

## Evaluation of fibromyalgia syndrome in patients with rosacea

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### ABSTRACT

**Objectives:** This study aims to investigate the frequency of fibromyalgia syndrome (FMS) in rosacea patients and the relationship between disease disability score of FMS and quality of life score of rosacea.

**Patients and methods:** This cross-sectional controlled clinical trial was performed between December 2017 and December 2018. One hundred female rosacea patients (mean age 43.2±10.1; range, 21 to 65 years) and 100 age- and sex-matched control subjects (mean age 41.2±11.1; range, 22 to 68 years) with no history of skin disease and systemic diseases including diabetes, cardiovascular, renal and hepatic diseases were recruited. Dermatology Life Quality Index (DLQI) scores were calculated using a 10-item self-administered questionnaire. The diagnosis of FMS was established according to 2010 American College of Rheumatology diagnostic criteria. Fibromyalgia Impact Questionnaire (FIQ) was used to determine the clinical severity and functional disability, while Visual Analog Scale (VAS) was used to determine pain severity in the patients with FMS.

**Results:** The frequency of FMS in patient group was significantly higher than control group (p=0.019). The mean duration of FMS in patient group was significantly higher than control group (p=0.001). There was no significant difference in terms of the age of onset of FMS, FIQ and VAS scores between groups (p=0.53, p=0.54, p=0.07, respectively). DLQI scores were significantly correlated with FIQ scores in the patient group (r=0.43, p=0.008).

**Conclusion:** The frequency of FMS in rosacea patients was significantly higher than control subjects without any skin disease and there was a correlation between disability score of FMS and quality of life score of rosacea. Investigating fibromyalgia symptoms in rosacea patients may be helpful for providing patient-based therapeutic approaches where neurologically based treatments may also be beneficial for rosacea.

**Keywords:** Female, fibromyalgia, frequency, quality of life, rosacea.

Rosacea is a chronic inflammatory skin disorder with unknown etiology. Vascular abnormalities, environmental factors and microorganisms such as *Demodex folliculorum* and *Helicobacter pylori* have been documented to play a potential role in the development of the disease.<sup>1</sup> Dysfunction of innate immune system, disruption of the epidermal skin barrier, activation of cutaneous nerves by triggering factors like sun exposure and emotional stress result with skin sensitivity.<sup>2-4</sup> Coexistence

of neurological and neuropsychiatric diseases with rosacea has been reported, supporting the role of neurophysiological mechanisms in disease etiopathogenesis.<sup>5,6</sup>

Fibromyalgia syndrome (FMS) is a chronic noninflammatory rheumatic disorder that is characterized by generalized musculoskeletal pain.<sup>7</sup> Although the etiopathogenesis is not clear, the abnormalities in central pain mechanisms have been thought to play a crucial role.<sup>8</sup>

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Recently, the role of peripheral nerves and neurogenic inflammation has been implicated in the pathophysiology of FMS.<sup>9,10</sup> Skin related symptoms including hyperhidrosis, burning sensation of the skin or mucous membranes and increased frequency of cutaneous disorders like neurotic excoriations, lichen simplex chronicus, dermatographism, seborrheic dermatitis and tinea pedis have been reported in FMS patients.<sup>11</sup> Rosacea is another skin disease which has been reported to accompany FMS.<sup>11</sup> However, the relationship between rosacea and FMS has not been investigated as far as we are aware. Therefore, in this study, we aimed to investigate the frequency of FMS in rosacea patients and the relationship between disease disability score of FMS and quality of life score of rosacea.

## PATIENTS AND METHODS

This cross-sectional controlled clinical trial was performed in Kırşehir Training and Research Hospital between December 2017 and December 2018. We included 130 consecutive female patients with rosacea. Thirty patients met the exclusion criteria and therefore were excluded from the study and a total of 100 patients were recruited. The control group was selected from our hospital staff by snowball technique and included 100 consecutive female controls. The mean ages of rosacea patients and control subjects were 43.21 (range, 21 to 65) years and 41.2 (range, 22 to 68) years, respectively ( $p=0.18$ ). Patients aged under 18 years, pregnant or lactating patients, those

having a history of systemic or inflammatory diseases were excluded. The control group was selected from female subjects with no history of skin disease and systemic diseases including diabetes, cardiovascular, renal and hepatic diseases. The study protocol was approved by the Ahi Evran University Ethics Committee (approval no: 2017-18/219, date: 28.11.2017). A written informed consent was obtained from each participant. The study was conducted in accordance with the principles of the Declaration of Helsinki.

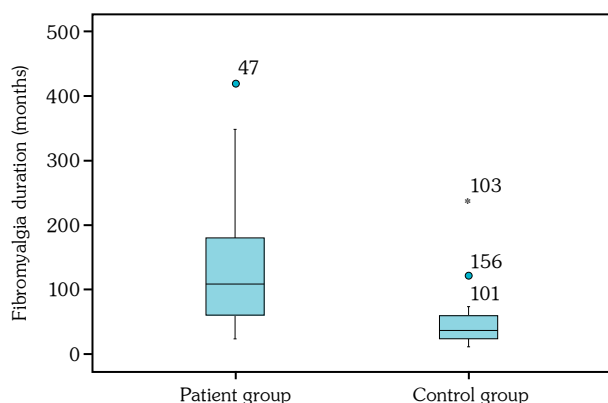
The patients were evaluated by a physical medicine and rehabilitation specialist and the diagnosis of FMS was established according to 2010 American College of Rheumatology diagnostic criteria.<sup>12,13</sup> A validated Turkish version of the Fibromyalgia Impact Questionnaire (FIQ) was used to determine the clinical severity and functional disability of the patients diagnosed with FMS. The forms were filled out by the patients in the outpatient clinic and took approximately 5 min to complete. FIQ forms consist of 10 self-administered scales related to physical functioning, work status, depression, anxiety, sleep, pain, stiffness, fatigue and well being (scores between 0 to 80). Visual Analog Scale (VAS) (0 to 10) was used to determine the pain severity in FMS.<sup>14,15</sup>

Dermatology Life Quality Index (DLQI) scores were calculated using a 10-item self-administered questionnaire. The patients filled out the Turkish version of the DLQI form in approximately 3 to 4 min in the outpatient clinic. The DLQI consists of 10 questions regarding symptoms

**Table 1.** Characteristics of patient and control groups

	Patient group (n=100)			Control group (n=100)			p
	n	%	Mean±SD	n	%	Mean±SD	
Age (year)			43.21±10.1			41.2±11.1	0.18
Rosacea duration (month)			54.8±5.9			-	-
Fibromyalgia age onset			34.9±1.2			36.4 ±2.4	0.53
Subjective symptoms							
Itching	55	55		-	-		-
Burning sensation	53	53		-	-		-
Stinging sensation	11	11		-	-		-

SD: Standard deviation; \*  $p<0.05$ .



**Figure 1.** Comparison of fibromyalgia durations between patient and control groups.

and feelings, daily activities, leisure, work or school, personal relationships and treatment in the previous seven days. The questions have four alternative answers: not at all, a little, a lot and very much, which correspond to scores of 0, 1, 2 and 3, respectively. The total score is calculated by summing the score of each question ranging from a minimum of 0 to a maximum of 30.<sup>16,17</sup>

The age of patients, disease duration, skin types, symptoms like itching, burning and stinging sensations were recorded. Skin types were assessed based on Fitzpatrick scale.<sup>18</sup> FMS symptoms like fatigue, sleep disturbances, cognitive difficulties and stiffness were recorded.

### Statistical analysis

Statistical analysis was performed using the IBM SPSS version 21.0 software (IBM Corp., Armonk, NY, USA) and G\*Power Version 3.1.9.6 (Kiel Universität, Kiel, Germany). Shapiro-Wilk test was used for testing normality. Continuous

and discrete variables were presented as mean  $\pm$  standard deviation and median (min-max), respectively. Categorical variables were shown as number and percentage. Fisher's exact test was used for analyzing categorical variables. The statistical difference between the groups was analyzed using Student's t-test for mean values and Mann-Whitney U test for median values. Correlation analysis was performed using Spearman's correlation test.  $P < 0.05$  was considered to be statistically significant.

## RESULTS

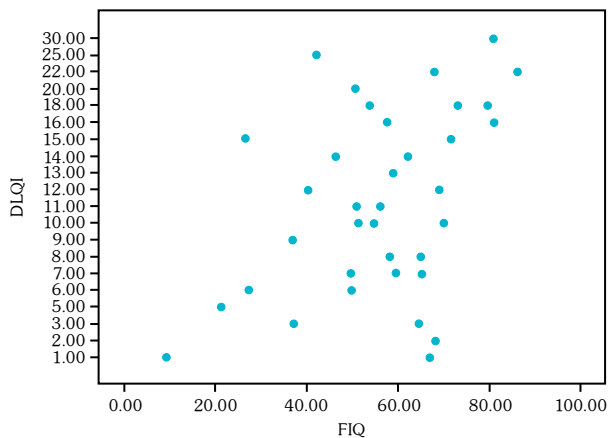
The mean age of onset of rosacea was  $38.8 \pm 1.1$  years. Fifteen patients had a family history of rosacea. As for skin types; 24 were of skin type I, 47 were of skin type II and 29 were of skin type III. Fifty-five patients described itching, 53 burning and 11 stinging sensation (Table 1).

Thirty-seven (37%) patients were diagnosed with FMS in patient group; 10 patients already had a diagnosis of FMS at the time of examination. Twenty-one (21%) subjects were diagnosed with FMS in the control group. The frequency of FMS was significantly higher in the patient group than in the control group ( $p = 0.019$ ). The mean duration of FMS was  $138.5 \pm 17.0$  months in the patient group and  $52.0 \pm 11.5$  in the control group ( $p = 0.001$ ) (Figure 1). In 24 (64.8%) of the patients FMS started before rosacea symptoms. The mean FIQ scores did not differ between groups. ( $p = 0.54$ ) (Table 2). DLQI scores were significantly correlated with FIQ scores in the patient group. ( $r = 0.39$ ;  $p = 0.017$ ) (Figure 2).

**Table 2.** Dermatology Life Quality Index scores of patient group, Fibromyalgia Impact Questionnaire and Visual Analog Scale scores of patient and control groups

	Patient group (n=100)					Control group (n=100)					p
	n	%	Mean $\pm$ SD	Median	Min-Max	n	%	Mean $\pm$ SD	Median	Min-Max	
DLQI score				9	1-30				-	-	
FIQ score			54.9 $\pm$ 3.0					50.8 $\pm$ 5.0			0.54
Pain severity (VAS scale)				7	2-10				6	2-10	0.07

SD: Standard deviation; Min: Minimum; Max: Maximum; DLQI: Dermatology Life Quality Index; FIQ: Fibromyalgia Impact Questionnaire; VAS: Visual Analog Scale; \*  $p < 0.05$ .



**Figure 2.** Correlation between Dermatology Life Quality Index and Fibromyalgia Impact Questionnaire in patient group.

DLQI: Dermatology Life Quality Index; FIQ: Fibromyalgia Impact Questionnaire.

## DISCUSSION

The pathophysiology of rosacea has not yet been fully elucidated and is considered as multifactorial.<sup>19</sup> Neuroimmune and neurovascular interactions are noted among the mechanisms in disease etiopathogenesis leading to flushing, erythema and induction of leukocyte infiltration. Rosacea has been reported to be accompanied by neurological and neuropsychiatric disorders including headaches, complex regional pain syndrome, essential tremor, depression and obsessive-compulsive disorder.<sup>5</sup> Another striking coexistence with rosacea is migraine which is also a chronic paroxysmal disorder involving the trigeminal innervated area.<sup>2,6</sup>

Rheumatologic disorders including FMS, lupus, rheumatoid arthritis, mixed connective tissue disease and psoriatic arthritis are also reported to be common in rosacea patients.<sup>5</sup> Dermatological disorders including dermatographism, lichen simplex chronicus, tinea pedis and seborrheic dermatitis have been reported to be more common in FMS patients than the healthy population as well.<sup>20</sup> FMS is a chronic pain syndrome characterized by generalized pain, fatigue, sleep disorders and cognitive function disorders. In our study, in which we evaluated the relationship between rosacea and FMS, we found that the frequency of FMS was higher in rosacea patients than controls and the frequency

of FMS was higher in both patient and control groups than that of the normal population which is estimated to be around 0.5 to 5%.<sup>21</sup> This result may be related to the selection of the control group from our hospital staff who work under stressful conditions as work-related stress has been shown to contribute to the development of FMS.<sup>22,23</sup> Recent studies have demonstrated the role of peripheral nerves and neurogenic inflammation in FMS.<sup>9,10</sup> Increased frequency of FMS in rosacea patients may be attributed to the common role of neurogenic inflammation in which substance P, mast cells, interleukin-1 beta and tumor necrosis factor-alpha are involved in both diseases.<sup>4,24-28</sup>

On the other hand, the similarity of the triggering factors of rosacea and FMS is noteworthy. FMS patients are highly sensitive to various environmental factors including heat, light, cold, chemical exposure, sound and smell, most of which also affect rosacea symptoms.<sup>24</sup> Furthermore, both rosacea and FMS can be aggravated with consumption of certain foods and food additives such as caffeine, chocolate and glutamate.<sup>29-33</sup>

Fibromyalgia syndrome is also closely associated with stress, which is another triggering factor for rosacea.<sup>22,23</sup> In addition, some skin changes including reticular skin discoloration, pressure hyperalgesia, reactive skin hyperemia and Raynauds phenomenon are seen in FMS supporting that neurovascular changes are not only limited to musculoskeletal system but they also affect the skin.<sup>34</sup>

In our study, the FMS duration in the patient group was significantly higher than that of the control group. This finding gives an impression that long-term exposure to neuromediators may cause a tendency to develop rosacea. The FIQ and VAS values did not differ between groups suggesting that the presence of rosacea was not associated with the increase in the severity of FMS. However, FIQ scores correlated with DLQI scores; this suggests that common pathophysiological mechanisms such as neuroinflammation may be involved in FMS and rosacea.

In addition to the four rosacea subtypes (erythematotelangiectatic, papulopustular, phymatous and ocular types), Scharschmidt et al.,<sup>5</sup> described the term neurogenic rosacea as

another subgroup which is refractory to classical treatments and necessitates neurologically based treatment approaches including gabapentin, duloxetine, pregabalin, tricyclic antidepressants or topical doxepin, glycopyrrolate, capsaicin and ketamine. Gabapentin, duloxetine and tricyclic antidepressants are also used in FMS treatment, which supports that there are common therapeutic targets in the treatment of both diseases.

In this study, whether patients with FMS were using such medications at the time of the study, which can also affect rosacea symptoms, was not evaluated in detail and this is a limitation. The high frequency of FMS in rosacea patients in our study can be explained by the role of common pathophysiological mechanisms in both diseases.

In conclusion, in this study, we found that the frequency of FMS in rosacea patients was significantly higher than control group without skin disease and there was a correlation between DLQI and FIQ scores, suggesting a close relationship between FMS and rosacea. Questioning rosacea patients for FMS symptoms may be helpful for planning a patient-based treatment approach where neurologically based treatments may also be beneficial for rosacea. Further studies on the pathophysiological relationship of rosacea and FMS are warranted.

#### Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

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