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Relationship between fibromyalgia clinical and laboratory parameters with obesity

Fibromyalji klinik ve laboratuar parametreleri ile obezite ilişkisi

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Abstract

Purpose: Fibromyalgia syndrome (FMS) is a common disease characterized by diffuse pain. Obesity is also a common disease characterized by excessive fat accumulation in adipose tissue. Obese individuals are known to have more musculoskeletal pain than normal people. In this study, we aimed to evaluate the relationship between obesity and fibromyalgia clinical and laboratory parameters.

Materials and methods: The study included 50 FMS patients and 35 healthy control groups. FMS patients were divided into two subgroups according to their BMI: obese (BMI≥30) and non-obese (BMI<30). Clinical comparisons were made with Visual Analogue Scale (VAS), Fibromyalgia Impact Questionnaire (FIQ, Short Form-36 (SF-36), and Beck Depression Inventory (BDI). In addition, serum CRP, vitamin B12, folate, TSH levels were compared.

Results: BDI, SF-36 physical function score was significantly higher in the obese group compared to the non-obese and healthy control group (p<0.001). Paresthesia and restless sleep symptoms were also significantly higher in the obese group than the non-obese group (p<0.05). Serum vitamin B12 levels were significantly lower and serum CRP values were significantly higher in the obese FMS group than the non-obese FMS group (p<0.001 and p<0.05, respectively). There was no statistically significant difference between groups in terms of VAS, FIQ score, pain duration, tender point count, serum TSH and folate levels.

Conclusion: Obesity is thought to have an impact on the pathogenesis and prognosis of the disease in patients with FMS. The findings of our study partially support the FMS-obesity relationship in the literature. To clarify this relationship, prospective studies involving more patient groups and using better homogenized patients and control groups are needed.

Key words: Fibromyalgia, Obesity, Short Form-36, Beck Depression İnventory, Vitamin B12.

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Özet

Amaç: Fibromiyalji sendromu (FMS) yaygın ağrı ile karakterize sık görülen bir hastalıktır. Adipoz dokuda aşırı yağ birikimi ile karakterize olan obezite de sık görülen bir hastalıktır. Obez bireylerde normal kişilere göre daha fazla kas iskelet sistemi ağrıları olduğu bilinmektedir. Biz de bu çalışmamızda obezite ile fibromyalji klinik ve laboratuar parametreleri arasındaki ilişkiyi değerlendirmeyi amaçladık.

Gereç ve yöntemler: Çalışmaya 50 FMS hastası ve 35 sağlıklı kontrol grubu alındı. FMS hastaları VKİ'lerine göre obez (VKİ≥30) ve non-obez (VKİ<30) olarak iki alt gruba ayrıldı. Gruplar arasında Vizual Analog Skalası (VAS), Fibromyalji Etki Anketi (FEA), Kısa Form-36 (KF-36), Beck Depresyon ölçeği (BDÖ) ile klinik olarak, serum CRP, vitamin B12, folat, TSH düzeyleri ile laboratuar olarak karşılaştırmalar yapıldı.

Bulgular: BDÖ, KF-36'nın fiziksel fonksiyon skoru obez grupta non-obez ve sağlıklı kontrol grubuna göre anlamlı olarak daha yüksekti (p<0.001). Parestezi ve dinlendirmeyen uyku semptomları da obez grupta non-obez gruptan anlamlı derecede daha yüksekti (p<0.05). Obez FMS grupta serum vitamin B12 değerleri non-obez FMS gruptan anlamlı düzeyde düşük, serum CRP değerleri ise anlamlı düzeyde yüksek bulundu (sırasıyla p<0.001 ve p<0.05). VAS, ağrı süresi, hassas nokta sayısı, FEA, TSH, folat düzeyleri açısından gruplar arasında istatiksel anlamlı farklılık gözlenmedi.

Sonuç: Obezitenin, FMS'li hastalarda hastalığın patogenez ve prognozuna etkisi olabileceği düşüncesi hakimdir. Bizim çalışmamızdaki bulgular da kısmi olarak literatürdeki FMS-obezite ilişkisini destekler niteliktedir. Bu ilişkinin daha net ortaya konulabilmesi için daha geniş sayıda hasta gruplarını içeren ve daha iyi homojenize edilmiş hasta ve kontrol gruplarının kullanıldığı prospektif çalışmalara ihtiyaç vardır.

Anahtar kelimeler: Fibromyalji, obezite, kısa form-36, beck depresyon ölçeği, vitamin B12.

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Introduction

Fibromyalgia syndrome (FMS) is a chronic pain syndrome characterized by diffuse pain, stiffness, fatigue, sleep disturbance, increased pain sensitivity to pressure, psychological comorbidities, and adversely affects quality of life [1]. FMS is a common syndrome with a worldwide prevalence of 2-7% [2]. Although the etiopathogenesis of FMS is not clearly understood yet, it is thought that impairments in the autonomic nervous system and neuroendocrine system, cytokines, genetic factors and environmental stress factors may play various roles in etiopathogenesis. However, the most accepted pathophysiological mechanism explained in recent years is the increased sensitivity of the central nervous system to pain [3]. FMS is more common in women than in men [4]. It has been shown that especially physically inactive individuals and obese patients have an increased risk of developing FMS [5]. FMS is often associated with severe functional impairment and disability, similar to other rheumatic disorders such as osteoarthritis or rheumatoid arthritis [6].

Obesity is a complex disease defined as excessive fat accumulation in adipose tissue [7]. Evidence in the literature shows that obese individuals have musculoskeletal pain and physical dysfunction more frequently than normal weight people [8]. Obesity is a well-known aggravating factor for certain rheumatologic conditions such as knee osteoarthritis. Epidemiological data show that the prevalence of obesity and excess weight is higher in fibromyalgia patients compared to healthy subjects. However, when we look at the relationship between fibromyalgia and obesity in terms of cause and effect, it does not seem possible to determine the possible causes and the results. Mechanisms for explaining the relationship between fibromyalgia and obesity include reduced physical activity, cognitive dysfunction and sleep disorders, psychiatric comorbidity and depression, dysfunction of the thyroid gland, GH / IGF-1 axis dysfunction, endogenous opioid system disruption.

The purpose of this cohort study was to examine the associations among obesity measurements and numerous FMS-related clinical and laboratory findings.

Materials and methods

Fifty female patients with a mean age of 38.35±5.35 years diagnosed with FMS according to American College of Rheumatology 1990 criteria and 35 healthy controls with a mean age of 35.0±5.1 years were included in the study [9]. Corporate ethics committee permission was obtained for the study. Patients who agreed to participate in the study were informed in detail about the study and their written informed consent was obtained. Patients with diagnose of any systemic disease, chronic inflammatory disease, major psychiatric disease, endocrine disease, cervical radiculopathy, cervical myelopathy, pregnancy and history of malignancy, were not included in the study. In addition, patients whose laboratory tests (hemoglobin, hematocrit, erythrocyte sedimentation rate (ESR), CRP) were abnormal suggesting a systemic, inflammatory or infective disease were also excluded. The healthy control group consisted of volunteer hospital staff who had no physical or mental disorder, were in the same age range as the patient group and accepted to participate in the study with signed consent forms. Detailed physical examination and other clinical assessments were performed by the same clinician in all of the subjects in the study. Complete blood count, CRP, ESR, thyroid function tests, serum vitamin B12 and folate levels and other biochemical parameters of blood (creatinine, AST, ALT) were analyzed in patient and control groups.

Demographic data and body mass index (BMI) of the participants (kg/m^2) were recorded at the first visit. The patient group was subdivided into two groups as obese (BMI≥30) and non-obese (BMI<30) patient groups according to their BMI [10]. In the second visit, Visual Pain Scale (VAS), tender point count (TPC), Beck Depression Scale (BDI), Fibromyalgia Impact Questionnaire (FIQ), Short Form-36 Health Survey Questionnare (SF-36) scores of the participants were determined. Within 24 hours prior to the second visit, participants were asked not to take painkillers or exercise to prevent VAS, TPC, BDI, FIQ and SF-36 scores from being affected.

Pain severity was evaluated with a 0-10 cm VAS scale. On this scale, there is the definition of ‘’no pain’’ at the left end and “severe pain” at the right end on a 10 cm long horizontal

line. The patients graded the pain intensity by placing a mark on this line. VAS is a frequently used scale because of its easy application in pain assessment and its validity and reliability [11]. Tender points, although controversial, are the only objective physical examination findings that can be detected in FMS. Eighteen spesific tender point sites have been identified in patients with FMS [12]. Tender points detected on physical examination were recorded as TPC. BDI was used to evaluate depression in the patients. BDI was developed by Beck in 1961 to evaluate depressive symptoms in patients and Turkish validity and reliability studies were carried out [13]. FIQ is used in FMS to assess both the clinical severity of the disease and the effectiveness of different treatments. The Turkish version of FIQ is used to evaluate the clinical severity of the disease. The validity and reliability studies of the Turkish version of FIQ were conducted [14]. In order to evaluate the functional status of the patients, the SF-36 quality of life scale, of which the Turkish version was found to be reliable and valid, was used [15]. The SF-36 includes 36 questions and is composed of 8 multi-item scales assessing physical function, role limitations due to physical health problems, bodily pain, general health, vitality, social functioning, role limitations due to emotional problems and emotional well-being.

Descriptive analyzes were conducted to give information about the general characteristics of the study groups. Data of continuous variables were expressed as median (min.-max.) and categorical variables were given as n(%). Mann Whitney U test was used to compare two independent continuous variable groups. Categorical data were analyzed by Chi-square test. The relationship between numerical variables was examined by Spearman Correlation Analysis. The p-value used to determine statistical significance was ≤0.05. The Statistical Package for the Social Sciences (IBM SPSS Statistics 17, SPSS inc., An IBM Co., Somers, NY) was used for data analysis.

Results

The median BMI of the subjects in the obese-FMS group was 30 (30.1-41.6); which was significantly higher than non-obese group 25.1 (20.4-27.6) and control group 23.6(18.3-28.4) BMI values (p<0.001). The mean values of BDI and SF-36 physical function sub-parameters were significantly higher in obese-FMS group than non-obese FMS group and control group (p<0.001). Serum vitamin B12 levels were significantly lower in obese-group than non-obese FMS group. Serum CRP levels were significantly higher in obese-FMS group than non-obese FMS group and control group. However, no statistically significant difference was observed between the groups in terms of VAS, pain duration, number of tender points, FIQ, serum TSH and folate levels (Table 1)

When we compared the incidence of fibromyalgia symptoms in the obese and non-obese patient groups, 20 (76.9%) of the 26 obese FMS patients had paresthesia and only 10 (43.5%) of the non-obese FMS group had paresthesia. The difference was statistically significant (p=0.021). Likewise, the frequency of restless sleep symptoms was significantly higher in the obese group (88.5%) than the non-obese group (52.2%) (p=0.010) (Table 2).

When the correlation analysis of the BMI and clinical evaluation scales of the patient group was performed, only a weak negative correlation was found between BMI and physical function sub-parameter values of SF-36 (r:-0.324, p=0.022), and a weak positive correlation between BMI and CRP values (r:-0.359, p=0.011) was determined (Table 3).

Table 1. Comparison of clinical and laboratory data of patient and control groups.

	Obese-FMS Group n:26	**Non-Obese FMS Group n:24**	**Control group n:35**	***p* value**
Age (year)	38.5±6.9	38.1±3.8	35.0±5.1	>0.05
BMI (kg/m^2)	33.4±2.3	24.9±2.3[a]	24.8±4.3[a]	<0.001*
VAS (cm)	7.9±2.2	7.8±1.2	-	>0.05
Pain duration (month)	5.6±4.7	5.3±4.8	-	>0.05
TPC	13.8±1.9	13.1±3.3	-	>0.05
BDI	25.8±12.2	19.8±7.9[b]	6.1±5.2[a,,c]	<0.001*
FIQ	63.9±18.3	62.1±16.9	-	>0.05
SF-36/physical function	47.1±15.6	57.1±16.9[b]	86.1±16.7[a,,c]	<0.001*
Folate (ng/mL)	8.9±2.3	9.1±1.9	8.5±3.2	>0.05
Vitamin B12 (pikogram/mL)	309.9±109.1	432.9±232.9[a,b]	257.9±95.1	<0.001*
CRP(mg/L)	4.7±5.3 7.2 (1-28)	1.4±1.3 1.72 (0.3-6.4)	2.2±2.5 1.68 (0.1-5.4)	<0.05*
TSH (µIU/mL)	2.0±1.4	1.9±1.1	1.8±1.4	>0.05

[a] Significance level between obese-FMS group $p<0.001$
[b] Significance level with obese-FMS group $p<0.05$
[c] Significance level with the control group $p<0.001$
[d] Significance level with the control group $p<0.001$
ANOVA multiple comparison test (Tukey HSD)

BMI: Body Mass Index **VAS:** Visual Analogue Scale **TPC:** Tender point count **BDI**: Beck Depression Inventory **FIQ:** Fibromyalgia Impact Questionnaire **SF-36**: Short Form-36 Quality of Life Scale **CRP:** C-Reactive Protein **TSH:** Thyroid Stimulating Hormone

Table 2. Comparison of the prevalence of fibromyalgia symptoms between obese and non-obese patient groups.

	Obese-FMS Group n: 26	**Non-obese FMS Group n:24**	***p* value**
Sleeping disorder	22 (%84.6)	15 (%65.2)	0.107
Fatigue/weakness	25 (%96.2)	23 (95.8)	0.724
Concentration difficulty	22 (%84.6)	21 (%87.0)	0.571
Headache	22 (%84.6)	18 (%78.3)	0.418
Paresthesia	20 (%76.9)	10 (%43.5)	0.021*
Morning stiffness	18 (%69.2)	11 (%47.8)	0.109
Subjective swelling	14 (%53.8)	9 (%37.5)	0.318
Unresponsive sleep	23 (%88.5)	12 (%52.2)	0.010*
Irritable bowel syndrome	7 (%26.9)	10 (%41.7)	0.273
Anxiety	17 (%65.4)	15 (%62.1)	0.487
Dysmenorrhea	7 (%26.9)	11 (%45.8)	0.112

Chi-square test

Table 3. Relationship between BMI and clinical scales.

	BMI	
	r	***p* value**
Pain duration	0.069	0.634
VAS	0.049	0.738
TPC	0.127	0.379
BDI	0.269	0.059
FIQ	0.161	0.263
SF-36/physical function	-0.324	0.022*
SF-36/ physical role limitation	-0.182	0.207
SF-36/pain	0.022	0.882
SF-36/general health perception	-0.247	0.084
SF-36/ energy / vitality	-0.265	0.063
SF-36/ social function	0.037	0.798
SF-36/ emotional role limitation	0.205	0.152
SF-36/ mental health	-0.236	0.099
Vitamin B12 (pikogram/mL)	-0.221	0.124
CRP (µIU/mL)	0.359	0.011*

Pearson correlation analysis

BMI: Body Mass Index **VAS:** Visual Analogue Scale **TPC:** Tender point count
BDI: Beck Depression Inventory **FIQ**: Fibromyalgia Impact Questionnaire
SF-36: Short Form-36 Quality of Life Scale **CRP**: C-Reactive Protein

Discussion

Obesity is a common health problem, which is an important cause of mortality and morbidity, playing an important role in the etiology of metabolic, cardiac and musculoskeletal diseases. Overweight and obesity have been considered as risk factors for chronic pain disorders [16]. In addition, in a study using electrophysiological methods in healthy and painless obese women, a negative correlation was found between pain threshold and weight [17]. In another similar study evaluating the mechanical pain threshold by applying continuous force with the thumb, it was found that the mechanical pain threshold was lower in healthy and painless obese people compared to non-obese people [18].

Several studies have reported that BMI of patients with FMS is higher than that of the healthy population and 62-73% of patients with FMS are overweight or obese [19-21]. The mean BMI of the patients with FMS included in our study was 29.15±2.66 kg/m^2. According to BMI, 48% of our patients were obese.

Mork et al. studied the effect of BMI and physical exercise on FMS development in a large 11-year longitudinal study with 15990 patients. These patients did not initially

have FMS or any physical impairment. After 11 years, 380 of these patients were

diagnosed as FMS. There was a weak dose-response relationship between FMS and physical exercise level, but BMI was found to be an independent risk factor for FMS [5].

The BMI and clinical features were compared in patients with FMS and various results have been obtained in the studies [19-21]. In a study including 211 women with FMS to evaluate the relationship between BMI and FMS characteristics, Yunus et al. found a positive correlation between BMI and Health Assessment Questionnaire score. In the same study, they have found a positive correlation between BMI and both age and TPC, but have not found a relationship between BMI and VAS scores. In conclusion, they have reported that obesity may aggravate the symptoms of FMS [20].

In a study including 100 female patients with FMS; Neumann et al. have found a negative correlation between BMI and both SF-36 and pain threshold. In the same study, a positive

correlation has been found between BMI and both TPC and FIQ. In conclusion, they have reported that obese patients with FMS have lower quality of life and higher pain sensitivity [21]. In our study, the quality of life of the patients was evaluated with SF-36 and we found that physical function sub-scores of SF-36 were significantly lower in the obese group.

In a study conducted with 38 patients with FMS, Okifuji et al. have reported that BMI is associated with sleep disturbance. In addition, when they divided patients into three groups in terms of being in normal weight, overweight and obese, they could not detect a difference between the groups in terms of depression and anxiety rates [19]. In our study, the mean BDI score of the obese-FMS group was significantly higher than that of the non-obese group. In order to discriminate whether this was a condition related to FMS-obesity relationship or only obesity, we think that it would be useful to conduct future studies involving both the obese and non-obese control groups in larger patient samples.

Some authors have shown the relationship between obesity and FMS symptom severity, and thus suggest that FMS symptoms may be more severe in patients with increased BMI [22]. In our study, no significant correlation was found between increased BMI values and FIQ. There are many factors that increase the severity of FMS symptoms. Although there are many factors that may increase the symptoms of FMS, there is no study that excludes all these factors and only evaluates the effect of BMI on FMS symptoms in the literature. In our study, the reason for the absence of a relationship between BMI and FIQ may be that other factors could not be excluded.

There are very few studies examining the relationship between FMS and serum vitamin B12 in the literature. In none of these studies, a statistically significant difference in serum vitamin B12 levels has been shown between healthy control group and FMS patients [23, 24]. On the other hand, there is a greater number of studies examining the relationship between obesity and serum vitamin B12 in the literature. Furthermore, there is a clear relationship between obesity and low serum vitamin B12 levels in these studies [25, 26]. In our study, mean serum vitamin B12 level was found to be lower in obese-FMS patients than non-obese FMS patients. However, this decrease was not correlated with BMI. Another result of our study was that the incidence of paresthesia was higher in obese-FMS patients than non-obese patients. These results suggest that vitamin B12 deficiency may be responsible for the development of paresthesia in obese-FMS patients.

Obesity has been associated with higher CRP levels in several meta-analyzes and reviews, as well as in several cross-sectional studies [27, 28]. In addition, pathophysiological mechanisms that associate obesity with high CRP levels are well known [27, 29, 30]. Adipose tissue is an active endocrine organ releasing various hormones and cytokines that contribute to CRP elevation [31]. In our study, when we examined CRP levels in obese FMS patients, we found that CRP levels were higher in obese patients and it was associated with BMI. This result suggests that hormones and cytokines released from adipose tissue may play a role in the development of FMS in obese people.

The relationship between FMS and CRP is controversial. CRP is thought to reflect chronic systemic inflammation also in the absence of infection and tissue injury [32]. In studies examining the relationship between fibromyalgia and CRP, only a few studies have found positive correlation between them [33-35].

FMS is a common pain syndrome. Obesity is also a common disease and can be seen predisposing or comorbid to various clinical conditions. In recent years, the relationship between FMS and obesity has been investigated with increasing interest. Although the results of the literature suggest that obesity increases the presence and severity of the clinical findings in fibromyalgia patients, there are contradictory results in this regard.

In conclusion, although some of the results of our study supported this relationship between obesity and FMS, prospective studies involving larger patient samples in addition to patient and control groups with better homogenization are needed to clarify the relationship between fibromyalgia and obesity.

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

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