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Investigation of Serum Plasma Total Oxidant/Antioxidant, Thiol-Disulfide, and Asprosin Levels in Fibromyalgia Patients

Fibromiyalji Hastalarında Serum Plazma Total Oksidan/Antioksidan, Tiyol-Disülfit ve Asprosin Düzeylerinin İncelenmesi

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Abstract

Background: Fibromyalgia is defined as a chronic syndrome of uncertain etiology, accompanied by musculoskeletal findings and numerous somatic symptoms. In this study, we aimed to contribute to understanding the etiopathogenesis of fibromyalgia syndrome by examining total antioxidant status, total oxidant status, thiol-disulfide homeostasis, and asprosin levels.

Materials and Methods: Newly diagnosed female patients with fibromyalgia syndrome between the ages of 20-50 and healthy female volunteers in the same age range were included in the study. Plasma native thiol, total thiol, disulfide, native thiol/total thiol, disulfide/native thiol, disulfide/total thiol, total antioxidant level, total oxidant level, oxidative stress index, and asprosin values of both groups were measured.

Results: Total antioxidant level, total oxidant level and total thiol levels were lower in the patient group; the disulfide/native thiol ratio was higher in the patient group; the differences were statistically significant (p=0.024, p<0.001, p=0.050, p=0.050). In the fibromyalgia syndrome group, there was a positive correlation between age and total antioxidant level and total thiol values (r=0.361, p=0.020; r=0.314, p=0.045, respectively) and a negative correlation with native thiol (r=-0.354, p=0.023). There was a positive correlation between body mass index (BMI) and asprosin and total oxidative level in the fibromyalgia syndrome group (r=0.743, p<0.001; r=0.356, p=0.022, respectively); there was a negative correlation between BMI and total antioxidant level in the control group (r=-0.429, p=0.005). The Widespread Pain Index was positively correlated only with asprosin (r=0.309, p=0.049).

Conclusions: Although no significant difference was found between the groups in terms of serum asprosin levels in fibromyalgia syndrome, the positive correlations of asprosin with BMI and the Widespread Pain Index may suggest an association with metabolic status and pain extent. In addition, our findings indicate partial alterations in oxidative-antioxidative balance and thiol-disulfide homeostasis in fibromyalgia syndrome rather than a uniform disturbance across all parameters.

Keywords: Fibromyalgia, Oxidative Stress, Adipokines, Biomarkers

Öz

Amaç: Fibromiyalji; etiyolojisi belirsiz olan, kas iskelet sistemi bulguları ve birçok somatik semptomun eşlik ettiği kronik bir sendrom olarak tanımlanmaktadır. Bu çalışmada, total antioksidan seviye, total oksidan seviye, tiyol-disülfit homeostazı ve asprosin düzeylerini inceleyip, Fibromiyalji sendromu etyopatogenezine katkı sağlamayı amaçladık.

Materyal ve metod: Yeni tanılı 20-50 yaş aralığındaki Fibromiyalji sendromlu kadın hastalar ile aynı yaş grubunda sağlıklı gönüllü kadınlar çalışmaya dahil edildi. Her iki grubun plazma natif tiyol, total tiyol, disülfit, natif tiyol/total tiyol, disülfit/natif tiyol, disülfit/total tiyol, total antioksidan seviye, total oksidan seviye ve oksidatif stres indeksi değerleri ile asprosin değerlerine bakıldı.

Bulgular: Total antioksidan seviye, total oksidan seviye ve total tiyol seviyeleri hasta grubunda daha düşük; disülfit/natif tiyol oranı hasta grubunda daha yüksek olup; aradaki farklar istatistiksel olarak anlamlı idi (p=0,024, p<0,001, p=0,050, p=0,050). Fibromiyalji sendromu grubunda yaş ile total antioksidan seviye, total tiyol değerleri arasında pozitif korelasyon (r=0,361 p=0,020, r=0,314 p=0,045) ve natif tiyol ile negatif korelasyon (r=-0,354 p=0,023) vardı. Fibromiyalji sendromu grubunda vücut kitle indeksi ile asprosin ve total oksidatif seviye arasında pozitif korelasyon (r=0,743 p<0,001, r=0,356 p=0,022); kontrol grubunda vücut kitle indeksi ile total antioksidan seviye arasında negatif korelasyon vardı (r=-0,429 p=0,005). Yaygın ağrı indeksi sadece asprosin ile pozitif koreleydi (r=0,309 p=0,049).

Sonuç: Fibromiyalji sendromunda, serum asprosin düzeyleri gruplar arasında anlamlı farklılık göstermemekle birlikte, vücut kitle indeksi ve yaygın ağrı indeksi ile olan pozitif korelasyonları olası bir ilişkiye işaret edebilir. Bulgularımız ayrıca oksidatif-antioksidatif denge ve tiyol-disülfit homeostazında kısmi bir değişiklik olabileceğini düşündürmektedir.

Anahtar Kelimeler: Fibromiyalji, Oksidatif Stres, Adipokinler, Biyobelirteçler

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Introduction

Fibromyalgia syndrome (FMS) affects the musculoskeletal system with widespread pain, tenderness in certain anatomical areas, disturbances in sleep and cognitive functions, fatigue, depression, anxiety, and many somatic symptoms. Its etiology remains unknown (1). Although FMS affects individuals of all ages and both sexes, it is most commonly seen in women between the ages of 30 and 50 (2,3).

The diagnosis of FMS is made by the presence of typical symptoms and the exclusion of other diseases that cause the similar symptoms. Various FMS classifications and diagnostic criteria have been developed and tested to ensure homogeneity in clinical studies and evaluations. After FMS was recognized as a syndrome, the American College of Rheumatology (ACR) released the initial diagnostic criteria in 1990 (1). While the ACR's 1990 classification criteria included widespread pain and tender points, in 2010, other somatic symptoms, such as fatigue, waking up tired in the morning, and impairment in cognitive functions were added (4).

The etiology and pathophysiology of FMS remain unclear and are thought to be multifactorial. According to information obtained from research, multiple factors and systems, such as genetic factors, psychosocial variables and environmental stress, the neurohormonal system, and the autonomic nervous system contribute to the pathophysiology of FMS (5). Additionally, the literature indicates that oxidative stress may contribute to the pathophysiology of FMS (6, 7).

Reactive atoms or molecules containing one or more unpaired electrons in their outermost orbitals are known as free radicals (8, 9). The types of free radicals in the biological environment are reactive nitrogen species and reactive oxygen species. Free oxygen radicals are formed during metabolic events and are eliminated and kept in balance by antioxidant mechanisms in aerobic organisms. Free oxygen radicals are produced at high rates during treatment, hyperoxia, ischemia-reperfusion, radiation, aging, exposure to chemical substances or when the defense system is inadequate. It causes tissue damage through toxic effects on lipids, DNA, fractions, and enzymes in the cell. The imbalance between free radicals and the antioxidants that help biological systems detoxify them is known as oxidative stress. In other words, they are the negative effects caused by the accumulation of free radicals within cells (10).

The body contains compounds called antioxidants that stop reactive oxygen radicals from forming and from causing damage, and this system is called the antioxidant defense system (11). An organism's overall antioxidant capacity against free radicals is referred to as its total antioxidant status (TAS), and the entire amount of oxidative stress is known as the total oxidant status (TOS). Simple and reliable detection of TAS and TOS in the body were developed by Erel et al. (12, 13). Thiols, also known as mercaptans, are chemical compounds with a sulfhydryl group that is composed of sulphur and hydrogen bound to a single carbon (14). They are those containing thiols in their important antioxidant structure, which are responsible for defense against oxidative stress due to their reducing properties (15, 16). The neutralization of destructive exogenous and endogenous oxidants occurs through binding by thiols, and during this interaction, free disulfide bonds are released. Thiol/disulfide homeostasis is reduced again by binding the hydrogen atom to free disulfide, thus forming a native thiol (NT) (17, 18). The NT which shows antioxidant activity, and the disulfide, which shows oxidant activity, are in a dynamic balance. This makes it possible to control transcription, apoptosis, detoxification, antioxidant defence, enzyme activity modulation, and cellular signal transmission systems. Thiol-disulfide balance may be disrupted negatively or positively in the case of cellular pathologies (19).

Some studies have shown that antioxidant defense is impaired and the oxidant burden is increased in patients with FMS; accordingly, lower TAS levels together with higher TOS and/or oxidative stress index (OSI) levels have been reported (20-22). In contrast, there are also studies reporting no significant differences in TAS, TOS, or OSI values in patients with FMS compared with the control group (23). In addition, the limited number of studies investigating thiol-disulfide homeostasis in FMS have identified alterations in native thiol, disulfide, and related ratios; however, these findings have not been entirely consistent across studies (23–26). Therefore, although current evidence supports the presence of oxidative imbalance in FMS, data regarding TAS/TOS and, in particular, thiol-disulfide homeostasis remain limited and partly conflicting.

Profibrillin's C-terminal cleavage produces the hormone asprosin, which has a 140 amino acid polypeptide structure (27). It is secreted by white adipose tissue, and, stimulated by fasting, it induces hepatic glucose production and regulates glucose homeostasis. It has been observed that the administration of intravenous asprosin causes appetite stimulation via the hypothalamus and can cause obesity in the long term (28). Since obesity has been reported to be more common in patients with FMS and to be associated with more severe pain, poorer functional status, and a higher symptom burden, adipokine-related mediators such as asprosin have been considered

potential contributors to this disorder (29, 30). In this context, we considered asprosin a potential biomarker in FMS because of its capacity to reflect metabolic disturbances and mechanisms that may be associated with widespread pain in FMS.

In the literature, there are studies on TAS, TOS, and thiol-disulfide homeostasis, but there is no study examining asprosin levels in FMS. Our aim in this study is to examine TAS, TOS, thiol-disulfide homeostasis, and asprosin levels to contribute to understanding the etiopathogenesis of FMS.

Materials and Methods

The study was conducted in accordance with the Declaration of Helsinki and was approved by the Harran University Clinical Research Ethics Committee (decision number: 20/14/27, dated: August 17, 2020). Informed consent forms were obtained from the patients.

This study comprised women aged 20-50 years with widespread pain, classified according to the 2010 ACR fibromyalgia diagnostic criteria (Table 1), and healthy female volunteers in the same age range. Women with diabetes mellitus, hypertension, hypercholesterolemia/hypertriglyceridemia, history of thyroid hormone disorder, alcohol consumption and/or smoking, antidepressant/antiepileptic use, coronary artery disease, pacemaker use, heart failure, renal failure, or hepatic failure, autoimmune disease, inflammatory rheumatic disease, acquired immunodeficiency syndrome (AIDS), hepatitis B, hepatitis C, brucellosis, tuberculosis, and active infection, cerebrovascular accident, neuromuscular junction disease, Parkinson's disease, multiple sclerosis, malignancy history, pregnancy, or breastfeeding history were excluded from the study.

Table 1. Fibromyalgia criteria; modified from American College of Rheumatology (ACR) diagnostic criteria 2010

A patient satisfies modified ACR 2010 fibromyalgia diagnostic criteria if the following 3 conditions are met: (1) Widespread Pain Index ≥ 7 and Symptom Severity Score ≥ 5 or Widespread Pain Index between 3–6 and Symptom Severity Score ≥ 9. (2) Symptoms have been present at a similar level for at least 3 months. (3) The patient does not have a disorder that would otherwise sufficiently explain the pain.			
Ascertainment			
1) Widespread Pain Index (WPI): Indicate the number of body areas in which the patient has experienced pain over the past week. In how many areas has the patient had pain? The total score ranges from 0 to 19.			
Shoulder girdle, Left.	Hip (buttock, trochanter), Left.	Jaw, Left.	Upper Back
Shoulder girdle, Right.	Hip (buttock, trochanter), Right.	Jaw, Right.	Lower Back
Upper Arm, Left.	Upper Leg, Left.	Chest	Neck
Upper Arm, Right.	Upper Leg, Right.	Abdomen	
Lower Arm, Left.	Lower Leg, Left.		
Lower Arm, Right.	Lower Leg, Right.		
2) Symptom Severity Score: Fatigue; Waking unrefreshed; Cognitive symptoms.			
For the each of these 3 symptoms, indicate the level of severity over the past week using the following scale: 0 = No problem; 1 = Slight or mild problems; generally mild or intermittent; 2 = Moderate; considerable problems; often present and/or at a moderate level; 3 = Severe: pervasive, continuous, life-disturbing problems.			
The Symptom Severity Score is the sum of the severity of the 3 symptoms (fatigue, waking unrefreshed, and cognitive symptoms) plus the sum of the number of the following symptoms occurring during the previous 6 months: headaches, pain or cramps in lower abdomen, and depression (0–3). The final score is between 0 and 12.			

Two groups of participants were formed for our investigation: newly diagnosed patients with FMS and healthy volunteers. Sociodemographic data for these groups were recorded. FMS diagnosis was made according to the ACR's 2010 diagnostic criteria. The patients' ages, body mass index (BMI), occupations, marital statuses, and disease duration were documented, and detailed physical examinations were performed. The symptom severity score (SSS) and Widespread Pain Index (WPI) of the patients were recorded.

A 5-cc blood sample was collected from each woman and stored at -80°C until the trial commenced. Serum asprosin, TAS, TOS, and thiol/disulfide levels were studied according to the kit manufacturers' recommendations and expiration dates.

TOS: Rel Assay brand commercial kits, which work on the principle of a completely automated technique developed by Erel, were used for TOS measurement (MEGA TIP Medical Industry and Trade Co. Ltd., Gaziantep, Turkey).

Test principle: In this method, the Fe^{2+}-o-dianisidine complex in the sample undergoes oxidation to ferric ions by the action of oxidants, while the presence of glycerol markedly accelerates the reaction, approximately threefold. Ferric ions create a coloured complex with xylenol orange in an acidic medium, and the intensity of the colour, which correlates with the quantity of oxidants, is quantified spectrophotometrically (13).

TAS: Rel Assay brand commercial kits, which work on the principle of a completely automated technique developed by Erel, were used for TAS measurement (MEGA TIP Medical Industry and Trade Co. Ltd., Gaziantep, Turkey).

Test Principle: In this method, hydroxyl radicals are generated through a Fenton-type mechanism initiated by the interaction between hydrogen peroxide and the Fe^{2+}-o-dianisidine complex. OH interacts with the colourless o-dianisidine molecule at an acidic pH, leading to the generation of yellow-brown dianisidyl radicals. Dianisidyl radicals engage in advanced oxidation processes, leading to increased colour formation; however, antioxidants inhibit these reactions and prevent further colour development (12).

Oxidative Stress Index (OSI): To compute the OSI of the samples, the units of TOS and TAS were initially determined in µmol. The OSI was subsequently computed using the formula OSI (AU) = [(TOS, µmol/L) / (TAS, µmol/L)] × 100 (31).

Thiol-Disulfide Homeostasis Parameters: Parameters of serum thiol-disulfide homeostasis were assessed utilising a novel automatic measuring approach devised by Erel and Neselioğlu (15).

Test Principle: Under oxidative stress, thiols engage with oxidants and undergo oxidation, resulting in the formation of reversible disulphide linkages. Reduction of these disulphide bonds regenerates thiol groups, a process referred to as thiol–disulphide homeostasis. Total thiol (TT) includes the sum of reduced and oxidized thiols, while native thiol denotes only the thiols in their reduced state. In the first stage of the experiment, free functional thiol groups were generated through the reduction of disulphide bonds. In the second step, the unutilised reductant sodium borohydride was depleted and eliminated using formaldehyde. In the final step, all thiol groups were treated with 5,5'-dithiobis-(2-nitrobenzoic) acid to quantify the native and reduced thiol groups. One-half of the value obtained by subtracting native thiols (NT) from total thiols (TT) was recorded as the amount of dynamic disulfide (DS). Following the determination of NT and TTs, the quantities of disulphides, the percentage ratios of disulphides to total thiols (DS/(NT+DS)), the percentage ratios of disulphides to native thiols (DS/NT), and the ratio of native thiols to total thiols (NT/TT) were calculated. Percentage ratios (NT/(NT+DS)) were subsequently computed (15).

Asprosin: The Bioassay Technology Laboratory brand (Zhejiang, China), catalog number E4095Hu, Human Asprosin ELISA kit was used for measurement.

Test Principle: This kit is based on an enzyme-linked immunosorbent assay (ELISA). Asprosin present in the sample was introduced and adhered to the plates previously coated with asprosin antibodies in the wells. The asprosin in the sample was bound by the addition of a biotinylated anti-human asprosin antibody. The biotinylated asprosin antibody was then coupled to streptavidin-HRP. Following incubation, free Streptavidin-HRP was eliminated through washing. Subsequently, the substrate solution was applied, resulting in a color change proportional to the concentration of human asprosin. The reaction was stopped with an acidic stop solution, and absorbance was subsequently read at 450 nm. Absorbance measurements were performed using the Thermo Scientific Varioskan LUX Microplate Reader.

Statistical Analysis

Statistical analyses were performed using SPSS (version 20; IBM Corp., Armonk, NY, USA). The Shapiro–Wilk test was utilised to assess the distribution of quantitative data. For data that did not follow a normal distribution, the Mann–Whitney U test was used and results were expressed as median (min–max).

For normally distributed data, Student's t test was applied and results were presented as mean ± standard deviation (SD). Categorical variables were analyzed using the chi-square test. A p-value less than 0.050 was deemed statistically significant.

Results

A total of 82 female cases, 41 with FMS and 41 healthy volunteers, were included in the study. All participants provided informed consent to participate in the study after receiving information about the study. The mean age of the participants was 36.92±7.64 years in the FMS group and 34.56±5.37 years in the control group. Statistical analysis showed that the groups did not differ significantly (p=0.110). The mean BMI was 26.39±3.69 kg/m2 in the patient group and 27.90±4.59 kg/m^2 in the control group. No statistically significant difference was detected between the groups (p=0.104) (Table 2).

Table 2. Age and BMI values of study participants

	FMS (n=41)	Control (n=41)	p
Age	36.92±7.64	34.56±5.37	0.110
BMI	26.39±3.69	27.90±4.59	0.104
FMS: Fibromyalgia syndrome, BMI: Body Mass Index			

The mean duration of widespread pain was 11.78±6.24 (5-30) months. The mean WPI was 10.00±2.24, and SSS values was 8.26±1.39. The most frequently reported pain localizations were lowerback, upperback, andneck at 75.60%, 73.17%, and 70.73%, respectively. Jaw pain was reported at the lowest rate at 29.27%. Pain localizations and frequency of occurrence are summarized in Table 3.

Table 3. Pain areas of participants with fibromyalgia syndrome

Lower back	31 (75.60%)
Upper back	30 (73.17%)
Neck	29 (70.73%)
Upper leg (Left)	28 (68.29%)
Upper arm (Left)	27 (65.85%)
Upper arm (Right)	25 (60.97%)
Forearm (Left)	25 (60.97%)
Hip (Right)	24 (58.53%)
Forearm (Right)	22 (53.66%)
Upper leg (Right)	22 (53.66%)
Lower leg (Right)	22 (53.66%)
Shoulder (Left)	21 (51.22%)
Lower leg (Left)	21 (51.22%)
Chest-Abdomen	20 (48.78%)
Hip (Left)	20 (48.78%)
Shoulder (Right)	19 (46.34%)
Jaw (Right)	12 (29.27%)
Jaw (Left)	12 (29.27%)

While TAS, TOS and TT levels were lower, the DS/NT ratio was higher in the FMS group. In the FMS group, the differences reached statistical significance (p=0.024, p<0.001, p=0.050, and p=0.050, respectively). There was no statistically significant difference between the groups in terms of asprosin, OSI, NT, DS, DS/TT, or NT/TT levels (p=0.089, p=0.756, p=0.650, p=0.507, p=0.882, and p=0.882, respectively). The data are summarized in Table 4.

Table 4. Comparison of Oxidative Stress Tests of FMS and Control Groups

	FMS (n=41)		**Control (n=41)**		**p***
	Median	**Min-max**	**Median**	**Min-max**	
Asprosin	16.377	7.17-53. 36	13.991	5.55-53.82	0.089*
TAS (mmol Trolox/L)	0.948	0.64-1. 80	1.532	0.64-1.80	0.024*
TOS (µmol H_2O_2/L)	6.929	5.74-12. 50	8.673	4.65-25.77	<0.001*
OSI (arbitrary unit)	0.786	0.34-1.18	0.544	0.33-2.10	0.756*
Disulfide/Native thiol (%)	5.806	1.48-15.58	5.528	2.13-18.09	0.050*
	Mean±SD		**Mean±SD**		
Total thiol (µmol/L)	304.49±68.86		330.4±46.93		0.050**
Native thiol (µmol/L)	270.85±65.14		294.44±47.69		0.065**
Disulfide (µmol/L)	16.82±7.22		17.97±8.43		0.507**
Disulfide/Total thiol (%)	5.57±2.28		5.50±2.45		0.882**
Native thiol/Total thiol (%)	88.84±4.56		88.99±4.90		0.882**
* Mann-Whitney U test, TAS: Total Antioxidant Status, TOS: Total Oxidative Status, OSI: Oxidative Stress Index, FMS: Fibromyalgia syndrome, ** Student's t test, SD: Standard deviation					

Table 5 summarizes the correlations of demographic and clinical profiles of the groups with oxidative stress tests. In the FMS group, age correlated positively with TAS and TT values (r=0.361, p=0.020; r=0.314, p=0.045, respectively) and negatively with NT (r=-0.354, p=0.023). There was a positive correlation between BMI and asprosin and between BMI and TOS in the FMS group (r=0.743, p<0.001; r=0.356, p=0.022). A negative correlation was observed between BMI and TAS in the control group (r=-0.429, p=0.005). No correlation was observed between SSS and complaint duration and oxidative stress parameters. WPI was positively correlated only with asprosin (r=0.309, p=0.049).

Table 5. FMS Patients and Healthy Control Group; Correlations of Demographic and Clinical Characteristics with Oxidative Stress Tests

		Age		**BMI**		**SSS**		**WPI**		**Symptom Duration**	
		p	***r***	***p***	***r***	***p***	***r***	***p***	***r***	***p***	***r***
Asprosin	**FMS**	0.675	-0.076	0.000	**0.743****	0.572	0.091	0.049	**0.309***	0.072	0.284
	Control	0.433	-0.126	0.271	0.176						
TAS	**FMS**	0.020	**0.361***	0.665	-0.070	0.824	0.036	0.529	-0.101	0.205	0.202
	Control	0.768	0.048	0.005	**-0.429****						
TOS	**FMS**	0.684	-0.066	0.022	**0.356***	0.110	0.248	0.069	0.287	0.966	0.007
	Control	0.622	0.079	0.640	-0.075						
OSI	**FMS**	0.090	-0.268	0.102	0.259	0.389	0.138	0.060	0.296	0.254	-0.182
	Control	0.533	0.100	0.340	0.153						
TT	**FMS**	0.045	**0.314***	0.093	-0.266	0.564	0.093	0.472	0.116	0.513	0.105
	Control	0.346	-0.151	0.965	0.007						
NT	**FMS**	0.023	**-0.354***	0.921	0.016	0.476	0.114	0.712	0.059	0.476	0.115
	Control	0.259	-0.180	0.786	-0.044						
DS	**FMS**	0.547	0.097	0.846	0.031	0.476	0.114	0.074	0.282	0.926	-0.015
	Control	0.579	0.089	0.370	0.144						
DS/NT	**FMS**	0.175	0.216	0.972	-0.006	0.617	0.080	0.266	0.178	0.947	-0.011
	Control	0.522	0.103	0.416	0.131						
DS/TT	**FMS**	0.108	0.255	0.653	0.072	0.595	0.086	0.090	0.268	0.655	-0.072
	Control	0.412	0.132	0.270	0.176						
NT/TT	**FMS**	0.108	0.255	0.953	-0.072	0.595	-0.086	0.090	0.268	0.655	0.075
	Control	0.412	-0.132	0.270	-0.176						

FMS: Fibromyalgia syndrome, BMI: Body Mass Index, SSS: Symptom severity scale, WPI: Widespread pain index, TT: Total Thiol, NT: Native Thiol, DS: Disulfide, DS/NT: Disulfide/Native Thiol, DS/TT: Disulfide /Total Thiol, NT/TT: Native Thiol/Total Thiol, TAS: Total Antioxidant Status, TOS: Total Oxidative Status, OSI: Oxidative Stress Index

Discussion

In this study, patients with FMS had lower TAS, TOS, and TT levels and a higher DS/NT ratio than healthy controls. In contrast, serum asprosin, OSI, NT, DS, DS/TT, and NT/TT values did not differ significantly between the groups. Overall, these findings suggest partial alterations in oxidative-antioxidative balance and thiol-disulfide homeostasis in FMS rather than a uniform disturbance across all measured parameters. We found that FMS patients had more upper back, lower back, and neck pain; that pain was more frequent on the left side of the body.

In a study examining 729 patients with FMS based on Rheumatic Diseases Bank data, WPI was found to be 10.0, and SSS was 6.4 (32). In our study, WPI was 10.00±2.24. Although the SSS was found to be 8.26±1.39, it was similar to the value found in the literature.

To the best of our knowledge, no previous study has examined the association between asprosin and FMS. In this respect, our study may be considered the first to explore this relationship. Asprosin has mixed roles in the central nervous system, peripheral tissues, and organs, and these roles are mainly related to appetite, glucose metabolism, insulin resistance, and cell apoptosis. Research indicates that it has a significant function in the pathophysiology of diabetes mellitus, obesity, cardiovascular diseases, and polycystic ovary syndrome (33-37). The relationship between FMS and obesity has been previously demonstrated (38,39).

Although serum asprosin levels were higher in the FMS group, the difference between the groups did not reach statistical significance. Therefore, our findings do not support a definitive role for asprosin in the pathophysiology of FMS. Nevertheless, the positive correlations of asprosin with BMI and WPI in the FMS group may indicate a possible association with metabolic status and pain extent in these patients.

Previous studies have suggested that oxidative imbalance may contribute to the pathophysiology of FMS (6, 7). Altındağ et al. reported lower TAS levels and higher oxidative stress-related parameters in patients with FMS (20). In our study, TAS was also significantly lower in the FMS group. However, unlike some previous reports, TOS was also lower in our patients, and although OSI was numerically higher, the difference was not statistically significant. Therefore, our findings suggest a disturbance in redox balance rather than unequivocal evidence of increased oxidative stress.

Fidan et al. (24) reported lower DS/NT and DS/TT ratios and higher NT/TT ratios in patients with FMS compared with controls. In our study, the pattern was only partially different: the DS/NT ratio was significantly higher in the FMS group, whereas DS/TT and NT/TT did not differ significantly between groups. This discrepancy may be related to differences in sample characteristics, exclusion criteria, or unmeasured lifestyle factors such as smoking and alcohol use.

Some studies have reported higher NT and NT/TT values together with lower DS-related ratios in FMS, whereas others have found no significant associations between thiol-disulfide parameters and clinical variables such as pain severity or symptom duration (24,25). Our findings do not indicate a uniformly opposite pattern; rather, they suggest a partially different thiol-disulfide profile. In addition, we did not observe significant correlations between symptom duration, SSS, and oxidative stress parameters. Our correlation analysis showed that age was positively correlated with TAS and TT, whereas NT was negatively correlated with age in the FMS group.

In some studies, TAS levels and antioxidant enzymes, including superoxide dismutase and catalase, were reported to be reduced in patients with FMS (21, 40). Similarly, we found TAS levels to be lower in the FMS group. However, TAS was not correlated with BMI in the FMS group; instead, a negative correlation between BMI and TAS was observed in the control group.

Neyal et al. reported elevated TOS and OSI levels together with reduced TAS levels in patients with FMS (22). In our study, TAS was similarly lower in the FMS group; however, TOS was also lower, and OSI did not differ significantly between groups. These discrepancies may be related to differences in patient characteristics, disease stage, exclusion criteria, or laboratory methodology.

One of the main limitations of our study was that only female participants were included. This approach was adopted because FMS is more prevalent in women and because it allowed us to establish a more homogeneous study population by minimizing sex-related variability. However, this selection limits the generalizability of our findings, particularly to male patients and to the broader population of individuals with FMS. Therefore, our results should be interpreted with caution, and further studies including both sexes and more diverse patient populations are needed to validate these findings.

Another limitation of our study was that detailed data on potential confounding factors that may influence oxidative stress and/or asprosin levels, such as dietary habits, physical activity level, and mood disorders, were not collected. Since fibromyalgia is a multifactorial condition, these factors may affect both metabolic and oxidative pathways, and their absence may have influenced the observed associations. Future studies in which nutrition, exercise, depression, and anxiety are assessed using standardized methods may allow for a more comprehensive interpretation of these biomarkers in FMS.

Conclusion

In conclusion, our findings do not support a definitive role for asprosin in FMS; however, its correlations with BMI and WPI may represent a preliminary signal of potential relevance. Similarly, the observed changes in TAS, TOS, TT, and DS/NT suggest a partial disturbance in redox balance and thiol-disulfide homeostasis rather than a consistent increase in oxidative stress. Further studies with larger cohorts are required to confirm these findings and better define their role in the etiopathogenesis of FMS.

** This is derived from the medical specialty thesis titled "Investigation of serum/plasma total oxidant/antioxidant, thiol-disulfide, and asprosin levels in fibromyalgia patients," completed by Ali Güneri under the supervision of Serap Satış at the Department of Physical Medicine and Rehabilitation, Harran University.*

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