Ayhan Aşkın, Ayten Özkan*, Seciye Eda Bıyıklı, Aliye Tosun**

Could There Be a Possible Link Between Vitiligo and Fibromyalgia Syndrome?

Vitiligo ve Fibromiyalji Sendromu Arasında Muhtemel Bir Bağlantı Olabilir mi?

Abstract

Objective: In this study, it was aimed to determine the frequency of Fibromyalgia syndrome (FMS) in vitiligo patients and to evaluate its relation with clinical parameters.
Methods: Thirty-five generalized vitiligo patients and 45 sex- and age-matched healthy controls were included in the study. Participant's demographic and clinical characteristics were determined. All participants were questioned in detail from the point of symptoms and signs of FMS. Clinical and functional evaluations were performed with Fibromyalgia Impact Questionnaire (FIQ), Vitiligo Area Scoring Index (VASI), Pittsburgh Sleep Quality Index (PSQI), visual analogue scale and hospital anxiety and depression scales (HADS).
Results: Vitiligo patients' fatigue, depression, anxiety and sleep quality scores were significantly higher ($p<0.05$). The frequency of FMS was significantly high in patients with vitiligo than in controls (34.3% vs 11.1%, $p=0.015$). The vitiligo patients with FMS had higher pain, fatigue, stiffness, FIQ, VASI, HADS and PSQI scores ($p<0.05$). Significant correlations were obtained between vitiligo severity and clinical parameters. FIQ, VASI, HADS and PSQI scores were detected as an important indicator which a sign of the presence of FMS in vitiligo patients.
Conclusion: This study revealed that the frequency of FMS was significantly higher in patients with vitiligo. While the presence of FMS deteriorates the psychological state and sleep quality in vitiligo patients, it also exacerbates the severity of the disease. Therefore, clinicians should be aware of the FMS, which can worsen the clinical and functional status on vitiligo patients.

Keywords: Vitiligo, fibromyalgia, pain, depression, anxiety, sleep quality

Öz

Amaç: Bu çalışmada vitiligo hastalarında Fibromiyalji sendromu (FMS) sıklığını belirlemek ve klinik parametreler ile ilişkisini değerlendirmek amaçlanmıştır.
Yöntemler: Çalışmaya 35 jeneralize vitiligo hastası ve 45 yaş-cinsiyet uyumlu sağlıklı kontrol alınmıştır. Katılımcıların demografik ve klinik karakteristikleri belirlenmiştir. Tüm katılımcılar FMS'nin semptom ve belirtileri yönünden ayrıntılı olarak sorgulanmıştır. Klinik ve fonksiyonel değerlendirmeler Fibromiyalji Etki Anketi (FIQ), Vitiligo Alan Skorlama İndeksi (VASI), Pittsburg Uyku Kalitesi İndeksi (PSQI), görsel analog skala ve hastane anksiyete ve depresyon skalası (HADS) ile yapılmıştır.
Bulgular: Vitiligo hastalarının yorgunluk, depresyon-anksiyete ve uyku skorları anlamlı olarak daha yüksekti ($p<0,05$). FMS sıklığı vitiligo hastalarında kontrollere göre anlamlı yüksekti (%34,3 vs %11,1, $p=0,015$). FMS'li vitiligo hastaları daha yüksek ağrı, yorgunluk, tutukluk, FIQ, VASI, HADS ve PSQI skorlarına sahipti ($p<0,05$). Vitiligo şiddeti ile klinik parametreler arasında anlamlı kolerasyon vardı. FIQ, VASI, HADS ve PSQI skorları, vitiligo hastalarında FMS varlığını işaret eden önemli belirteçler olarak saptandı.
Sonuç: Bu çalışmada vitiligo hastalarında FMS sıklığı anlamlı olarak yüksek bulunmuştur. Ayrıca, FMS varlığı vitiligo hastalarında psikolojik durum ve uyku kalitesini bozduğu gibi ek olarak hastalığın şiddetini de kötüleştirmektedir. Bu nedenle, klinisyenler vitiligo hastalarının klinik ve fonksiyonel durumunu kötüleştirebilen FMS'nin farkında olmalıdırlar.

Anahtar kelimeler: Vitiligo, fibromiyalji, ağrı, depresyon, anksiyete, uyku kalitesi

Katip Çelebi University Faculty of Medicine, Department of Physical Medicine and Rehabilitation, İzmir, Turkey

*Selçuk State Hospital, Clinic of Physical Medicine and Rehabilitation, İzmir, Turkey

**Selçuk State Hospital, Clinic of Dermatology, İzmir, Turkey

Correspondence/ Yazışma Adresi:
Ayhan Aşkın,
Katip Çelebi University Faculty of Medicine, Department of Physical Medicine and Rehabilitation, İzmir, Turkey
E-mail: ayhanaskin@hotmail.com
ORCID ID: orcid.org/0000-0001-9445-4430
Submitted/Geliş Tarihi: 31.01.2018
Accepted/Kabul Tarihi: 19.03.2018

Introduction

Vitiligo is a chronic depigmenting disease of the skin resulting from destruction of melanocytes (1). The prevalece of the disease is about 1% in the United States and in European countries. Both women and men are affected equally, but women often apply for treatment more frequently due to cosmetic problems and negatory social outlook (2). Although the underlying pathophysiologic causes of vitiligo is still unclear, several factors have been suggested to contribute to the pathophysiology of vitiligo, including genetic, neuronal, autocytotoxic, biochemical, oxidative and autoimmune factors. The autoimmune theory is the leading hypothesis for causation with strong evidence (3,4). The proinflammatory cytokines and other inflammatory factors (e.g., free radicals and reactive oxygen species) are present in vitiligo patients. Their systemic increase may be the result from an autoimmune process, as well as oxidative and cytotoxic activities. In addition, we also detect more autoimmune diseases (e.g., thyroid disorders, some rheumatological disease, diabetes mellitus and endocrinopathies, urticaria and atopic dermatitis, alopecia areata, lupus) in these patients (2,5). Likewise it has been suggested that there is a neuro-immune interactions with mental stress, neuropeptides, nerve growth factors and the onset or progression of vitiligo (6-8).

Skin is the widest, most notable and most visible part of our body and it carries great socio-psychological importance. Skin diseases can significantly affect the psychological well-being of the patients, which can lead to impaired social relations. Anxiety, depression, sleep disturbance, impairments in health related quality of life have been shown in vitiligo patients (9-11).

Fibromyalgia syndrome (FMS) is a chronic, common pain syndrome associated with fatigue, non-restorative sleep, cognitive and mood problems. The prevalence of FMS is higher in women (12) and true pathophysiology of this disease is still unknown. Increased evidence supports the problem of central nervous system nociceptive processing and stress changes. However, more recently studies have begun exploring the role of peripheral factors and neurogenic inflammation in the formation of pain (13-15). FMS is not classically thought to be a disease with related cutaneous findings, but several studies have showed that patients with FMS have increased inflammatory cytokines in the skin. They also have dysfunction of nervous system (autonomic) and increased cutaneous opioid receptors levels (16). FMS accompanies with some other conditions which share similar underlying pathophysiologies such as irritable bowel syndrome, cystitis and tension headache; or seen as a comorbidity in patients with autoimmune disorders, rheumatologic diseases, osteoarthritis and some psychiatric conditions (12,17).

FMS and vitiligo have several similar features (e.g., similarity of pathophysiologic causes, comorbid conditions, association with psychiatric disorders, sleeping problems), but to our knowledge there is no study in English literature that investigated the relationship between FMS and vitiligo. Therefore, in this study we aimed to determine the frequency of FMS in patients with vitiligo and its relationship with clinical parameters.

Methods

Participants

Thirty-seven patients with generalized vitiligo and 45 sex- and age-matched healthy controls were enrolled in this study. Subjects with the history of any systemic disease including musculoskeletal, oncological, neurological, autoimmune-inflammatory, endocrine, psychiatric or the other clinically significant chronic diseases and under treatment due to vitiligo were excluded from the study. Demographical characteristics, pain, fatigue and stiffness values of the participants and disease durations of the patients were recorded. Information was given about the study and provided written informed consent from participants. The study was approved by the Katip Çelebi University Local Ethical Committee (approval number: 04.10.2017/213). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Clinical and Functional Evaluations

All patients with vitiligo and controls were questioned and examined in detail to search for symptoms and signs of FMS. American College of Rheumatology (ACR) 2010 criteria were used to determine the presence of FMS (18). Functional health status of the participants was assessed with the Fibromyalgia Impact Questionnaire (FIQ), which measures 10 different features (physical functioning, missed days of work, depression, anxiety, feeling good, morning tiredness, pain, stiffness, fatigue, and well-being over the past week) (19).

Vitiligo Area Scoring Index (VASI) was used to assessed the degree of depigmentation and vitiligo severity. In this outcome measure, the patient's body is divided into five separate regions: the hands, upper extremities, trunk, lower extremities and the feet. The percentage of vitiligo involvement for each body region is calculated by using the palmar method. Each site is clinically evaluated by visual assessment for the pattern of skin depigmentation using a visual scale. The VASI is then derived by multiplying the values assessed for the vitiligo involvement by the percentage of affected skin (20).

Sleep quality was calculated with the Pittsburgh Sleep Quality Index (PSQI) (21). PSQI is a 19-item, self-rated measure assessing sleep quality and disturbance during the past month. The scale consists of seven subscales [subjective sleep quality, sleep latency (i.e., how long it takes to fall asleep), sleep duration, sleep efficiency (i.e., the percentage of time in bed that one is asleep), sleep disturbances, use of sleeping medication, and daytime dysfunction]. A total PSQI score greater than five indicates a lower sleep quality. Lower scores show a healthier sleep quality (21).

The symptoms of depression and anxiety were assessed by the hospital anxiety and depression scale (HADS). It consists of 14 items divided into two subscales of seven items each. Each subscale ranges in value from 0-21 for either depression or anxiety (22).

The severity of the pain, fatigue and stiffness (during the last 7 days) were assessed by a 10 cm visual analogue scale (VAS).

Statistical Analysis

All statistical analyses were performed by using SPSS 16.0 (IBM Corporation, Armonk, New York, United States) and MedCalc 14 (Acacialaan 22, B-8400 Ostend, Belgium) softwares. Normal distribution of the data was studied by Kolmogorov-Smirnov test and the homogeneity of variance tested using Levene's test of equality of variances. Independent sample t test or Mann-Whitney U (exact) test were used to compare independent two groups quantitative data samples. Pearson correlation, Kendall's tau-b or Spearman's rho tests were performed to determine the relations of clinical variables. Pearson chi-square or Fisher exact tests were used to assess differences in categorical variables. Odds ratio was used to determine the most important risk factors of the categorical significant risk factors. Sensitivity, specificity values aimed at detecting the diagnostic value of clinical parameters were calculated using receiver operating characteristic (ROC) analysis. Categorical variables were defined as number and percentage. Numeric data are expressed as mean ± SD and median (min-max). The variables examined in the 95% confidence level and p values less than 0.05 were considered significant.

Results

Two patients with vitiligo were excluded because of the histories of Hashimoto's thyroiditis. A total of 35 patients with generalized vitiligo and 45 sex- and age-matched healthy controls completed the study. The groups were comparable in respect to age, gender, educational status, marital status and body mass index (BMI). Mean disease duration was 117.4±99.9 months and mean VASI score was 4.46±3.13 in vitiligo patients. Patients with vitiligo had significantly higher fatigue, HAD-depression, HAD-anxiety and PSQI scores (all $p<0.05$), and higher frequency of FMS than controls (34.3% vs 11.1%, $p=0.015$). Demographical and clinical features of the participants are shown in Table 1.

There was no difference regarding gender, BMI and duration of the disease between vitiligo patients with or without FMS ($p>0.05$). Vitiligo patients with FMS were significantly older than patients without FMS ($p<0.05$). The vitiligo patients with

Table 1. Demographic and clinical characteristics of the subjects

	Vitiligo patients (n=35)				Controls (n=45)				
	n	%	Mean ± SD	Median (min-max)	n	%	Mean ± SD	Median (min-max)	p value
Age (years)	-	-	44.23±13.19	-	-	-	46.60±12.04	-	0.415
Gender	-	-	-	-	-	-	-	-	0.999
Female	17	48.6	-	-	22	48.9	-	-	-
Male	18	51.4	-	-	23	51.1	-	-	-
BMI (kg/m^2)	-	-	26.17±4.85	-	-	-	24.56±2.82	-	0.104
Educational status	-	-	-	-	-	-	-	-	0.634
Primary school	11	31.4	-	-	15	33.3	-	-	-
High school	12	34.3	-	-	19	42.2	-	-	-
University	12	34.3	-	-	11	24.4	-	-	-
Marital status	-	-	-	-	-	-	-	-	0.111
Married	24	68.6	-	-	38	84.4	-	-	-
Single	11	31.4	-	-	7	15.6	-	-	-
Presence of FMS	12	34.3	-	-	5	11.1	-	-	**0.015**
Pain-VAS score	-	-	-	2 (0-9)	-	-	-	1 (0-9)	0.058
Fatigue	-	-	-	2 (0-10)	-	-	-	1 (0-10)	**0.033**
Stiffness	-	-	-	1 (0-6)	-	-	-	1 (0-7)	0.445
FIQ score	-	-	-	12 (1-58.34)	-	-	-	14.2 (1-62)	0.634
Duration of vitiligo (month)	-	-	117.4±99.9	-	-	-	-	-	-
VASI	-	-	4.46±3.13	-	-	-	-	-	-
HAD-depression	-	-	-	8 (0-17)	-	-	-	3 (0-12)	**0.001**
HAD-anxiety	-	-	-	11 (0-17)	-	-	-	3 (0-16)	**0.001**
PSQI	-	-	-	5 (1-13)	-	-	-	3 (1-9)	**0.008**

BMI: Body mass index, FMS: Fibromyalgia syndrome, VAS: Visual analog scale, FIQ: Fibromyalgia Impact Questionnaire, VASI: Vitiligo Area Scoring Index, HAD: Hospital anxiety and depression scale, PSQI: Pittsburgh Sleep Quality Index, SD: Standard deviation, Min: Minimum, Max: Maksimum

FMS had significantly higher scores in VAS (p<0.05), fatigue (p<0.05), stiffness (p<0.05), FIQ (p<0.05), VASI (p=0.001), HAD-depression (p=0.001), HAD-anxiety (p=0.001) and PSQI scores (p=0.008). Clinical characteristics of vitiligo patients with and without FMS are given in Table 2.

There was a significant correlation between vitiligo severity (VASI) and VAS pain score (r=0.429, p=0.010), fatigue score (r=0.511, p=0.002), stiffness score (r=0.525, p=0.001), FIQ score (r=0.487, p=0.003), HAD-depression score (r=0.377, p=0.026), HAD-anxiety score (r=0.340, p=0.046) and PSQI score (r=0.446, p=0.007). Correlation values between VASI and other clinical parameters in vitiligo patients are given in Table 3. We also demonstrated that FIQ, HAD-depression/anxiety scores, PSQI and VASI were accurate and significant predictors of the presence of FMS on the ROC curve (p<0.001). The cut-off value of VASI was 4.8, with a sensitivity of 75%, a specificity of 87% (Figure 1). The area under the curve and the best cut-off values of variables to predict the presence of FMS are given in Table 4.

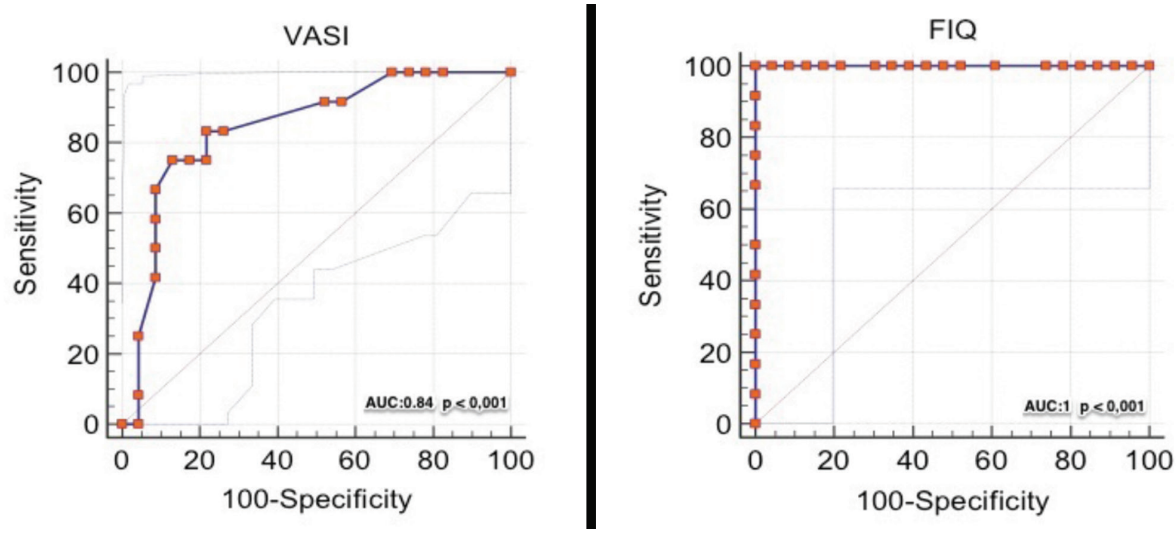

Figure 1. Receiver operating characteristic curve analysis of Vitiligo Area Scoring Index and Fibromyalgia Impact Questionnaire for the presence of Fibromyalgia syndrome

VASI: Vitiligo Area Scoring Index, FIQ: Fibromyalgia Impact Questionnaire

Table 2. Clinical characteristics of vitiligo patients with and without fibromyalgia syndrome

	Vitiligo patients without FMS (n=23)				Vitiligo patients with FMS (n=12)				
	n	%	Mean ± SD	Median (min-max)	n	%	Mean ± SD	Median (min-max)	p value
Age (years)	-	-	41.96±14.33	-	-	-	48.58±9.80	-	**0.016**
Gender	-	-	-	-	-	-	-	-	0.035
Female	8	34.8	-	-	9	75.0	-	-	-
Male	15	65.2	-	-	3	25.0	-	-	-
BMI (kg/m^2)	-	-	25.19±4.12	-	-	-	28.05±5.76	-	0.070
Pain-VAS score	-	-	-	1 (0-5)	-	-	-	7 (5-9)	**<0.001**
Fatigue	-	-	-	1 (0-6)	-	-	-	7 (5-10)	**<0.001**
Stiffness	-	-	-	0 (0-2)	-	-	-	4.5 (3-6)	**<0.001**
FIQ score	-	-	-	8 (1-20.36)	-	-	-	46 (35-58.3)	**<0.001**
Duration of vitiligo (month)	-	-	-	72 (12-360)	-	-	-	96 (12-360)	0.572
VASI	-	-	-	3 (1-12)	-	-	-	7.65 (2-10.5)	**0.001**
HAD-depression	-	-	-	5 (0-13)	-	-	-	10.5 (5-17)	**0.005**
HAD-anxiety	-	-	-	3 (0-16)	-	-	-	14 (5-17)	**0.001**
PSQI	-	-	-	3 (1-9)	-	-	-	7 (4-13)	**<0.001**

BMI: Body mass index, FMS: Fibromyalgia syndrome, VAS: Visual analog scale, FIQ: Fibromyalgia Impact Questionnaire, VASI: Vitiligo Area Scoring Index, HAD: Hospital anxiety and depression scale, PSQI: Pittsburgh Sleep Quality Index, SD: Standard deviation, Min: Minimum, Max: Maksimum

Discussion

Our results showed that the frequency of FMS was significantly higher in patients with vitiligo than in controls. In addition, we found higher scores in terms of pain, fatigue, stiffness, depression, anxiety, sleep quality and VASI in vitiligo patients with FMS, namely coincidence of FMS was worsening the clinical and functional outcomes of vitiligo. Furthermore, FIQ, HAD-depression/anxiety scores, PSQI and VASI were found to be significant predictors of the presence of FMS in patients with vitiligo.

Although etiology of vitiligo remains unclear, several hypotheses have been proposed in literature. The most up-to-date and most acceptable theory is the immune etiology. It is clear that vitiligo may be relevant with various autoimmune diseases. Gill et al. (5) recently revealed that 217 of 1098 patients with vitiligo had one other comorbid autoimmune disease and they found a higher prevalence of thyroid disease, pernicious anemia, alopecia areata, inflammatory bowel disease, lupus erythematosus in vitiligo patients. The authors also reported that older age, later onset age, and vitiligo duration may be a factor in the development of these comorbid autoimmune problems. Furthermore, the presence of high levels of autoantibodies against tyrosinase, activation of cell mediated immunity, autoreactive T lymphocytes, increase in tumor necrosis factor-α, interferon-γ and interleukin-10 were shown in vitiligo patients (4). Kemp et al. (23) have identified tyrosine hydroxylase as a B-cell autoantigen and antibodies in active vitiligo disease. Likewise, neuropeptides and skin have been the subject of various skin diseases, including vitiligo. Evidence is increasing regarding the role of neuropeptide Y, calcitonin gene-related peptide, nerve growth factor in vitiligo pathogenesis (6).

Table 3. Correlation values between Vitiligo Area Scoring Index and other clinical parameters in vitiligo patients

Correlations with r	VASI	p value
Pain-VAS score	0.429	**0.010**
Fatigue	0.511	**0.002**
Stiffness	0.525	**0.001**
FIQ score	0.487	**0.003**
HAD-depression	0.377	**0.026**
HAD-anxiety	0.340	**0.046**
PSQI	0.446	**0.007**
Duration of vitiligo (month)	0.029	0.868

r: Correlation coefficient, VAS: Visual analog scale, FIQ: Fibromyalgia Impact Questionnaire, VASI: Vitiligo Area Scoring Index, HAD: Hospital anxiety and depression scale, PSQI: Pittsburgh Sleep Quality Index

Although the relationship between autoimmune diseases and FMS is not well known; there are quite a few reports supporting this. Various studies demonstrated that FMS was accompanying autoimmune diseases like lupus and rheumatologic arthritic conditions. Higher cytokine levels were found in patients with FMS, suggesting that an immune process is involved in the pathogenesis (24). Another idea that supports the autoimmune process of FMS is the presence of autoantibodies. Klein and Berg (25) revealed that antibodies to 5-hydroxytryptamine, gangliosides and phospholipids have been found to be high in patients with FMS. Therefore, it can be assumed that neuropeptides may also be playing a role in etiopathogenesis of FMS. Torresani et al. (26) hypothesized that dysfunctional cutaneous nerve fibers of patients with FMS may release neuropeptides. These literature data show that both vitiligo and FMS share similar etiopathogenetic mechanisms (e.g., autoimmun theory, autoantibodies, cytokines, neuropeptides), however up to date no study had evaluated the potential association between vitiligo and FMS. Our study is the first study that evaluated the FMS frequency and its relationship with clinical and functional scales in patients with vitiligo.

Several studies have evaluated the prevalence of FMS in some other dermatologic diseases. Torresani et al. (26) revealed that

Table 4. Receiver operating characteristic curve analysis of the clinical parameters in vitiligo patients

		FMS				AUC ± SE	Odds ratio (95% CI)	p value
		Negative		Positive				
	Cut off	n	%	n	%			
FIQ	≤20.36	23	**100.0***	0	0.0	1±0	1175 (21.9-62857.4)	**<0.001**
	>20.36	0	0.0	12	**100.0****			
HAD-depression	≤7	15	**65.2***	1	8.3	0.786±0.077	20.6 (2.2-189.8)	**<0.001**
	>7	8	34.8	11	**91.7****			
HAD-anxiety	≤8	14	**60.9***	1	8.3	0.833±0.067	17.1 (1.9-156.2)	**<0.001**
	>8	9	39.1	11	**91.7****			
PSQI	≤5	18	**78.3***	2	16.7	0.875±0.057	18 (2.9-110.3)	**<0.001**
	>5	5	21.7	10	**83.3****			
VASI	≤4.8	20	**87.0***	3	25.0	0.844±0.072	20 (3.4-118.9)	**<0.001**
	>4.8	3	13.0	9	**75.0****			

FMS: Fibromyalgia syndrome, AUC: Area under the curve, SE: Standard error, CI: Confidence interval, FIQ: Fibromyalgia Impact Questionnaire, HAD: Hospital anxiety and depression scale, PSQI: Pittsburgh Sleep Quality Index, VASI: Vitiligo Area Scoring Index
*Specificity, **Sensitivity

almost 70% of chronic urticaria patients get diagnosed with FMS and this relationship can be seen as a kind of neuropathic skin inflammation. Yener at al. (27) suggested that FMS slightly, but not significantly, more frequent in patients with chronic urticaria and severity of disease was also correlated with duration of FMS symptoms, number of the tender point, FIQ and VAS scores. In contrast to these studies Hapa et al. (28) revealed that the frequency of FMS in chronic urticaria was not increased and they could not find any association with urticaria severity, duration and serum skin test. Yazmalar et al. (29) also determined that FMS was high frequency (21.6%) in patients with acne vulgaris and Thune (30) found 8% of patients with psoriasis that four times higher than normal frequency of 2%. In our study, we determined that FMS was significantly higher in vitiligo patients than controls (34.3% vs 11.1%). Pain, fatigue stiffness, FIQ, VASI, HADS and PSQI scores were also found to be significant predictors of the concomitant FMS in vitiligo patients.

Skin disease is often recognized by other people and can cause psychological distress in patients suffering from these dermatological diseases. On the other hand, it is known that psychological distress can result in elevated levels of neuropeptides and cytokines that can exacerbate existing skin disease (6). There are numerous reports showing that vitiligo has negative psychological effects. Mattoo et al. (31) found that 25% of vitiligo patients were found to have psychiatric morbidity and they concluded that psychiatric morbidity is significantly related to disease-induced dysfunction. Sangma et al. (32) have shown that the quality of life in vitiligo patients decreased and the incidence of depression increased. Noh et al. (33) found that patients with vitiligo experienced more severe anxiety. Ramakrishna and Rajni (34) also found that lesions were strongly associated with high incidence of major depressive disorder, high incidence of social phobia, lower quality of life, and lower self-esteem. Sharma et al. (10) determined that the prevalence of depression was 10% and sleep disturbance was present in 20% of the vitiligo patient group. Karelson et al. (35) found 30% of their vitiligo patients had sleep disturbances. In our study we found that depression and anxiety incidences were higher and sleep quality was poorer in vitiligo patients than in controls. The presence of FMS is found to be a further worsening factor of the psychological status and sleep qualities of the patients. Moreover, severity of the vitiligo is also found to be increased with accompanying FMS.

Study Limitations

There are limitations of our study. First, relatively a small number of patients were included. Further studies with larger sample sizes will yield more reliable results. Second is the lack of specific measurement techniques of other variables such as vitiligo specific stressors or quality of life. Third, we did not use a standardized interview for assessing psychiatric diseases in order to exclude comorbid disorders.

Conclusion

This study revealed that the frequency of FMS was significantly higher in patients with vitiligo. Moreover, the presence of FMS was not only associated with worsening in psychological status and sleep qualities of the vitiligo patients, but also with increased severity of the disease itself. Therefore, clinicians should be aware of FMS as concomitant disease which worsens the clinical and functional outcomes in patients with vitiligo. There is a need for further studies with larger samples to explain the link between FMS and vitiligo.

Ethics

Ethics Committee Approval: The study was approved by the Katip Çelebi University Local Ethical Committee (approval number: 04.10.2017/213).

Informed Consent: A consent form was completed by all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.A., A.T., Concept: A.A., Design: A.A., A.T., Data Collection or Processing: A.Ö., S.E.B., Analysis or Interpretation: A.T., Literature Search: A.Ö., S.E.B., Writing: A.A.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

References

1. Ezzedine K, Eleftheriadou V, Whitton M, et al. Vitiligo. Lancet 2015;386:74-84.
2. Alikhan A, Felsten LM, Daly M, et al. Vitiligo: a comprehensive overview Part I. Introduction, epidemiology, quality of life, diagnosis, differential diagnosis, associations, histopathology, etiology, and work-up. J Am Acad Dermatol 2011;65:473-91.
3. Rork JF, Rashighi M, Harris JE. Understanding autoimmunity of vitiligo and alopecia areata. Curr Opin Pediat 2016;28:463-9.
4. Iannella G, Greco A, Didona D, et al. Vitiligo: Pathogenesis, clinical variants and treatment approaches. Autoimmun Rev 2016;15:335-43.
5. Gill L, Zarbo A, Isedeh P, et al. Comorbid autoimmune diseases in patients with vitiligo: A cross-sectional study. J Am Acad Dermatol 2016;74:295-302.
6. Yu R, Huang Y, Zhang X, et al. Potential role of neurogenic inflammatory factors in the pathogenesis of vitiligo. J Cutan Med Surg 2012;16:230-44.
7. Liu PY, Bondesson L, Löntz W, et al. The occurrence of cutaneous nerve endings and neuropeptides in vitiligo vulgaris: a case-control study. Arch Dermatol Res 1996;288:670-5.
8. Lazarova R, Hristakieva E, Lazarov N, et al. Vitiligo-related neuropeptides in nerve fibers of the skin. Arch Physiol Biochem 2000;108:262-7.
9. Linthorst Homan MW, Spuls PI, de Korte J, et al. The burden of vitiligo: patient characteristics associated with quality of life. J Am Acad Dermatol 2009;61:411-20.
10. Sharma N, Koranne RV, Singh RK. Psychiatric morbidity in psoriasis and vitiligo: a comparative study. J Dermatol 2001;28:419-23.
11. Mattoo SK, Handa S, Kaur I, et al. Psychiatric morbidity in vitiligo and psoriasis: a comparative study from India. J Dermatol 2001;28:424-32.
12. Clauw DJ. Fibromyalgia and related conditions. Mayo Clin Proc 2015;90:680-92.
13. Sluka KA, Clauw DJ. Neurobiology of fibromyalgia and chronic widespread pain. Neuroscience 2016 Jun 9. doi: 10.1016/j.neuroscience.2016.06.006.
14. Bradley LA. Pathophysiology of fibromyalgia. Am J Med 2009;122(12 Suppl):22-30.
15. Üçeyler N, Zeller D, Kahn AK, et al. Small fibre pathology in patients with fibromyalgia syndrome. Brain 2013;136:1857-67.
16. Laniosz V, Wetter DA, Godar DA. Dermatologic manifestations of fibromyalgia. Clin Rheumatol 2014;33:1009-13.
17. Yunus MB. Fibromyalgia and overlapping disorders: the unifying concept of central sensitivity syndromes. Semin Arthritis Rheum 2007;36:339-56.

18. 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 (Hoboken) 2010;62:600-10.
19. Sarmer S, Ergin S, Yavuzer G. The validity and reliability of the Turkish version of the Fibromyalgia Impact Questionnaire. Rheumatol Int 2000;20:9-12.
20. Hamzavi I, Jain H, McLean D, et al. Parametric modeling of narrowband UV-B phototherapy for vitiligo using a novel quantitative tool: the Vitiligo Area Scoring Index. Arch Dermatol 2004;140:677-83.
21. Buysse DJ, Reynolds CF, Monk TH, et al. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res 1989;28:193-213.
22. Zigmond AS, Snaith PR. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983;67:361-70.
23. Kemp EH, Emhemad S, Akhtar S, et al. Autoantibodies against tyrosine hydroxylase in patients with non-segmental (generalised) vitiligo. Exp Dermatol 2011;20:35-40.
24. Rodriguez-Pinto´ I, Agmon-Levin N, Howard A, et al. Fibromyalgia and cytokines. Immunol Lett 2014;161:200-3.
25. Klein R, Berg PA. High incidence of antibodies to 5-hydroxytryptamine, gangliosides and phospholipids in patients with chronic fatigue and fibromyalgia syndrome and their relatives: evidence for a clinical entity of both disorders. Eur J Med Res 1995;1:21-6.
26. Torresani C, Bellafiore S, De Panfilis G. Chronic urticaria is usually associated with fibromyalgia syndrome. Acta Derm Venereol 2009;89:389-92.
27. Yener M, Erturan I, Ceyhan AM, et al. The evaluation of prevalence of fibromyalgia in patients with chronic urticaria. Med Sci Monit 2013;19:757-61.
28. Hapa A, Ozdemir O, Evans SE, et al. Evaluation of the frequency of fibromyalgia in patients with chronic urticaria. Turkderm 2012;46:202-5.
29. Yazmalar L, Çelepkolu T, Batmaz İ, et al. High Frequency of Fibromyalgia in Patients With Acne Vulgaris. Arch Rheumatol 2016;31:170-5.
30. Thune PO. The prevalence of fibromyalgia among patients with psoriasis. Acta Derm Venereol 2005;85:33-7.
31. Mattoo SK, Handa S, Kaur I, et al. Psychiatric morbidity in vitiligo: prevalence and correlates in India. J Eur Acad Dermatol Venereol 2002;16:573-8.
32. Sangma LN, Nath J, Bhagabati D. Quality of life and psychological morbidity in vitiligo patients: a study in a teaching hospital from north-East India. Indian J Dermatol 2015;60:142-6.
33. Noh S, Kim M, Park CO. Comparison of the Psychological Impacts of Asymptomatic and Symptomatic Cutaneous Diseases: Vitiligo and Atopic Dermatitis. Ann Dermatol 2013;25:454-61.
34. Ramakrishna P, Rajni T. Psychiatric morbidity and quality of life in vitiligo patients. Indian J Psychol Med 2014;36:302-3.
35. Karelson M, Silm H, Kingo K. Quality of life and emotional state in vitiligo in an Estonian sample: comparison with psoriasis and healthy controls. Acta Derm Venereol 2013;93:446-50.