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Original Article

The relationship of serum vaspin level with clinical parameters in patients with fibromyalgia syndrome

Muhammet Şahin Elbastı[1*], Emine Kaçar[2]

[1] *Elazığ Medical Hospital, Department of Physical Medicine and Rehabilitation, Elazig, Türkiye*
[2] *Firat University, Faculty of Medicine, Department of Physiology, Elazig, Türkiye*

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Abstract

Vaspin plays a regulatory role in lipid and glucose metabolism and is a therapeutic adipokine against impaired glucose intolerance in obese individuals. We aimed to investigate serum vaspin levels in patients with FMS and whether there was any relationship between vaspin levels and metabolic and clinical parameters in fibromyalgia. A total of 64 female patients who applied to an outpatient clinic due to widespread pain lasting more than three months were included in the study. The patients were divided into two groups: 32 in the fibromyalgia group and 32 in the healthy controls. The socio-demographic characteristics of the patients were evaluated with the standard evaluation form. Age, weight, height, blood pressure, body mass index (BMI), waist circumference, presence of menopause were recorded. Pain intensity was evaluated with visual analogue scale (VAS). The Fibromyalgia Impact Scale (FIS) was utilized to measure quality of life and functional status. Metabolic syndrome components were significantly different in the fibromyalgia group compared to the control group ($p < 0.05$). While 22 patients (68.8%) in the fibromyalgia group met the diagnostic criteria for metabolic syndrome, three patients (9.4%) in the control group met these criteria. In the fibromyalgia intra-group correlation, vaspin was significantly positively correlated with BMI and waist circumference ($p<0.05$). In the control group, vaspin indicated a statistically significant positive correlation with BMI. This study elaborated that waist circumference, insulin, and insulin resistance were significantly higher in the fibromyalgia patients compared to the healthy control group. This was confirmed by the finding that significantly more patients met the diagnostic criteria for metabolic syndrome. Additionally, vaspin was considerably higher in fibromyalgia patients and thus it was positively correlated with BMI and waist circumference.

Keywords: FMS (fibromyalgia syndrome); Metabolic Syndrome; Obesity; Vaspin; Waist Circumference

1. Introduction

Fibromyalgia syndrome (FMS) is a chronic musculoskeletal disease of unknown etiology, characterized by widespread body pain and the presence of subjective tender points in specific anatomical regions. In many patients, chronic widespread pain may be accompanied by various complaints such as sleep disturbance, fatigue, stiffness, drowsiness, depression, dysmenorrhea, sicca symptoms, irritable bowel syndrome, palpitations, urethral syndrome, memory and cognitive disorders [1].

Fibromyalgia is defined as a chronic syndrome of unknown cause that progresses with widespread body pain, fatigue, sleep disturbance, impairment in cognitive functions, and anxiety, and genetic, neurological, psychological, sleep-related, and immunological factors are listed among its possible causes [2]. The prevalence of fibromyalgia is between 0.2% and 6.6%, 2.4% to 6.8% in women, 0.7% to 11.4% in cities, 0.1% to 5.2% in rural areas, and 0.1% to 5.2% in special populations. It has been stated that it varies between 0.6 and 15% [3]. Its prevalence in the general population is 2% [4]. The disease is 6 – 9 times more common in women [3]. Although fibromyalgia is usually seen in middle-aged women, it can also affect children, adolescents, and the elderly [5].

Fibromyalgia is in a group called central sensitization syndromes. This group also includes chronic fatigue syndrome, functional dyspepsia, interstitial cystitis, irritable bowel syndrome, temporomandibular joint dysfunction, myofascial pain, posttraumatic stress disorder, and restless legs syndrome. Fibromyalgia can be seen together with these diseases or other regional musculoskeletal pain syndromes. Fibromyalgia is also considered in the group of functional somatic syndromes because the physical symptoms cannot be fully explained [6].

Vaspin is secreted from both visceral fat tissue and subcutaneous fat tissue in humans. However, studies reveal that vaspin expression is higher in visceral fat tissue. In addition to white adipose tissue, it is stated that vaspin is expressed in tissues such as liver, stomach, pancreas, skin and hypothalamus. Studies reveal that vaspin plays a regu-

* Corresponding author.
E-mail address: muhammetsahinelbasti@gmail.com (M. Ş. Elbastı).
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latory role in lipid and glucose metabolism and is a therapeutic adipokine against impaired glucose intolerance in obese individuals [7]. It is stated that serum vaspin expression decreases with progressive diabetes, but this level reaches normal levels with insulin treatment. It is noted that serum vaspin levels also increase in obese individuals. It is speculated that increased vaspin may be a metabolic defense against insulin resistance [8]. On the other hand, it is stated that vaspin suppresses hormones such as Leptin, TNF-α, and Resistin, which increase with obesity and stimulate the synthesis of the adiponectin hormone, which decreases with obesity [9].

Seeger et al. (2008), found that vaspin levels were higher in women and that gender was an independent predictor of circulating vaspin in the study population. They reported that gender-dependent regulation also occurs in adiponectin and leptin. Surprisingly, vaspin serum concentrations were low in lean individuals and competitive athletes engaged in long-term physical activity but increased in cases of weight loss associated with a physical activity program [10]. According to Youn et al. (2008), the explanation for this paradox is that serum vaspin concentration is regulated differently after rest and exercise. This is also true for other adiponectins [11].

Within the scope of this research, we aimed to investigate serum vaspin levels in patients with FMS and whether there was any relationship between vaspin levels and metabolic and clinical parameters in patients with FMS.

2. Materials and Methods

This study was designed from a perspective. A total of 64 female patients who applied to Şırnak State Hospital Physical Medicine and Rehabilitation outpatient clinic due to widespread pain (pain in the left, right, lower, and upper quadrants of the body and axial skeleton) lasting more than three months were included in the study.

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Ethics committee approval has been granted from our institution with protocol number 10275, and informed consent has been obtained from all participants.

The patients were divided into two groups: 32 in the fibromyalgia group and 32 in the healthy controls. The socio-demographic characteristics of the patients were evaluated with the standard evaluation form. Age, weight, height, blood pressure, body mass index (BMI), waist circumference, presence of menopause were recorded. The waist circumference measurement points were adjusted according to World Health Organisation (WHO) recommendations from the middle of the distance between the lower edge of the rib and the spina iliac point. Pain intensity was evaluated with visual analogue scale (VAS). The Fibromyalgia Impact Scale (FIS) was utilized to measure quality of life and functional status. International Diabetes Foundation (IDF) - 2005 criteria were followed for the diagnosis of metabolic syndrome. These criteria are abdominal obesity (waist circumference: ≥ 94 cm in men and ≥ 80 cm in women) and at least two of the following: Triglycerides ≥ 150 mg/dl HDL: < 40 mg/dl in men, < 50 mg/dl in women) Blood pressure ≥ 130/85 mmHg or receiving hypertension treatment Fasting blood glucose ≥ 100 mg/dl or previously diagnosed Type 2 DM .

Serum vaspin levels were measured using the ELISA (Enzyme-Linked Immunosorbent Assay) method. This method offers high sensitivity (12.371 pg/mL) and specificity; the reference range for mean serum vaspin concentration ranges from 15 to 3500 pg/mL. The kit used was performed according to the protocols provided by the manufacturer and the results were calibrated with standard curves.

2.1. Inclusion Criteria

Women between the ages of 20 and 50 who met the ACR 2013 fibromyalgia diagnostic criteria and had widespread body pain lasting more than 3 months were included in the study.

2.2. Exclusion Criteria

Patients who cannot be contacted cognitively, individuals with uncontrolled endocrine diseases (Thyroid, Parathyroid), those with systemic inflammatory rheumatic diseases (Rheumatoid arthritis, Ankylosing spondylitis), those with diabetes mellitus, those with malignancy, fracture, stroke, organ failure, pregnant women, those who entered menopause were excluded.

2.3. Statistical Analysis

Patient data collected within the scope of the study were analyzed with the IBM Statistical Package for the Social Sciences (SPSS) for Windows 26.0 (IBM Corp., Armonk, NY) package program. Frequency and percentage for categorical data and mean and standard deviation for continuous data were given as descriptive values. For comparisons between groups, the "Independent Sample T-test" was used for two groups, and the "Pearson Chi-Square Test" was used to compare categorical variables. The results were considered statistically significant when the p-value was less than 0.05.

3. Results

The clinical and demographic characteristics of both groups are denoted in Table 1. No significant difference was observed between the two groups regarding demographic data ($p>0.05$). When the two groups were compared in terms of BMI ($p>0.663$) and weight ($p>0.877$), there was no statistically significant difference. At the same time, waist circumference was significantly different between the two groups ($p=0.041$). Insulin resistance was detected in 23 people (71.9%) in the FMS group and 13 people (40.6%) in the control group ($p = 0.012$). Insulin and insulin resistance were significantly higher in the FMS group compared to the control group ($p<0.05$) (Table 1). Similarly, the VAS score and FIS score were significantly higher in the FMS group compared to the control group ($p<0.05$) (Table 1). Vaspin was significantly higher in the FMS group compared to the control group ($p = 0.03$) (Table 1).

When the groups were compared in terms of metabolic syndrome components, a significant difference was observed in all metabolic syndrome parameters in the FMS group compared to the control group ($p <0.05$) (Table 2). While 22 patients (68.8%) in the FMS group met the diagnostic criteria for metabolic syndrome, three patients (9.4%) in the control group met these criteria.

In the FMS intra-group correlation, Vaspin was significantly positively correlated with BMI and waist circumfe-

rence ($p<0.05$) (Table 3). No significant relationship was found between vaspin and other parameters (Table 3). In the control group, vaspin indicated a statistically significant moderated positive correlation only with BMI, while no statistically significant relationship was found with other parameters (Table 3).

4. Discussion

Vaspin was concluded higher in the FMS group compared to the control group. Vaspin was found to be positively correlated with BMI in both groups and waist circumference in FMS patients in thşs study. In addition, a significant difference was observed in all metabolic syndrome parameters in the FMS group compared to the control group. This study was concluded higher levels of vaspin in FMS patients with the relationship between vaspin and metabolic syndrome.

Vaspin (visceral adipose tissue-derived sprinkle) was first described by Hida et al. (2000) and consists of 415 amino acids [13]. Vaspin is secreted from both visceral fat tissue and subcutaneous fat tissue in humans. However, studies reveal that vaspin expression is higher in visceral fat tissue [14]. In addition to white adipose tissue, it is stated that vaspin is expressed in tissues such as liver, stomach, pancreas, skin and hypothalamus [15]. Various studies noted that the average serum vaspin concentration is ~ 1 ng/mL, and the reference range is between 0.01 and 6.74 ng/mL. The recently discovered vaspin has a paracrine effect on visceral tissue and an endocrine effect on the central nervous system [16]. There is limited information on the direct effects of vaspin on pain and inflammation, but some studies have suggested that vaspin may play a role in inflammatory processes [17]. Since fibromyalgia is characterised by chronic pain and inflammation, vaspin may have an effect on these processes. The effect of vaspin on fibromyalgia symptoms is important, especially in terms of the relationship between insulin resistance and pain. High levels of vaspin may be indicative of insulin resistance and metabolic dysfunction [18]. This is associated with chronic inflammatory processes that cause worsening of symptoms in fibromyalgia patients. Further research is needed to understand how the effects of vaspin in adipo-

Table 1. Clinical, laboratory and demographic data between groups.

Parameters (Mean±SD)	**FMS Group (n=32)**	**Control Group (n=32)**	**P-value**
Age/year	37,63±6,80	38,53±7,56	,455
Kilogram/kg	70,09±11,72	69,72±7,27	,877
Height/cm	161,94±6,49	162,75±5,21	,463
BMI/kg/cm^2	26,78±4,60	26,31±2,37	,663
Insulin	13,93±6,22	9,22±4,63	**,003****
Insulin Resistance	3,58±1,90	2,14±1,16	**<,001****
VAS	8,69±1,49	4,50±1,13	**<,001****
FEA	75,02±10,84	27,34±6,37	**<,001****
Vaspin/(pg/mL)	1919,98±1647,57	1010,77±920,20	**,030***

Table 2. Metabolic Syndrome parameters between groups.

Parameters (Mean±SD)	**FMS Group (n=32)**	**Control Group (n=32)**	**P-value**
Waist Circumference/cm	88,68±9,09	82,34±9,28	**,041***
SBP/ mmHg	128,90±9,30	113,43±8,92	**<,001****
DBP/ mmHg	80,93±7,77	73,12±5,64	**<,001****
Fasting Blood Glucose/ (mg/dL)	102,46±19,22	93,40±20,68	**,013***
Triglyceride/ (mg/dL)	201,31±131,86	120,93±56,63	**,001****
HDL/ (mg/dL)	47,15±7,82	55,03±10,54	**,001****

Table 3. Vaspin Correlation of both groups.

	FMS Group Vaspin		**Control Group Vaspin**	
	Spearman r	**P**	**Spearman r**	**P**
Age	-,077	,673	-,224	,218
BMI	,502	**,003****	,455	**,009****
FEA	,326	,068	,105	,566
VAS	,090	,625	-,283	,117
Waist Circumference	,608	**<,001****	,118	,521
SBP	-,207	,255	-,241	,183
DBP	-,219	,228	,134	,463
Insulin Resistance	,146	,426	,129	,480
Triglyceride	-,187	,305	-,174	,340
HDL	,267	,139	,276	,127

se tissue are linked to pain in the muscular and nervous system. For example, it could be examined whether increased levels of vaspin affect the release of neurotransmitters in the brain that modulate pain perception.

It is stated that serum vaspin levels also increase in obese individuals. It is estimated that increased vaspin may be a metabolic defense against insulin resistance [19]. On the other hand, it is stated that vaspin suppresses hormones such as Leptin, TNF-α, and Resistin, which increase with obesity and stimulates the synthesis of adiponectin hormone, which decreases with obesity [13]. Researchers state that vaspin serum concentrations and mRNA expressions increase in parallel with obesity, metabolic syndrome, and Type 2 DM. Additionally, studies are showing that vaspin serum concentration may be related to an individual's food consumption [20]. Metabolic disorders and obesity are also common in fibromyalgia patients, therefore vaspin levels may be different in this population. Studies have shown that vaspin levels are associated with BMI and waist circumference in fibromyalgia patients [7, 21]. The significant relationship between obesity and vaspin in our study may be due to the relationship between FMS and vaspin. According to the authors' knowledge, no study investigating vaspin levels in FMS patients was found. Jian et al. (2014) compared serum vaspin levels in 148 diabetic patients and 193 control groups and found that vaspin showed a positive correlation with HDL in the control group and with BMI in the diabetic patient group [21]. Von Loeffelholz et al. (2010) reported that normal-weight individuals had higher serum vaspin concentrations than underweight, obese, and overweight individuals [22]. Another study reported that vaspin concentration was higher in women than men [11]. Saboori et al. (2015) reported that vaspin concentration was higher in obese women aged between 20 and 50 compared to thin women. There was no significant relationship between vaspin level and fasting glucose, LDL-C, HDL-C, and triglyceride levels [23]. Another study reported that individuals with central obesity had higher serum vaspin concentrations than healthy individuals [24]. The results of our study are compatible with these studies in the literature. Another study reported that vaspin concentration was higher in women than men [11].

It has been stated that the BMI values of patients diagnosed with FMS are significantly higher than those of healthy individuals and that these individuals are in the risk group for metabolic syndrome. Therefore, it is essential to provide nutrition education to individuals diagnosed with FMS, monitor their diet, and gain physical activity habits [25]. In a study conducted with patients diagnosed with FMS, it was found that there was no significant difference in symptoms between obese and slightly obese patients. Still, patients with normal BMIs had a significant improvement in their symptoms compared to somewhat overweight and obese patients [26]. Vaspin was positively correlated with BMI and waist circumference. In the control group, vaspin indicated a statistically significant positive correlation with BMI. Vaspin was considerably higher in the FMS group compared to the control group. In a study conducted to determine the prevalence of overweight and overweight in female patients diagnosed with FMS, it was found that the prevalence of obesity in patients diagnosed with FMS (61%) was higher than the prevalence of obesity in society (38%) [27]. In a study investigating the body composition of women diagnosed with FMS in Southern Spain, it was found that the prevalence of obesity (33.7%) was higher than the reference values (26.4%) of women of the same age in the country [28]. A study evaluating the body composition of individuals diagnosed with FMS found that the body fat percentages of individuals diagnosed with FMS were significantly higher compared to the reference body fat percentages of healthy women [29]. Additionally, considering that patients are usually diagnosed with FMS at the age of 40 – 50, it can be concluded that the individuals are in the pre-menopausal period. Therefore, when the body composition of individuals is examined during this period, it is known that there is an increase in body fat tissue, especially abdominal fat tissue, and a decrease in estrogen levels and physical activity [30].

Obesity is a risk factor for various metabolic complications, and among these complications, impaired blood sugar regulation is one of the most important, and the most common is Type 2 DM. Parallel to the increase in the prevalence of obesity, there has also been a significant increase in the prevalence of Type 2 DM. Our study found that waist circumference was significantly different between the two groups. Insulin and insulin resistance were significantly higher in the FMS group compared to the control group: 23 patients (71.9%) in the FMS group and 13 people (40.6%) in the control group. Similarly, the VAS and FIS scores were significantly higher in the FMS groups than in the control groups. The findings of our research correlated with these studies. A significant difference was observed in all metabolic syndrome parameters in the FMS group compared to the control group ($p<0.05$). While 22 patients (68.8%) in the FMS group met the diagnostic criteria for metabolic syndrome, three patients (9.4%) in the control group met these criteria.

Our study has some limitations. The small sample size may make it difficult to generalise the findings. In addition, the focus of the study on only one gender caused us to miss the opportunity to evaluate the relationship between vaspin and fibromyalgia with differences between genders.

Future studies should be conducted on a larger and heterogeneous population. Further studies should investigate the longterm effects of vaspin on metabolic syndrome in FMS patients.

5. Conclusion

This study elaborated that waist circumference, insulin, and insulin resistance were significantly higher in the fibromyalgia patients compared to the healthy control group. This was confirmed by the finding that significantly more patients met the diagnostic criteria for metabolic syndrome. Additionally, vaspin was considerably higher in fibromyalgia patients and thus it was positively correlated with BMI and waist circumference.

Abbreviations

BMI: Body mass index; FBG: Fasting Blood Glucose; FIS: Fibromyalgia Impact Scale; FMS: Fibromyalgia syndrome; SPSS: Statistical Package for the Social Sciences; TNF-α: Tumor Necrosis Factor Alfa; VAS: Visual Analogue Scale; VASPIN: Visceral Adipose Tissue-Derived Sprinkle; WHO: World Health Organisation.

Competing interests
The authors declare that they have no competing interests.

Consent for Publication
The original article is not under consideration by another publication, and its substance, tables, or figures have not been published previously and will only be published elsewhere.

Ethical Declaration
All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Ethics committee approval has been granted from our institution. Informed consent has been obtained from all participants.

Data Availability
This review article does not include any personal or patient data.

Authors' contributions
All of the authors have participated in the design, execution, and analysis of the study, and they have approved the final version.

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