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ORIGINAL ARTICLE

Cutaneous findings in fibromyalgia syndrome and their effect on quality of life

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ABSTRACT

Background/Objective: Fibromyalgia syndrome (FMS) is a chronic, generalized pain condition characterized with widespread soft-tissue pain, fatigue, sleep disturbances, and tender points on physical examination. Although, there are numerous articles about the frequency of FMS in dermatologic diseases such as psoriasis and chronic urticaria, few studies have been reported concerning skin findings in FMS. Our objective was to evaluate the skin findings and skin-related symptoms in FMS patients and determine the quality of life in FMS patients with dermatologic diseases.
Methods: A total 105 female patients ages between 18 years and 65 years and diagnosed with FMS were included in the study. A total of 105 healthy volunteers were age and sex matched in the control group.
Results: Skin related symptoms such as pruritus, burning, tingling, and increased sweating were more common in FMS patients than in the control group. Xerosis, dermographism, lichen simplex chronicus, neurotic excoriations, tinea pedis, and seborrheic dermatitis were more frequent in FMS patients and the differences were statistically significant. Presence of dermatologic disease or skin-related symptoms in FMS patients did not affect the quality life of the FMS patients.
Conclusion: Genetic and pathophysiological studies to clarify the relationship between FMS and dermatologic disorders will provide more information on the association and common treatment of these disorders.

Introduction

Fibromyalgia syndrome (FMS) is a chronic pain syndrome characterized by widespread pain, fatigue, sleep and cognitive function disorders.[1,2]

The disorder affects 2% of the population and is seven times more common in females.[3] A study from our country has reported the FMS incidence in women aged 20–65 years as 3.6%.[4]

The etiopathogenesis is not clear but abnormalities in the central pain mechanisms are thought to play a central role.[2] The role of peripheral nerves and neurogenic inflammation in FMS pathogenesis has also attracted interest recently.[5,6] FMS can also accompany many disorders with a common pathogenetic mechanism such as irritable bowel syndrome, chronic fatigue syndrome, anxiety, and depression.[7] Pathologic examination of FMS patients' skin has revealed various changes such as oxidative stress and increased numbers of cytokines and mast cells.[8–10]

Although there are studies that have investigated the FMS incidence in dermatologic disorders such as psoriasis,[11] chronic urticarial,[12–15] and Behçet's disease,[16,17] there are only a few studies on skin findings in FMS patients.[18,19] The aim of our study was to determine the possible accompanying skin findings in FMS patients, the incidence of cutaneous symptoms, and the quality of life in FMS patients with dermatological disease.

Conflicts of interest: The authors declare that they have no financial or non-financial conflicts of interest related to the subject matter or materials discussed in this article.

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Methods

The study included a total of 105 female patients aged 18–65 years who had been diagnosed with FMS by a Physical Therapy and Rehabilitation specialist using the 2010 American College of Rheumatology (ACR) FMS diagnostic criteria at the Physical Therapy and Rehabilitation Department of our hospital. The new diagnostic criteria specified by the ACR in 2010 do not include tender points examination, require exclusion of other causes of pain, include symptoms other than pain, and evaluate the symptom severity.[20] The control group consisted of 105 age-matched female patients with no systemic and rheumatoid disorder who had presented to the Ophthalmology Department of our hospital. Patients with congestive heart failure, pulmonary failure, coronary heart disease, neurological disorder, inflammatory rheumatologic disease, hypothyroidism, hyperparathyroidism, diabetes mellitus, those who had started psychotropic or antihistaminic treatment within the past month, and pregnant or breastfeeding patients were excluded.

We obtained Erciyes University Ethics Committee (Kayseri/Turkey) approval and written patient consent stating that they had been informed about the study. The sociodemographic features, cutaneous symptoms such as pruritus, burning, increased sweating, numbing and tingling; personal history, and the family history of FMS were queried. A detailed dermatologic examination was performed by a dermatologist. The quality of life scale short form-36 (SF-36) was administered to the FMS patients.

SPSS version 22.0 package software (SPSS Inc., Chicago, IL, USA) was used to analyze the data. We used the Kolmogorov Smirnov test to evaluate the distribution of the variables. The Mann–Whitney *U* test and the independent samples t test were used for the analysis of quantitative data. The Chi-square test was used for qualitative data and the Fischer's test was used when the Chi-square test conditions were not met. A p value < 0.05 was considered statistically significant.

Results

The mean age was 45.5 ± 8.7 years in the study group and 46.6 ± 9.7 years in the control group. There was no significant difference between the patient and control groups regarding age, occupation, marital status, accompanying disorder, smoking, and alcohol use. Stress ($p = 0.019$), accompanying psychiatric disorder ($p = 0.009$), and family history of FMS ($p < 0.001$) were significantly more common in the patient group (Table 1).

The percentage of at least one cutaneous symptom was 92.4% in FMS patients and 42.9% in the control group ($p < 0.001$). The rates of other cutaneous symptoms such as pruritus at 69.5% ($p < 0.001$), burning at 49.5% ($p < 0.001$), hyperhidrosis at 67.6% ($p < 0.001$), and numbness and tingling at 34.3% were more common in the FMS group than in the control group ($p < 0.001$; Table 2).

At least one dermatologic disorder was found in 78.1% of FMS patients and in 46.7% of the control group. This difference was statistically significant ($p < 0.001$). The most common dermatologic disorders in the FMS patients were xerosis (44.7%), lichen simplex chronicus (15.2%), acne (10.4%), contact dermatitis (8.5%), neurotic excoriation (6.6%), tinea pedis (6.6%), melasma (4.7%), and seborrheic dermatitis (3.8%). Dermographism was present in 30.5% of the FMS patients and 8% of the control group ($p < 0.001$; Table 3).

Comparison of common disorders between the two groups showed that xerosis ($p = 0.002$), lichen simplex chronicus ($p = 0.011$), neurotic excoriation ($p = 0.031$), tinea pedis ($p = 0.007$), and seborrheic dermatitis ($p = 0.043$) were more common in the FMS group than the control group (Table 3).

We found that the presence of a dermatologic disorder or cutaneous symptoms in FMS patients did not create a significant difference in the SF-36 physical function, physical role, pain, general health, vitality, social function, emotional role, and mental health scores.

Discussion

FMS is frequently accompanied by some medical, organic, and psychiatric disorders and this concurrence has been named the "central sensitization syndrome".[7] Some disorders that can accompany FMS are obsessive-compulsive disorder, major depression, dysthymia, panic disorder, generalized anxiety disorder, irritable bowel syndrome, migraine, and temporomandibular joint disorders.[21–24] We found a statistically significantly higher percentage of stress and accompanying psychiatric disorder in FMS

Table 2 Comparison of cutaneous symptoms between FMS and control groups.[a]

	FMS group	Control group	p
Cutaneous symptom	97 (92.4)	45 (42.9)	<0.001
Pruritus	73 (69.5)	26 (24.8)	<0.001
Burning	52 (49.5)	6 (5.7)	<0.001
Hyperhidrosis	71 (67.6)	35 (33.3)	<0.001
Others	36 (34.3)	0 (0)	<0.001

Data are presented as *n* (%).
[a] Mann–Whitney *U* test.

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

		FMS group	Control group	p
Age (y)		45.5 ± 8.7/45.0	46.6 ± 9.7/48.0	0.381
Occupation	Working	14 (13.3)	13 (12.4)	0.837
	House-wife	91 (86.7)	92 (87.6)	
Marital status	Single	5 (4.8)	9 (8.6)	0.268
	Married	100 (95.2)	96 (91.4)	
Family history of FMS		25 (23.8)	0 (0)	<0.001
Stress		25 (23.8)	12 (11.4)	0.019
Smoking		22 (21.0)	21 (20.0)	0.864
Alcohol usage		1 (1.0)	1 (1.0)	1.000
Accompanying disorder[b]		74 (70.5)	65 (61.9)	0.189
Accompanying psychiatric disorder[c]	Present	18 (17)	6 (6)	0.009
	Absent	87 (83)	99 (94)	

Data are presented as *n* (%) or mean ± standard deviation/median.
[a] Independent samples *t* test/Chi-square test
[b] Accompanying disorders were asthma, hypertension, anemia, hepatosteatosis, coronary artery disease, heart valve disease, gastroesophageal reflux, nephrolithiasis, and cyst hydatid
[c] Accompanying psychiatric disorders were depression, panic attack, and panic disorder.

Table 3 Comparison of dermatologic diseases between FMS and control groups.[a]

Dermatologic diseases	FMS group	Control group	*p*
At least one dermatologic disease	82 (78.1)	49 (46.7)	<0.001
Xerosis	47 (45)	26 (25)	0.002
Lichen simplex chronicus	16 (15)	5 (5)	0.011
Acne	11 (10)	6 (6)	0.206
Contact dermatitis	9 (9)	5 (5)	0.268
Neurotic excoriation	7 (7)	1 (1)	0.031
Tinea pedis	7 (7)	0 (0)	0.007
Melasma	5 (5)	1 (1)	0.098
Seborrheic dermatitis	4 (4)	0 (0)	0.043
Onychomycosis	4 (4)	1 (1)	0.174
Acrochordon	4 (4)	1 (1)	0.174
Urticaria	3 (3)	1 (1)	0.313
Rosacea	2 (2)	0 (0)	0.498
Verruca vulgaris	2 (2)	0 (0)	0.498
Brachioradial pruritus	1 (1)	0 (0)	1
Telogen effluvium	1 (1)	0 (0)	1
Vitiligo	1 (1)	2 (2)	1
Onychophagia	1 (1)	0 (0)	1
Psoriasis	0 (0)	2 (2)	0.498

Data are presented as *n* (%).
[a] Chi-square test (Fischer's exact test).

patients in our study. Anxiety, depression, and FMS have common pathogenetic mechanisms such as neurochemical dysfunction, serotonergic system hypofunction, and changes in hypothalamic-pituitary-adrenal axis activity.[24] The presence of stress and accompanying disorders in our study could be an indicator of these common pathogenetic mechanisms.

We found at least one cutaneous symptom such as pruritus, increased sweating, numbness, and tingling in 92.4% of the FMS patients in our study. Pathologic investigations of skin from FMS patients in other studies have revealed changes such as increased mast cells, mitochondrial dysfunction, coenzyme Q10 deficiency, increased oxidative stress, increased expression of δ and κ opiate receptors, increased interleukin (IL)-1β, IL-6, and tumor necrosis factor-α, microcirculation abnormalities at tender points, vasoconstriction, hypoxia and hypothermia, intradermal immunoglobulin G deposits, and increased Type 3 collagen reactivity.[5,6,8–10,21,25,26] Mitochondrial dysfunction, increased oxidative stress, and inflammation interdependently cause peripheral nerve damage and this is associated with the pain and allodynia seen in FMS.[26] Evaluation of the serum cytokine levels of the patients has revealed increased IL-6, IL-8, and IL-1 receptor antagonist and decreased T helper 2 cytokines.[27–29]

There is a complicated relationship between pain and pruritus. We found pruritus as a symptom in 69.5% of the FMS patients in our study. There are various similar mechanisms to explain the relationship between chronic pain and chronic pruritus such as peripheral and central sensitization, loss of inhibition in the spinal cord, and neuroimmune and neuroglial interactions. In the physiological conditions, itch and pain are encoded by labeled lines. But in pathological conditions, the crosstalk of the pain and itch labeled lines are disrupted. Pruritus and pain have both an antagonistic relationship and similar sensitization processes.[30,31] The high rate of pruritus in our study may support the presence of this common mechanism and common pathways.

Laniosz et al[19] retrospectively evaluated 845 FMS patients in their study on cutaneous symptoms and dermatologic disorders in FMS patients. They found hyperhidrosis (32%), skin and mucosal burning sensation (3.4%), various unusual cutaneous sensations (1.7%), pruritus of unknown origin (3.3%), neurotic excoriation, prurigo nodularis, lichen simplex chronicus (1.9%), and eczema other than lichen simplex chronicus (9.1%). They stated that FMS-related cutaneous problems can be present in FMS patients but there was no markedly increased dermatologic diagnosis other than a subjective increase in sweating.[19]

When accompanied dermatologic disorders are considered, psychocutaneous diseases concept should not be ignored. Psychiatric and dermatologic disorders are closely related and are evaluated within the dermatology practice as psychocutaneous disorders. The skin and brain originate from the ectoderm and are affected by the same hormones and neurotransmitters. The neuropeptides secreted from skin cells regulate the local neuroimmune reactions in the skin as a response to the stress. Neurogenic inflammation develops as a result of associated events and intercellular interactions.[24,32] Doğramacı and Yalcinkaya[18] found the incidence of xerosis and neurotic excoriation in FMS patients to be significantly higher than in the control group and concluded that some stress-induced dermatologic problems could be seen commonly in FMS patients. We also found incidences of 15.2% and 6.6%, respectively, for lichen simplex chronicus and neurotic excoriation, both psychocutaneous disorders. Any stressor can trigger skin findings while also causing FMS. Another possibility is that this relationship may not just be due to stress and that a certain type of personality predisposed to FMS, lichen simplex chronicus or neurotic excoriation may provide a suitable background for all three disorders. However, this is only speculation for now as there is no study supporting it.

In our study, we found that seborrheic dermatitis was more common in the FMS group. Also we found a higher percentage of stress in FMS patients. Stress is a well-known trigger of seborrheic dermatitis. So the higher percentage of seborrheic dermatitis in FMS patients can be explained by stress.

The third most common disorder in FMS patients was acne with an incidence of 10.4% while the control group had an incidence of 6%. Although, the number of patients with acne in the test group was more than in the control, the statistical difference between the two groups was not significant. Therefore, it may not indicate a meaningful coexistence of the two disorders, acne and FMS. By contrast, stress induces the hypothalamic-pituitary-adrenal axis and substance P, which also plays a role in FMS pathogenesis and is secreted from peripheral nerves, has recently been shown to stimulate sebaceous gland proliferation and increase lipid synthesis in the sebaceous cells.[24] A stress-related indirect relationship between FMS and acne is likely, but this needs to be clarified with other studies.

There are several studies on the link between allergic disorders and FMS in current literature. Tuncer et al[33] found higher rates of allergic disorders such as allergic rhinitis, atopic dermatitis, asthma, allergic conjunctivitis, and eruptions related to drugs and food in FMS patients. We found no increase in allergic disorders in FMS patients in our study. The role of mast cells in FMS pathogenesis is still not clear although increased numbers of mast cells have been shown in FMS patients and the concurrence of chronic urticaria and FMS has been reported.[6,8,12–15]

FMS has been reported at rates of 9.7%,[15] 23%,[13] 26%,[12] and 70.6%[14] in chronic urticaria patients. It has been speculated that the neuropeptides secreted from the dysfunctional nerve endings could cause vasodilation, plasma extravasation, and mast cell degranulation in the dermal vessels. It is suggested that the reason for the high FMS rate in chronic urticaria patients in these studies could be related to neurogenic inflammation and autoimmunity. The urticaria incidence was 3% in FMS patients and 1% in the control group while dermographism was positive at a rate of 30.5% in FMS patients and 8% in the control group. The low incidence of chronic urticaria in FMS patients despite the high rate of dermographism suggests that there is an increase in the number of mast cells but this is not reflected in the clinical findings. A study by Ang et al[34] on the effect of the mast cell stabilizer ketotifen on FMS symptoms has

shown no statistically significant difference between placebo and ketotifen (4 mg/d). We believe further clinicopathological studies are needed to clarify the relationship between FMS and urticaria or allergic disorders.

The FMS syndrome is known to cause functional disability and have a negative effect on the patient's quality of life.[35–37] Salaffi et al[37] found that the SF-36 physical component is related to widespread pain, educational level, and body mass index while the mental component is associated with widespread pain, sleep abnormalities, fatigue, age, and low educational level in FMS patients.

While we expected to find that the presence of a dermatologic disorder and cutaneous symptoms in FMS patients would create a significant change in the SF-36 scores, in the current study it did not. This result as similar to the findings of a study carried out by Doğramacı and Yalcinkaya.[18] These results indicate that widespread and chronic pain, sleep abnormalities, and chronic fatigue affect the quality of life in FMS patients more than the accompanying dermatologic problems.

In conclusion, some dermatologic problems such as xerosis, dermographism, lichen simplex chronicus, and neurotic excoriation are seen frequently in FMS patients. The higher incidence of some dermatologic disorders and cutaneous symptoms in FMS patients may be due to the common genetic basis and pathophysiological mechanisms instead of being a coincidence. We think that genetic and pathophysiological studies to clarify the relationship between FMS and dermatologic disorders will provide more information on the association and common treatment of these disorders. We also believe FMS needs a multidisciplinary approach with the participation of the dermatology and psychiatry departments as well as physical therapy and rehabilitation for optimal management of FMS patients.

References

1. Hawkins RA. Fibromyalgia: a clinical update. *J Am Osteopath Assoc* 2013;**113**:680–9.
2. Buskila D. Developments in the scientific and clinical understanding of fibromyalgia. *Arthritis Res Ther* 2009;**242**:1–8.
3. Lawrence RC, Felson T, Helmick CG, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. *Arthritis Rheum* 2008;**58**:26–35.
4. Topbas M, Cakirbay H, Gulec H, et al. The prevalance of fibromyalgia in women aged 20-64 in Turkey. *Scand J Rheumatol* 2005;**34**:140–4.
5. Kim DH, Oh DH, Clauw DJ. Characteristic electron microscopic findings in the skin of patients with fibromyalgia–preliminary study. *Clin Rheumatol* 2008;**27**:407–11.
6. Enestrom S, Bengtsson A, Frodin T. Dermal IgG deposits and increase of mast cells in patients with fibromyalgia-relevant findings or epiphenomena? *Scand J Rheumatol* 1997;**26**:308–13.
7. Yunus MB. Fibromyalgia and overlapping disorders: the unifying concept of central sensitivity syndromes. *Semin Arthritis Rheum* 2007;**36**:339–56.
8. Blanco I, Beritze N, Arguelles M, et al. Abnormal overexpression of mastocytes in skin biopsies of fibromyalgia patients. *Clin Rheumatol* 2010;**29**:1403–12.
9. Cordero MD, Moreno-Fernandez AM, Carmona-Lopez MI, et al. Mitochondrial dysfunction in skin biopsies and blood mononuclear cells from two cases of fibromyalgia patients. *Clin Biochem* 2010;**43**:1174–6.
10. Salemi S, Rethage J, Wollina U, et al. Detection of interleukin 1beta (IL-1beta), IL-6, and tumor necrosis factor-alpha in skin of patients with fibromyalgia. *J Rheumatol* 2003;**30**:146–50.
11. Thune PO. The prevalence of fibromyalgia among psoriasis patients. *Acta Derm Venereol* 2005;**85**:33–7.
12. Hapa A, Özdemir O, Evans SE, et al. Evaluation of the frequency of fibromyalgia in patients with chronic urticaria. *Turkderm* 2012;**46**:202–5.
13. Gözübüyükoğulları A, Onan DT, Allı N. Fibromyalgia syndrome in chronic urticaria patients. *Turkderm* 2014;**48**:215–8.
14. Torresani C, Bellafiore S, De Panfilis G. Chronic urticaria is usually associated with fibromyalgia syndrome. *Acta Derm Venereol* 2009;**89**:389–92.
15. Yener M, Erturan I, Ceyhan AM, et al. The evaluation of the prevalence of fibromyalgia in patients with chronic urticaria. *Med Sci Monit* 2013;**19**:757–61.
16. Melikoglu M, Melikoglu MA. The prevalence of fibromyalgia in patients with Behçet's disease and its relation with disease activity. *Rheumatol Int* 2013;**33**:1219–22.
17. Lee SS, Yoon HJ, Chang HK, et al. Fibromyalgia in Behçet's disease is associated with anxiety and depression, and not with disease activity. *Clin Exp Rheumatol* 2005;**23**:15–9.
18. Doğramacı AÇ, Yalcinkaya EY. Skin problems in fibromyalgia. *Nobel Medicus J* 2009;**5**:50–2.
19. Laniosz V, Wetter DA, Godar DA. Dermatologic manifestations of fibromyalgia. *Clin Rheumatol* 2014;**33**:1009–13.
20. Wolfe F, Clauw DJ, Fitzcharles MA, et al. The American College of Rheumatology preliminary diagnostic criteria for fibromyalgia and measurement of symptom severity. *Arthritis Care Res* 2010;**62**:600–10.
21. Jeschonneck M, Grohmann G, Hein G, et al. Abnormal microcirculation and temperature in skin above tender points in patients with fibromyalgia. *Rheumatology (Oxford)* 2000;**39**:917–21.
22. González E, Elorza J, Failde I. Fibromyalgia and psychiatric comorbidity: their effect on the quality of life patients. *Actas Esp Psiquiatr* 2010;**38**:295–300.
23. Bernik M, Sampaio TP, Gandarela L. Fibromyalgia comorbid with anxiety disorders and depression: combined medical and psychological treatment. *Curr Pain Headache Rep* 2013;**17**:358.
24. Altunay İK. Psychoneuroimmunology and Multifactorial Psychodermatological Diseases. *Turkderm* 2010;**44**:10–5.
25. Salemi S, Aeschlimann A, Wollina U, et al. Upregulation of delta-opioid receptors and kappaopioid receptors in the skin of fibromyalgia patients. *Arthritis Rheum* 2007;**56**:2464–6.
26. Sánchez-Domínguez B, Bullón P, Román-Malo L, et al. Oxidative stress, mitochondrial dysfunction and, inflammation common events in skin of patients with Fibromyalgia. *Mitochondrion* 2015;**21**:69–75.
27. Rodriguez-Pintó I, Agmon-Levin N, Howard A, et al. Fibromyalgia and cytokines. *Immunol Lett* 2014;**161**:200–3.
28. Uçeyler N, Häuser W, Sommer C. Systematic review with meta-analysis: cytokines in fibromyalgia syndrome. *BMC Musculoskelet Disord* 2011;**12**:245.
29. Sturgill J, McGee E, Menzies V. Unique cytokine signature in the plasma of patients with fibromyalgia. *J Immunol Res* 2014;**2014**:938576.
30. Liu T, Ji RR. New insights into the mechanisms of itch: are pain and itch controlled by distinct mechanisms? *Pflugers Arch* 2013;**465**:1671–85.
31. Ständer S, Schmelz M. Chronic itch and pain-similarities and differences. *Eur J Pain* 2006;**10**:473–8.
32. Mercan S, Kivanc Altunay I. Psychodermatology: a collaboration between psychiatry and dermatology. *Turk Psikiyatri Derg* 2006;**17**:305–13.
33. Tuncer T, Bütün B, Arman M, et al. Primary fibromyalgia and allergy. *Clin Rheumatol* 1997;**16**:9–12.
34. Ang DC, Hilligoss J, Stump T. Mast cell stabilizer (Ketotifen) in fibromyalgia: Phase 1 randomized controlled clinical trial. *Clin J Pain* 2014 [Epub ahead of print].
35. Turkyilmaz AK, Kurt EE, Karkucak M, et al. Sociodemographic Characteristics, Clinical Signs and Quality of Life in Patients with Fibromyalgia. *EAJM* 2012;**44**:88–93.
36. Campos RP, Vázquez Rodríguez MI. Health-related quality of life in women with fibromyalgia: clinical and psychological factors associated. *Clin Rheumatol* 2012;**31**:347–55.
37. Salaffi F, Sarzi-Puttini P, Girolimetti R, et al. Health-related quality of life in fibromyalgia patients: a comparison with rheumatoid arthritis patients and the general population using the SF-36 health survey. *Clin Exp Rheumatol* 2009;**27**:67–74.