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The impact of the presence of fibromyalgia on fatigue in patients with psoriatic arthritis: comparison with controls

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Abstract

Background: Coexisting fibromyalgia (FM) to psoriatic arthritis (PsA) has been identified and it has been associated with more severe symptoms, impaired function, and greater disability. It was aimed to explore the effect of the presence of FM on fatigue in patients with PsA comparing with controls.

Methods: Fifty patients with PsA and 34 sex-age matched controls were enrolled. In patients; pain was assessed by Visual Analogue Scale, disease activity by DAS-28, enthesitis by The Leeds Enthesitis Index. Fatigue level of all participants was evaluated by Multidimensional Assessment of Fatigue. In all participants, FM was determined according to 2010 American College of Rheumatology criteria.

Results: Seventeen patients with PsA (34%) and 4 controls (11.8%) were diagnosed with FM and all of them were women. There was significant difference between the patients and controls in terms of presence of FM ($p < 0.05$). Patients' fatigue scores were significantly higher than controls' ($p = 0.001$). There were significant differences between the PsA patients with and without FM with regard to gender, enthesitis, DAS-28 and pain scores ($p < 0.05$); fatigue scores ($p < 0.001$). The significant effect of the presence of FM on fatigue was found by univariate analysis of variance in patients ($p < 0.001$).

Conclusion: It was observed that FM presence and fatigue were more common in PsA patients than controls and comorbid FM had significant effect on fatigue in these patients. Physicians should be aware of the possibility of concomitant FM in patients with PsA.

Keywords: Psoriatic arthritis, Fibromyalgia, Fatigue, Disease activity

Introduction

Psoriatic arthritis (PsA) can be defined as an inflammatory arthritis associated with psoriasis. It is a part of the heterogeneous group of diseases, unified in the concept of spondyloarthritis. Clinically, PsA characterized by peripheral and/or axial joint inflammation with varying frequencies [1]. Peripheral arthritis, axial disease, enthesitis, dactylitis, skin disease, and nail disease have been defined as common clinical domains which should be considered in the treatment of patients with PsA [2].

Fibromyalgia (FM) is a chronic condition characterized by widespread bodily pain associated with somatic

symptoms including fatigue, sleep disturbance, and cognitive problems [3, 4]. Coexisting FM to the rheumatic diseases such as rheumatoid arthritis, systemic lupus erythematosus, scleroderma, primer Sjogren's syndrome, spondyloarthritis, PsA has been identified and it has been found associated with more severe symptoms, impaired function, and greater disability [5–12]. Moreover, presence of FM was one of the exclusion criteria in clinical trials of disease-modifying agents as it may influence study outcome [12].

Fatigue can be described as loss of force generation during a task or mismatch between expended effort and actual performance or exhaustion [13]. It is a common and important symptom in rheumatic diseases interfering with daily activities and causing disruption and disability [14]. Fatigue is related to pain, psychological

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distress, sleep quality, comorbidities, disability, fibromyalgia, and socio-demographic characteristics in rheumatic disorders [15–18]. As in other rheumatic diseases, fatigue levels are high in patients with PsA and are associated with emotional and social aspects of the disease beside disease related parameters [14, 19–23]. To date, little is known about the effect of the presence of FM on fatigue in patients with PsA. In one study, the association has been shown between the number of FM points and the level of fatigue in patients with PsA [19]. In another study, it has been found that PsA patients with FM reported greater fatigue than those without [14]. Magrey et al. [23] reported that FM associated fatigue is more frequent in patients with PsA compared to controls.

In this study the aim was to evaluate the effect of the presence of FM on fatigue in patients with PsA comparing with sex-age matched controls.

Material and methods

A case-control study was conducted in the Department of Physical Medicine and Rehabilitation of Medical Faculty of “Ondokuz Mayıs University” between February 2017 and June 2018. Fifty patients with PsA attending our institution who fulfilled the Classification Criteria for Psoriatic Arthritis (CASPAR) criteria [24] and 34 sex-age matched controls recruited from general population were enrolled in this study. Exclusion criteria were severe psoriatic skin lesions, other rheumatic diseases, any chronic diseases such as uncontrolled diabetes mellitus and heart or renal failure, thyroid disorders, severe somatic or psychiatric disorders, a history of cancer. Subjects with known FM and receiving chronic pain treatment were also excluded. The study protocol was approved by the Medical Research Ethics Committee at Ondokuz Mayıs University (B.30.2.ODM.0.20.08/ 530). All participants provided signed informed consent. The study was conducted in accordance with the principles of the Declaration of Helsinki.

All participants were questioned about age, number of education years completed, working status, medical comorbidities, and smoking habits. Durations of psoriasis and arthritis, current medications, and laboratory evaluations including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) were reported in the patients. The presence of skin lesions, dactylitis, and axial involvement were also evaluated in the patients.

Patients completed a 10-cm visual analogue scale (VAS) for pain (0 = no pain, 10 = very severe pain) [25]. Disease activity of the patients was evaluated using Disease Activity Score including 28 joints (DAS-28) [26]. Tender joint count, swollen joint count, erythrocyte sedimentation rate, and global assessment score were

used. It was reported to be useful method for assessing disease activity in PsA clinical trials [27].

The Leeds Enthesitis Index (LEI) was used to measure enthesitis. It consists of 6 sites: bilateral Achilles tendon insertions, medial femoral condyles, and lateral epicondyles of the humerus. Tenderness at each side is quantified on a dichotomous basis (0: non-tender and 1: tender) [28]. Fatigue level of the participants was evaluated by Multidimensional Assessment of Fatigue (MAF) [29]. This scale contains five dimensions of fatigue: degree, severity, distress, impact on activities of daily living and timing. Each 100-mm VAS was converted to a 10-point numerical rating scale. The scores range from 0 (no fatigue) to 50 (severe fatigue) [30]. The assessment of the presence of FM in all participants was based on the 2010 American College of Rheumatology (ACR) criteria [3].

Statistical analyses

The data were analyzed using the IBM SPSS version 22.0 for Windows. The sample size was calculated for the main outcome, fatigue, which was measured using MAF [30] by a statistician with PASS 2011. It was calculated as a minimum of 50 patients and 30 controls with an alpha value 0.05 and 96% power, based on the data of a study conducted by Alkan et al. [31]. The Kolmogorov-Smirnov test was used to analyze normal distribution assumption of the quantitative outcomes and all data were not normally distributed. Descriptive data were presented as minimum–maximum (median). The sociodemographic characteristics of the patients and controls were compared by Chi-square test. Mann–Whitney *U* test was used to compare clinical parameters of patients and controls. In patients, univariate analysis of variance was used to assess the effect of the presence of FM on MAF scores.

Results

The sample consisted of 50 patients aged between 23 and 64 years and 34 controls aged between 25 and 67 years. Demographic and clinical characteristics of the participants are shown in Table 1. There was no significant difference with regard to demographic characteristics (age, gender, years of education, smoking) among patients and controls ($p > 0.05$). Patients' MAF scores were significantly higher than controls' ($p = 0.001$) (Table 1).

Of the patients 16 (32%) had controlled hypertension and 2 (4%) had benign prostate hypertrophy. Skin lesions in 25 (50%) patients, axial involvement in 7 (14%) patients, and dactylitis in one (2%) patient were detected. Of the controls 7 (20.6%) had controlled hyperlipidemia and 12 (35.3%) had controlled hypertension.

Table 1 Comparison of demographic and clinical characteristics of the patients with psoriatic arthritis and controls

Characteristics	Patients (n = 50) Median (minimum-maximum)	Controls (n = 40) Median (minimum-maximum)	p
Age	47 (23–64)	45 (25–67)	0.480
Years of education (years)	5 (0–16)	11 (0–15)	0.057
MAF score (0–50)	17.6 (1–43.5)	1 (1–42.9)	0.001*
Psoriasis duration (years)	16 (1–50)	–	–
Arthritis duration (years)	6.5 (1–30)	–	–
ESR (mm/h)	13 (2–97)	–	–
CRP (mg/l)	0.7 (0.1–18.2)	–	–
DAS-28	2.9 (1.2–5.2)	–	–
VAS pain score (0–10)	4.5 (0–9)	–	–
LEI score (0–6)	0 (0–3)	–	–
	n (%)	n (%)	
Presence of FM	17 (34)	4 (11.8)	0.023*
Gender			
female	36 (72)	21 (61.8)	0.350
male	14 (28)	13 (38.2)	
Smoking	15 (30)	7 (20.6)	0.450
Occupation			
housewife	28 (56)	10 (29.4)	0.024*
office worker	11 (22)	19 (55.9)	
retired	11 (22)	5 (14.7)	
Medication use			
Biological agents	50 (100)	–	–
DMARDs	39 (78)		
Corticosteroid	8 (16)		
NSAIDs	13 (26)		

MAF Multidimensional Assessment of Fatigue, ESR Erythrocyte Sedimentation Rate, CRP C-Reactive Protein, DAS-28 Disease activity score-28, BASDAI Bath Ankylosing Spondylitis Disease Activity Index, VAS visual analogue scale, LEI Leeds Enthesitis Index, FM Fibromyalgia, DMARDs Disease-modifying anti-rheumatic drugs, NSAIDs non-steroidal anti-inflammatory drugs

* $p < 0.05$

Seventeen of 50 patients with PsA (34%) and 4 of 34 controls (11.8%) were diagnosed with FM. There was significant difference between the patients and controls in terms of presence of FM ($p < 0.05$) (Table 1). All of the PsA patients with FM (17 patients) and controls with FM (4 patients) were women. Information on regarding the demographical and clinical features in PsA patients with and without FM is presented Table 2. There were significant differences between the PsA patients with and without FM with regard to gender, LEI scores, DAS 28 scores, and VAS pain scores ($p < 0.05$). MAF scores were significantly higher in PsA patients with FM than those without FM ($p < 0.001$) (Table 2). Age and gender were not significantly different in controls with and without FM ($p > 0.05$). On the other hand; MAF scores were significantly high in controls with FM compared to

controls without FM ($p = 0.009$). The significant effect of the presence of FM on fatigue was found by univariate analysis of variance in patients with PsA ($p < 0.001$).

Discussion

This study explored the influence of the concomitant FM on fatigue in patients with PsA comparing with sex-age matched controls. The results of this study showed that patients with PsA had higher frequency of FM and higher fatigue level compared to controls, and comorbid FM had significant effect on fatigue level of these patients.

There is limited data on the prevalence of FM in patients with PsA [8, 9, 11, 23, 32, 33]. There are difficulties to distinguish the two conditions because both PsA and FM share similar complaints such as extraarticular

Table 2 Comparison of the clinical parameters in the psoriatic arthritic patients ($n = 50$) with and without fibromyalgia

Characteristics	Patients with FM ($n = 17$) n (%)	Patients without FM ($n = 33$) n (%)	p
Gender			
female	17 (34%)	19 (38%)	0.002*
male	0 (0%)	14 (28%)	
	Median (min-max)	Median (min-max)	
Age (years)	48 (25–66)	47 (23–64)	0.264
Psoriasis duration (years)	17 (5–50)	15 (1–38)	0.324
Arthritis duration (years)	10 (1–30)	5 (1–25)	0.271
ESR (mm/h)	20 (4–97)	12 (2–57)	0.263
CRP (mg/l)	3 (0.2–18.2)	0.56 (0.1–14.6)	0.050
DAS 28	3.5 (2.1–5.2)	2.8 (1.2–5.1)	0.012*
VAS pain score (0–10)	6 (3–7)	3 (0–9)	0.002*
LEI score (0–6)	0 (0–3)	–	0.004*
MAF score (0–50)	33.4 (3.1–43.2)	12.9 (1–43.5)	0.000**

ESR Erythrocyte Sedimentation Rate, CRP C-Reactive Protein, DAS-28 Disease activity score-28, BASDAI Bath Ankylosing Spondylitis Disease Activity Index, VAS visual analogue scale, LEI Leeds Enthesitis Index, MAF Multidimensional Assessment of Fatigue

* $p < 0.05$

** $p < 0.001$

pain, chronic back pain associated with morning stiffness, fatigue, depression, anxiety, and sleep disturbance. In the studies, comorbid FM has been reported to occur in 15 to 50% of patients with PsA with a higher prevalence in women [8, 9, 11, 23, 32, 33]. FM has been identified mostly using ACR 1990 criteria or ACR 2010 criteria [8, 9, 11, 32, 33]. Unlike, Magrey et al. [23] determined the frequency of FM using the London Fibromyalgia Epidemiologic Study Screening Questionnaire and Symptoms Intensity Scale. In a study by Fan et al. [8], rheumatologist opinion was also used for the diagnosis of FM besides ACR 1990 criteria. In the current study, FM was detected in 34% of PsA patients according to ACR 2010 criteria. We also found that FM was more frequent in patients with PsA than controls. In the literature, Magrey et al. reported statistically higher frequency of FM among PsA patients compared to controls [23]. On the other hand, the percentage of the FM presence was 11.4% in controls which was higher than expected. The prevalence of FM in our country was reported as 3.6% in 2005 [34]. The possible explanations for this difference may be the small sample size, differences in case detection strategies, and use of different criteria to diagnose FM in our study. Nevertheless, it seems that patients with PsA were at greater risk for FM compared to controls. The fact that patients and controls with FM were women also supports the female preponderance in FM.

The number of studies on fatigue in PsA patients has increased recent years and fatigue was defined as

a potential core domain in clinical trials in these patients [35]. In the literature, most researchers studied the severity of fatigue in patients with PsA, and reported that fatigue levels were high and moderate to severe in the majority of the patients [19–22]. However there is only one study comparing fatigue level in PsA patients with the controls. They found that the percentage of the PsA patients complaining fatigue was higher than controls but fatigue scores of the patients and controls were comparable [23]. In our study, patients with PsA had significantly higher fatigue scores comparing to controls. It was shown that fatigue has priority in PsA patients and has multifactorial aspects. Both the disease related factors and patient related characteristics play important role in the etiology of fatigue in patients with PsA [14, 19–22]. Coexisting FM was reported as one of the factors that contribute to fatigue in PsA [14, 19, 23]. Husted et al. have studied the relationship between fatigue and disease-related and psychological variables in a large, cross-sectional sample of PsA [19]. They have found that higher number of FM tender points was related to fatigue assessed by modified fatigue severity scale. In a study describing the longitudinal course of fatigue in PsA, comorbid FM was found to be associated with greater fatigue [14]. In another study; fatigue was evaluated with a fatigue visual analog scale within Symptoms Intensity Scale which was used to measure the frequency of FM, and increased frequency of FM was found in PsA patients that contributes to fatigue [23]. The results of the current study were

in line with our expectations. The PsA patients with FM had higher fatigue scores than those without FM and presence of FM was found to be influential variable on fatigue in PsA patients. Although fatigue scores of the controls were lower than patients', controls with FM also reported that they had more fatigue than controls without FM. Because of the close relationship between fatigue and FM presence, fatigue in PsA patients should not be attributed only to the disease itself.

In a study by Husted et al. [14], significant interactions of disease duration, morning stiffness, and physical disability with FM have been detected in patients with PsA. In another study, FM-associated pain was more frequent in patients with PsA compared to controls [23]. Brikman et al. [11] showed that coexisting FM is related to higher disease activity in these patients. In a retrospective study assessing the frequency of clinical remission in PsA patients, initial presence of <11 tender points and the absence of FM were found to be predictors of remission [32]. In the current study; disease activity, pain, and enthesitis scores were worse in PsA patients coexisting FM. There was also significant difference in terms of gender which all PsA patients with FM were women. It can be stated that in patients with PsA who still have high pain and diseases activity scores despite effective treatment, concomitant FM should be considered.

This study is faced with certain limitations that should be considered. Because of the cross-sectional design, it is not possible to show how fatigue and the factors effecting fatigue change over time. Additionally, the presence of FM was evaluated only by the 2010 ACR criteria which have been shown to be useful and valid in multiple settings [3, 4]. These criteria are based on self-reporting painful body regions assessed by the widespread pain index and the severity of symptoms assessed by symptom severity scale. Therefore, PsA patients who fulfill 2010 ACR criteria might have worse scores on pain and activity indices. On the other hand, it was stated that the overlap of enthesitis sites with FM tender points causes a diagnostic confusion in the 1990 ACR criteria [9]. The clinical evaluation of PsA is complex and includes numerous domains of disease activity [11]. Another limitation of this study is the assessment of disease activity by DAS28 which is routinely used in our clinic. Future studies with other measures (such as Disease Activity Index for Psoriatic Arthritis comprises 68 tender and 99 swollen joints) may be planned to clarify the relationship between FM presence, fatigue and disease activity in patients with PsA. In other respects; although we determined our sample size with power analysis, future studies are needed to address the impact of FM on patients with PsA with

larger number of participants. Since the results belong to single center, they could not be generalized to broader population. Finally, the lack of evaluation of the parameters associated with fatigue and FM, such as sleep quality and emotional status, is another limitation of this study.

Although the association of FM with many rheumatic diseases is well defined, the impact of comorbid FM in PsA patients has been investigated in limited number of studies [11, 14, 23, 32]. The results of the current study are valuable because of investigating FM presence in PsA patients by comparing with controls. This study revealed the differences of the sociodemographic and clinical features among PsA patients with and without FM. In our study, fatigue level of participants was evaluated with MAF which has relatively low patient burden and has potential clinical utility. Despite the fact that there is no gold standard fatigue instrument for rheumatologic diseases, MAF provides data for a fuller description of fatigue in the population of interest. Almost all chronic diseases may cause fatigue, for this reason the participants were carefully selected for inclusion and exclusion criteria in our study.

Conclusion

In the current study it was observed that FM presence and fatigue were more common in PsA patients than controls. PsA patients with FM reported higher fatigue level compared to those without FM. Pain, enthesitis, and disease activity scores were also significantly worse in PsA patients with comorbid FM. These results have shown that coexisting FM may cause increased fatigue and may worsen disease related factors such as pain, enthesitis, disease activity in patients with PsA. The unrecognized comorbid FM in patients with PsA may lead to misinterpretation of treatment failure. In PsA patients who have the complaints of fatigue and pain, and who have high disease activity; the presence of FM should be assessed before upgrading of PsA treatment strategy. PsA patients with comorbid FM may benefit from interventions targeted for FM. Physicians should be aware of the possibility of concomitant FM in patients with PsA.

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Authors' contributions

Yasemin Ulus: Design of the work, Interpretation of data for the work, Analysis of data, Drafting the work, Final approval of the version to be published, Agreement to be accountable for all aspects of the work. *Yesim Akyol*: Contributions to the conception, Interpretation of data for the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agreement to be accountable for all aspects of the work. *Ayhan Bilgici*: Contributions to the conception, Analysis of data,

Revising the work critically for important intellectual content, Final approval of the version to be published. *Omer Kuru*: Contributions to the conception, Analysis of data, Revising the work critically for important intellectual content, Final approval of the version to be published. All authors read and approved the final manuscript.

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Availability of data and materials

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Ethics approval and consent to participate

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Consent for publication

All of the authors have approved the final version. Additionally, there are no conflicts of interest in connection with this paper, and the material described is not under publication or consideration for publication elsewhere.

Competing interests

There is no conflict of interest concerning the authors in conducting this study and preparing the manuscript.

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