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Dermatological Findings in Fibromyalgia Syndrome and Their Effects on Quality of Life, Clinical Findings, and Depression

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ABSTRACT

Purpose: The aim was to investigate the skin findings in patients with Fibromyalgia Syndrome (FMS), and the relations of these findings with the clinical symptoms of the disease, quality of life and depression levels of the patient.

Materials and Methods: A total of 77 patients with FMS were included in the study as the study group, 74 individuals were included as the control group. The pain levels were evaluated with Visual Analogue Scale (VAS). The short form-36 (SF-36) was used to evaluate the quality of life levels of the patients. The Beck Depression Scale (BDS) was used to evaluate the depression levels of the patients. All participants were evaluated by the same dermatology specialist.

Results: Although 37.1% patients who had FMS had at least one cutaneous symptom, 19.9% of the control group had at least one cutaneous symptom (p<0.01). According to the BDS, significant increases were detected in FMS patients (p=0.001). Significant decreases were detected in terms of all SF-36 parameters in the FMS group (p=0.001). There was at least one dermatological disease in 43% of the patients, and in 20.5% of the controls. Although no significant differences were detected between BDS and VAS scores of the FMS patients with and without dermatological findings, SF-36 total score and physical role strength score were found to be significantly lower in the patients who had dermatological symptoms.

Conclusions: It must be known that there may be dermatological symptoms in FMS, a more multidisciplinary approach must be used in treatment and follow-up.

Keywords: fibromyalgia syndrome, skin findings, quality of life, depression

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INTRODUCTION

Fibromyalgia Syndrome (FMS) is a chronic disease that is characterized by widespread pain and tender points on physical examination, and is often accompanied by sleep disturbance, anxiety, fatigue, headache, irritable bowel syndrome, and cognitive disorders [1-3]. The prevalence of Fibromyalgia Syndrome in the normal population varies between 1-4%, and is mostly detected in women [4]. In a previous study that was conducted in our country, the incidence of FMS in women who were aged 20-65 was reported to be 3.6% [5].

Although the true pathophysiological mechanism of FMS is not fully known yet, it may be caused by neuro-hormonal and

immunological disorders, genetic predisposition, infections, rheumatic diseases, physical traumas, or psychological diseases [6]. Some disorders, which may accompany FMS, are obsessive-compulsive disorder, major depression, dysthymia, panic attacks, generalized anxiety disorder, irritable bowel syndrome, migraine, and temporomandibular joint disorders [7,8]. Although the pathophysiology of FMS is complex, it is obvious that the roles of peripheral nerves in FMS is much greater than it was considered previously. Skin biopsies of FMS patients not only show specific receptors and characteristic electron microscopic findings, but also increases in axon reflex reactions to mechanical and chemical stimuli and reduced threshold for

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² Adiyaman University, Faculty of Medicine, Department of Dermatology, Adiyaman, Turkey capsaicin-induced inflammation, which support increased neurogenic inflammation. FMS is not classically considered to be a disease that is associated with skin findings, but various changes such as oxidative stress, increased cytokines and mast cells were detected in the pathological examination of the skin of FMS patients [3,9-10]. Although there are studies, which show increased fibromyalgia syndrome in skin diseases such as psoriasis, acne vulgaris, systemic lupus erythematosus, and urticaria, there are also studies, which investigated skin findings in fibromyalgia syndrome, which are clinical; and studies, which show its effectiveness on quality of life are very few in number [11-14].

In the present study, the purpose was to investigate the skin findings, and the relationship of these findings with the clinical symptoms of the disease in FMS patients, as well as to investigate whether the existing skin findings might affect the quality of life and depression of patients.

MATERIALS AND METHODS

The ethical approval of the study was obtained from the Local Ethics Committee of our hospital. All participants were given detailed information about the study before the evaluations, and their informed consent was obtained.

The study included 77 patients, who were aged 20-65 years, who applied to the Physical Therapy and Rehabilitation Clinic of our hospital, and who were diagnosed with FMS according to the 2010 American College of Rheumatology (ACR) Diagnostic Criteria. A total of 74 patients between the ages of 20-65 without any systemic or rheumatological disorders, who applied to our clinic with another complaint were included as the control group. Those who had a history of any rheumatic and/or inflammatory disease, history of malignancy, any dermatological disease diagnosed before, those who had cervical-lumbar disc hernia, those who had congestive heart failure, those who had coronary artery disease, those who had severe pulmonary failure, those with diabetes mellitus, those with thyroid disease, those with dysfunction, those who were treated with psychotropic or antihistamines in the last one month, those who were pregnant, and breastfeeding women were excluded from the study. The age, gender, sociodemographic characteristics, medications used, diseases, and family history of all participants were recorded. All patients who were included in the study were asked whether they had fatigue, general body pain, sleep disturbance, irritable bowel disease, headache, morning stiffness, menstrual cycle disorder, and joint pain complaints, which are the characteristic symptoms of FMS. The pain level was evaluated with 0-10 cm Visual Analogue Scale (VAS). The short form-36 (SF-36) of the Quality of Life Scale was used to evaluate the quality of life in FMS patients. The SF-36 was designed to evaluate the health status of the general population [15].

- 1. Physical function (FF) (10 items),
- 2. Physical Role Difficulty (FRD) (4 items),
- 3. Emotional Role Difficulty (ERD) (3 items),
- 4. Vitality (C) (4 items),
- 5. Mental Health (MH) (5 items),
- 6. Social Functionality (SF) (2 items),
- 7. Pain (P) (2 items), and
- 8. General Health Perception (GHP) (5 items).

Instead of a total score, the scale gives separate scores for each subscale. The Turkish validity and reliability study of the scale was conducted by Koçyiğit et al. [16].

Also, the Beck Depression Scale (BDS) was used to evaluate the depression levels of FMS patients. The Beck Depression Scale was developed in 1961 by including the most common emotional, somatic, cognitive, and motivational symptoms in depression patients [17]. The purpose of the scale is to determine the degree of depression symptoms in patients objectively. The BDS focuses on cognitive and emotional symptoms of depression, with little emphasis on somatic symptoms (i.e., only anorexia, weight loss, and decreased libido). For this reason, it is a suitable scale to screen depression in people with physical diseases. The validity of the scale was made in Turkey by Hisli and Tigin [18,19]. BDS is a self-assessment scale that consists of 21 items. The items of the scale were evaluated between 0 and 3; and the lowest total score that can be obtained from the scale is 0, and the highest total score is 63. Increased scores mean that the level of depression symptoms of the patient increases [20]. All of the participants were evaluated by the same dermatology specialist, and cutaneous symptoms e.g. itching, swelling, burning, sweating, numbness and tingling were questioned, and skin findings were recorded after a detailed examination.

Statistical Analysis

The SPSS version 22.0 package software (SPSS Inc., Chicago, II USA) was used for the analysis of the data. For continuous variables, descriptive statistics were expressed as mean±standard deviation, and median and categorical variables were expressed as numbers and percentages. The Kolmogorov Smirnov test was used to evaluate the distribution of variables. The Mann-Whitney U test and Independent Samples t-test were used for the analysis of the quantitative data. The Chi-square test and Fischer's test were used for the analysis of qualitative data. p-value≤0.05 was taken statistically significant.

RESULTS

The mean age of the FMS group that was included in the study was 42.3 ± 10.3 , and the mean age of the control group was 40.9 ± 9.8 . No significant differences were detected between the patient and control group in terms of age, gender, marital status, occupation, and smoking. Comorbid psychiatric disorders e.g. depression, stress, and panic attacks were significantly higher in the FMS group. The

The scale has 8 subscales evaluating eight parts:

Table 1. Demographic and clinical data of FMS patients and the control group

	FMS Group N(%)	Control Group N(%)	p-value
Age	42.3±10.3	40.9±9.8	0.41ª
Gender			
Female	69(45.7)	68(45.0)	0.42 ^b
Male	8(5.3)	6(4.0)	
Marital Status			
Single	13(8.6)	10(6.6)	0.56 ^b
Married	64(42.4)	64(42.4)	
Working Status			
Housewife	59(39.1)	45(29.8)	0.56 ^b
Working	18(11.9)	29(19.2)	
Smoking History	21(13.9)	13(8.6)	0.15 ^b
Concomitant Psychiatric Diseases ^c	69(45.7)	44(29.1)	0.001 ^b
Other Concomitant Diseases ^d	47(31.1)	31(20.5)	0.19 ^b

Analyzed by ^astudent t-test; ^bChi-square test, ^cDepression, panic attack, stress, and anxiety; ^dFatigue, weakness, and sleep disturbance; p<0.05 is significant

 Table 2. Comparison of cutaneous symptoms between FMS and control group

	FMS Group N(%)	Control Group N(%)	p-value
Cutaneous Symptoms	56(37.1)	30(19.9)	<0.01
Pruritus	15(9.9)	20(13.2)	0.27
Burning	56(37.1)	30(19.9)	< 0.01
Hyperhidrosis	56(37.1)	30(19.9)	<0.01
Others	19(6.1)	10(3.2)	0.12

Analyzed by Chi-square test; p<0.05 is significant

sociodemographic findings of FMS and control group are shown in **Table 1**.

Although 56 (37.1%) FMS patients had at least one cutaneous symptom, 30 (19.9%) of the control group had at least one cutaneous symptom (p<0.01). There were multiple symptoms e.g. burning in 37.1%, itching in 9.9%, sweating in 37.1%; and burning, sweating, itching, numbness, and hyperesthesia in 6.1% of the patients. The cutaneous symptoms of the patient and control group are shown in **Table 2**.

In the present study, statistically significant increases were detected in FMS patients when compared to the control group, according to the Beck Depression Scale, which was used to evaluate depression (p=0.001). The SF-36 short form was used to evaluate the quality of life of the participants, and significant decreases were detected in all SF-36 parameters in the FMS group when compared to the control group (p=0.001). The Beck Depression Scale and SF-36 data of FMS and control group are shown in **Table 3**.

The dermatological diseases of FMS and control group were evaluated by the same dermatologist, and it was found **Table 3.** Comparison of SF-36 and Beck depression scale betweenFMS and control group

FMS Group	Control Group	p-value
15(1-48)	3.5(0-20)	0.001
55(0-100)	85(50-100)	0.001
0.001(0-100)	75(0-100)	0.001
33.3(0-100)	66.6(0-100)	0.001
30 (0-70)	52.5(15-100)	0.001
48(4-84)	57(20-100)	0.001
50(0-100)	62.5(25-100)	0.001
32.5(0-77.5)	77.5(12.5-100)	0.001
35(0-80)	60(25-100)	0.001
7(5-10)	3.5(0-8)	0.001
	15(1-48) 55(0-100) 0.001(0-100) 33.3(0-100) 30 (0-70) 48(4-84) 50(0-100) 32.5(0-77.5) 35(0-80)	15(1-48) 3.5(0-20) 55(0-100) 85(50-100) 0.001(0-100) 75(0-100) 33.3(0-100) 66.6(0-100) 30 (0-70) 52.5(15-100) 48(4-84) 57(20-100) 50(0-100) 62.5(25-100) 32.5(0-77.5) 77.5(12.5-100) 35(0-80) 60(25-100)

FF: Physical Function;PRD: Physical Role Difficulty; ERD: Emotional Role Difficulties; MH: Mental Health; SF: Social Functionality; GHP: General Health Perception; VAS: Visual Analog Scale;Analyzed by Mann-Whitney U test; Described value by median (maximum-minimum); p<0.05 is significant

Table 4. Comparison of dermatologic diseases between FMS and control group

Dermatologic Disease	FMS Group N(%)	Control Group N(%)	p-value
At Least One	65(42.0)	31(20.5)	-0.01
Dermatologic Disease	65(43.0)		<0.01
Lichen Simplex	17/11 2)	6(4.0)	0.01
Chronicus	17(11.3)	6(4.0)	0.01
Xerosis	5(3.3)	11(7.3)	0.09
Acne	7(4.6)	6(4.0)	0.83
Telogen Effluvium	6(4.0)	3(2.0)	0.49
Neurotic Excoriation	8(5.3)	0(0)	0.07
Seboreik Dermatit	3(2.0)	3(2.0)	1
Tinea Pedis	3(2.0)	3(2.0)	1
Urticaria	3(2.0)	0(0)	1
Other (Contact			
Dermatitis, Keratosis			
Pilaris, Melasma,	14(0.2)	2(2.0)	-0.01
Onychomycosis,	14(9.3)	3(2.0)	<0.01
Rosacea, Seborrheic			
Keratosis)			

Analyzed by Chi-square test; p<0.05 is significant

that there was at least one dermatological disease in 43% of the patients and 20.5% of the controls. Different skin diseases e.g. licken simplex chronicus, xerosis, acne, telogen effluvium, neurotic excoriation, seborrheic dermatitis, tinea pedis, urticaria, and contact dermatitis were detected. The dermatological diseases in the patient and control groups and the comparison between the two groups are shown in **Table 4**.

As shown in **Table 4**, the presence of dermatological disease was at higher levels at significant levels in the FMS group compared to the control group. As a result of the statistical evaluations made to determine whether the presence of dermatological symptoms affected depression, pain and quality of life of patients in fibromyalgia patients, no significant differences were detected between FMS

Table 5. Comparison of Beck depression scale, pain and qualityof life between FMS patients having at least one dermatologicsymptom and no dermatologic symptom

	No Dermatologic Symptom	At Least One Dermatologic Symptom	p-value
Beck Depression Scale	2(1-4)	15(1-48)	0.67ª
SF36FF	45(20-70)	60(0-100)	0.02ª
PRD	0.0(0-25)	22.5(0-100)	<0.01ª
ERD	16.6(0-100)	33.3(0-100)	0.29 ^a
Vitality	32.5(10-70)	30 (0-55)	0.93ª
МН	52(16-80)	48.0(4- 84)	0.81ª
SF	50(0-100)	22.5(0-100)	0.34ª
Pain	22.5(10-70)	32.5(0-77.5)	0.37ª
GHP	37.5(0-65)	32.5(0-80)	0.76ª
VAS	7.5(5-9)	7(5-10)	0.32ª
Stress	9(6.0%)	17(13.7%)	
Sleeping Disorder	13(8.6%)	15(9.9%)	-
Multiple Symptoms (Depression, Sleep Disturbance, Stress)	10(6.6%)	49(32.5%)	0.01 ^b

FF: Physical Function;PRD: Physical Role Difficulty; ERD: Emotional Role Difficulties; MH: Mental Health; SF: Social Functionality; GHP: General Health Perception; VAS: Visual Analog Scale; ^aAnalyzed by Mann-Whitney U test; ^bDescribed value by median (maximumminimum); p<0.05 is significant

patients with and without dermatological symptoms in terms of BDS and VAS, and the SF-36 total score and FRG, which is the quality of life scale. The comparison of depression, pain, and quality of life in FMS patients with and without dermatological symptoms is shown in **Table 5**.

DISCUSSION

In the present study, the dermatological symptoms and signs of patients with fibromyalgia were compared with those of normal healthy individuals, and it was examined whether this was related to the mental status and quality of life of patients in those with or without skin findings. To the best of our knowledge, the number of studies investigating the skin findings of FMS patients is very few. Although studies that investigated the frequency of FMS in various skin diseases were reported in the literature, the number of clinical studies that examined skin problems in FMS patients is very few. The authors in [21] reported that the incidence of xerosis and neurotic excoriations increased in FMS patients. However, it was not investigated whether these were related to the clinical findings of patients. In the present study, at least one dermatological disease was detected in 43% of FMS patients, which was significantly higher than that of the control group. Several objective changes were detected when the skin of FMS patients was compared with that of the healthy controls. Especially, the number of increased mast cell and inflammatory cytokines, altered collagen metabolism, cutaneous microcirculation changes, autonomic nervous system dysfunction, and increased cutaneous opioid receptors were detected in the skins of FMS patients. It was reported that FMS patients experienced sweating (32%), dermatitis (9.1%), itching (3.3%), psoriasis (2.6%), acne (2.1%), rosacea (2.1%), skin reported burning sensation (2%), skin pain (1.7%), and urticaria (1.5%) [22]. In the present study, sweating was detected in 37.1%, burning 37.1%, and multiple symptoms such as sweating, burning, numbness, and tingling in 6.1% in FMS patients, which were higher than in the control group.

The relations between chronic pain and chronic pruritus were explained by various similar mechanisms such as peripheral and central sensitization, loss of inhibition in the spinal cord, and neuroimmune and neuroglial interactions [23]. In FMS patients, itching supports this common mechanism. However, no significant differences were detected in our study between the patient and control group in terms of the incidence of itching. We believe that more studies are required on this subject.

In the present study, it was also found that the mean BDS score of the patients was higher than that of the control group. The incidence of depressive disorder in FMS was reported to vary between 28.6% and 70% in some previous studies [24]. It was found that the BDS score was above 21 in 27% of FMS patients [25]. Anxiety, depression, and FMS have common pathogenetic mechanisms e.g., neurochemical dysfunction, serotonergic system hypofunction, and variations in hypothalamic-pituitary-adrenal axis activity [8]. When the dermatological disorders that accompany FMS are considered, the psychocutaneous disease concept must not be overlooked. Psychiatric and dermatological disorders are related closely, which is called *Psychocutaneous* Disorder in dermatology practice. In embryological terms, the skin and brain originate from the ectoderm, and are affected by the same hormones and neurotransmitters. Neuropeptides regulate local neuroimmune reactions in the skin as a response to stress secreted from skin cells [8,26].

In the present study, the presence of stress and depression in FMS patients may be an indicator of these common pathogenetic mechanisms. Although depression was investigated in fibromyalgia in most studies, to the best of our knowledge, the present study is the first one that examined the relations between skin manifestations and depression. The mean BDS score of FMS patients without skin findings was 2 in our study, and the mean BDS score of those with at least one dermatological finding was found to be 15.

In our study, urticaria was detected in 2% of FMS patients, and no significant differences were found in the frequency of urticaria between the FMS and Control Group. Similarly, in a study that investigated skin findings in FMS, this rate was reported to be 1.5%; however, it was not compared with any control group [21]. It was argued in recent studies that FMS, whose etiology has not yet been fully explained, is among the neuropathic pain syndromes accompanied by neurogenic inflammation [27,28]. There are

previous studies showing that this neurogenic inflammation may also play roles in the pathogenesis of chronic urticaria, whose etiology has not yet been fully explained [29]. Based on this common hypothesis, the frequency of fibromyalgia syndrome was reported to be much higher in patients with chronic urticaria than in the normal population in a recent study [30]. Also, it is considered that emotional stress plays important roles in the etiology of chronic urticaria, as in fibromyalgia syndrome [31].

In our study, acne was detected in 4.6% of FMS patients, which was similar to that of the control group. No studies were detected in the literature that investigated the frequency of acne in FMS patients. Acne vulgaris is a common inflammatory disease of the skin. Many factors such as stress, genetic predisposition, bacterial infections, hormonal disorders, cosmetics, solar exposure, smoking, or diet can cause acne [32]. Also, clinical symptoms related to FMS such as fatigue, sleep disturbance, or anxiety were mentioned in the literature in acne vulgaris patients [32,33]. Stress-related factors may be the etiopathogenetic mechanism between FMS and acne. It was shown in the past that stress increased the release of P substance from peripheral nerves after inducing the hypothalamic-pituitary-adrenal axis, which in turn, also stimulates the proliferation of sebaceous glands increasing lipid synthesis in adipose cells [8]. It was reported significantly reduced L-selectin and B2-integrin expressions on the surface of polymorphonuclear leukocytes in FMS patients. These adhesion molecules serve to destroy the infectious organisms removing toxic substances and debris from the body [34].

In the present study, according to the short form SF-36 test, which was used to evaluate the quality of life of patients with and without FMS, significantly lower values were detected in all scores of SF-36 in patients with FMS when compared to the control group. It was reported in previous studies that FMS causes functional disability affecting the quality of life of patients negatively [35,36]. In the present study, when the groups with and without skin findings were compared, significant differences were detected in the SF-36's Physical Function and Physical Role Difficulty scores. It was also found that there is only one study in the literature that investigated the relations between skin findings and quality of life. Although it was reported in various studies that SF-36 scores were lower in patients with FMS than in the control group, it was found that there was only one study that examined the relations between SF-36 and skin symptoms [37,38]. It was reported that there were no differences in SF-36 scores between patients with and without dermatological findings in FMS patients [14]. In our study, physical function and Physical Role Difficulty scores of SF-36 were significantly lower in the group with skin findings when compared to the group without skin findings. We believe that further studies are required on this subject.

There were some limitations in the study, which include the fact that the study had a cross-sectional design, it was conducted with a relatively small number of patients, and the medical treatment of the patients was not standardized.

As a conclusion, it is seen that the frequency of both skinrelated symptoms such as burning, sweating, numbness, and skin findings such as licken simplex chronicus is high in FMS patients. When the complex pathogenesis of fibromyalgia syndrome is considered, it can be argued that clinicians must approach more multidisciplinary approaches in the followups and treatments of such patients, consider that skin symptoms may also be detected in a detailed evaluation of a patient, and contact dermatologists if necessary.

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