	38.06 ± 9.07	14/1 (93 %)	6.1 ± 4.98	18.4 ± 12.07	7.26 ± 0.64
	Without FM	40.13 ± 12.3	44/60 (42 %)	19.5 ± 28.44	31.39 ± 43.97	5.01 ± 1.4
	p	NS	0.000[a]	NS	NS	0.000[a]
OA $n = 238$	With FM	57.12 ± 8.09	24/0 (100 %)	5.87 ± 9.71	15.83 ± 13.96	58.79 ± 3.34
	Without FM	61.88 ± 12.41	149/65 (69 %)	6.87 ± 57.02	23.52 ± 18.86	45.69 ± 4.12
	p	NS	0.002[a]	NS	NS	0.000[a]
BD $n = 53$	With FM	30 ± 4	3/0 (100 %)	7.56 ± 9.1	19.83 ± 19.9	3.03 ± 0.05
	Without FM	36.66 ± 11.25	19/31 (38 %)	24.3 ± 35.94	39.08 ± 32.92	1.98 ± 0.65
	p	NS	0.034[a]	NS	NS	0.008[a]
FMF $n = 14$	With FM	53	1/0 (100 %)	3.4	22	4
	Without FM	27.38 ± 13.61	7/6 (54 %)	72.06 ± 97.69	31.07 ± 24.17	5 ± 2.44
	p	NS	NS	NS	NS	NS

NS nonsignificant

* DAS-28 for RA, SLEDAI for SLE, BASDAI for AS, WOMAC for OA BDCAF for BD, and THKSS for FMF

[a] $p < 0.05$

Table 2 Age, gender ratio, laboratory investigations, and clinical features of rheumatologic patients with(out) FM

	SS patients $n = 25$			Vasculitis patients $n = 20$		
	With FM	Without FM	*p*	With FM	Without FM	*p*
Age	50.66 ± 0.57	52.22 ± 11.13	NS	36.8 ± 19.03	41.73 ± 14.54	NS
Gender (women/men)	3/0 (100 %)	21/1 (95 %)	NS	14/1 (93 %)	10/5 (66 %)	NS
CRP	7.06 ± 3.35	19.16 ± 46.48	NS	7.49 ± 7.62	42.97 ± 68.68	NS
ESR	25.66 ± 28	33.13 ± 26.02	NS	17.4 ± 11.21	20.53 ± 12.8	NS
ANA	1.66 ± 0.57	1.27 ± 0.45	NS			
Fatigue	3/0 (100 %)	8/14 (36 %)	0.037[a]	4/1 (80 %)	2/13 (13 %)	0.005[a]
Arthritis	1/2 (33 %)	7/15 (31 %)	NS	3/2 (60 %)	7/8 (46 %)	NS
Reynaud's syndrome	0/3 (0 %)	6/16 (27 %)	NS	1/4 (20 %)	3/12 (20 %)	NS

NS nonsignificant

[a] $p < 0.05$

Table 3 Age, gender ratio, laboratory investigations, and disease activity of rheumatologic patients with(out) FM

	Gout patients $n = 71$			PMR patients $n = 29$		
	With FM	Without FM	*p*	With FM	Without FM	*p*
Age	50	57.42 ± 15.59	NS	48 ± 18.38	74.85 ± 8.93	0.001[a]
Gender (women/men)	1/0 (100 %)	19/51 (27 %)	NS	2/0 (100 %)	19/8 (70 %)	NS
CRP	12.6	37.29 ± 94.61	NS	3.35 ± 0.21	23.47 ± 36.56	NS
ESR	24	31.51 ± 24.04	NS	10 ± 2.82	39.85 ± 28.6	NS
Fatigue	1/0 (100 %)	2/68 (2 %)	0.000[a]	1/1 (50 %)	3/24 (11 %)	NS
Arthritis	1/0 (100 %)	65/5 (92 %)	NS	1/1 (50 %)	27/0 (100 %)	0.000[a]

NS nonsignificant

[a] $p < 0.05$

Table 4 Somatic symptoms of rheumatologic patients with FM

	Existence/ nonexistence	(%)
Fatigue	76/0	100
Paresthesia	3/73	3.94
Gastric disturbance	32/44	42.1
Irritable bowel syndrome	12/64	15.78
Urticaria	5/73	6.57
Pain/cramps in the abdomen	34/42	44.73
Constipation	10/66	13.15
Diarrhea	3/73	3.94
Dry mouth	7/69	9.21
Dry eyes	7/69	9.21
Oral ulcers	20/56	26.31
Sun sensitivity	9/67	11.84
Reynaud's syndrome	9/67	11.84

significant for RA and PMR ($p < 0.05$). The presence of FM was significantly associated with fatigue for SS, vasculitis, and gout ($p < 0.05$). In addition, FM was significantly associated with arthritis in PMR ($p < 0.001$). There was no statistically significant difference between the groups, with regard to CRP and ESR.

We investigated the possible correlations between disease activity and total FIQ scores for almost all rheumatic diseases with concomitant FM ($p < 0.05$ and $r = 0.600$ for RA; $r = 0.950$ for SLE; $r = 0.887$ for AS; $r = 0.572$ for OA; and $r = 1$ for BD). We could not evaluate the correlation with FMF, because the number of patients was limited.

When we queried the somatic symptoms of rheumatologic patients with FM, we found that rates were high, as presented in Table 4. The prominent somatic symptoms were fatigue (100 %), pain in the abdomen (44.73 %), gastric disturbance (42.1 %), and oral ulcers (26.31 %). These symptoms were followed by irritable bowel syndrome (15.78 %), constipation (13.15 %), sun sensitivity (11.84 %), and Reynaud's syndrome (11.84 %). Other symptoms comorbid with FM were dry mouth, dry eyes, urticaria, diarrhea, and paresthesia.

Discussion

The prevalence of FM has been estimated at 2–7 % of the general population [1–3] and is frequently associated with some rheumatic diseases [5–8]. FM is a potentially debilitating disorder that can have a devastating effect on quality of life, impair patients' abilities, and result in economic and social burdens [34]. Since rheumatic diseases also cause chronic pain and affect the musculoskeletal system, a diagnosis of concomitant FM is particularly important. While previous studies have reported that FM prevalence is 12 and 15.4 % in patients with RA [4, 8, 9, 35], no data have been published on the relationship between FM and RA in the Turkish population. In our study, 6.6 % of the Turkish patients with RA had concomitant FM. The prevalence of FM that we observed was lower than in the other populations investigated.

While FM was associated with female patients with AS, OA, and BD, we did not find an association with RA. As shown in several previous studies, FM was more prevalent in females [9, 34–36]. In contrast with the published data, in our concomitant FM patients, there was no statistically significant difference between women and men with respect to RA. However, in accordance with FM epidemiology, the group with RA and FM had a lower mean age than those without FM [24, 35]. Further investigation is required to better understand the prevalence and related features of concomitant FM in RA patients for our population.

Confirming the results of a previous study [8, 9, 35], we observed an association between concomitant FM and a higher degree of disease activity. We also investigated the possible correlations of DAS-28 disease activity and the impact of FM on patients with a scoring system (FIQ). Likewise, there were similarities in the correlation for SLE (SLEDAI), AS (BASDAI), OA (WOMAC), and BD (BDCAF). In SLE patients, although there was no association between the presence of FM and disease activity scores, SLEDAI and FIQ were possibly correlated. These findings were consistent with the literature [5, 6, 9, 10, 35, 37–41], namely, both the presence of concomitant FM and the severity of FM suggest a higher degree of rheumatic disease activity.

We found concomitant FM in 13.4 % of the patients with SLE, 12.6 % of the patients with AS, and 10.1 % of the patients with OA in our study population. Although these degrees of prevalence were consistent with the literature, the prevalence of FM for BD and FMF as 5.7 and 7.1 %, respectively, did not correspond with previous findings. The presence of a limited number of patients with these diseases was the main weakness of our study. Confirming the results of a previous study [42], FM was found in three patients (12 %) with primary Sjögren's syndrome and was associated with fatigue.

The significance of our study is boosted by the fact that it was the first to investigate the prevalence of FM in patients with vasculitis (25 %), gout (1.4 %), and PMR (6.9 %). However, the main weakness of the study was the inability to carry out research into the relationship between FM and these diseases, due to the limited number of patients. We found FM in five patients (25 %) with vasculitis, and it was associated with fatigue and Sjögren's syndrome (1.4 %) in one patient. In the preliminary observation study, we found an increased prevalence of FM in vasculitis patients,

but no increase in gout patients, compared with the normal population. In our sample, 6.9 % of patients met the ACR classification criteria for PMR and FM simultaneously. The prevalence of FM in patients with PMR also did not differ from the normal population, but, as expected, FM was more common in young people with PMR [24, 35]. However, surprisingly, FM was associated with arthritis in PMR patients.

In this research, we queried many somatic symptoms that were comorbid with FM, such as fatigue, pain in the abdomen, gastric disturbance, oral ulcers, irritable bowel syndrome, constipation, diarrhea, sun sensitivity, Reynaud's syndrome, dry mouth, dry eyes, urticaria, and paresthesia. Emerging high prevalence supports a diagnosis of FM.

Future studies should, thus, be designed to identify other possible factors responsible for FM in patients with rheumatologic diseases beyond those already mentioned above. A direct case–control study with normal, age-matched controls would help to record the background prevalence of FM. In addition, future studies should include broader somatic symptoms of FM (such as headaches, cognitive dysfunction, balance problems, shortness of breath, and urinary problems, in addition to aforementioned symptoms), in order to improve the likelihood that a patient really does have both FM and rheumatic disease.

This study focuses on the relationship between disease activity and concomitant FM rather than the increased prevalence of FM in rheumatologic diseases. The clinical features of FM and rheumatologic diseases may also overlap. We found especially high correlations between disease severity and concomitant FM in rheumatologic diseases. The clinical overlap may also be responsible for the delay in diagnosing FM in rheumatologic patients. Furthermore, increased pain, physical limitations, and fatigue may be interpreted as increased activities of these diseases, and as such, patients are commonly prescribed higher doses of biologic agents or corticosteroids. However, centrally acting analgesics, such as pregabalin, duloxetine, and milnacipran, can be used to treat the FM.

In conclusion, concomitant FM is a common clinical problem in rheumatologic diseases, and an increased awareness of the possibility of its coexistence can contribute to the success of treatment.

Conflict of interest None.

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