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Evaluation of Metabolic Syndrome Prevalence and Parameters in Patients with Fibromyalgia

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ABSTRACT

Objectives: We aimed to evaluate the metabolic syndrome (MetS) parameters in patients with fibromyalgia syndrome.

Methods: Age, weight, height, body mass index, waist and hip circumferences, and blood pressure were recorded. Laboratory parameters included fasting blood glucose and insulin, high-density lipoprotein, and triglyceride, HOMA-IR.

Results: Thirty-five female patients aged 20-64 years with fibromyalgia and 29 age-matched healthy controls were included in this case-control study. Although MetS was more prevalent in fibromyalgia patients than the control group, the difference did not reach a statistically significant level [7 (20.0%) vs. 5 (17.2%), p=0.770]. The prevalence of high waist circumference was significantly higher in the fibromyalgia group than the control group [23 (65.7%) vs. 6 (20.7%), p<0.001]. High blood pressure was also more prevalent in fibromyalgia group [10 (28.6%) vs. 1 (3.4%), p=0.009]. Insulin resistance and dyslipidemia prevalence did not show a significant difference between groups (p=0.830 and p=0.250, respectively).

Conclusion: Although statistically insignificant, metabolic prevalence increases in patients with fibromyalgia, while some MetS parameters, including waist circumference, and systolic and diastolic blood pressures, were significantly higher in fibromyalgia. Therefore, fibromyalgia patients may be under greater risk of MetS than the general population. For a definitive conclusion on the MetS and fibromyalgia, further large-scale studies are needed.

Keywords: Fibromyalgia, metabolic syndrome, insulin resistance

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INTRODUCTION

Fibromyalgia is characterized by widespread musculoskeletal pain often associated with sleep disorders, mood changes, or irritable bowel syndrome.[1,2] It is a common noninflammatory chronic pain disorder affecting 2-5% of the general population.[3] Although fibromyalgia is a debilitating condition, it does not cause specific laboratory, imaging, and histopathological abnormalities, or permanent deformity and sequelae.[2] The underlying mechanism of fibromyalgia is mostly unknown; however, several risk factors, including neuroendocrinological abnormalities and stress, have been implicated in etiology.[4–7] Current knowledge indicates that it is a state of disordered pain regulation, i.e., central sensitization caused by hyperexcitement of the central nervous system as a result of the psychological or physical stress.[8–10]

Metabolic syndrome (MetS), on the other hand, refers to five risk factors, including obesity, insulin resistance, hypertension, hypertriglyceridemia, and dyslipidemia, which occur together

and increase the chance of having systemic diseases chiefly diabetes, cardiovascular disease, neurodegenerative disease, and cancer.[11] Although the exact pathophysiology of MetS is not known, insulin resistance, lipid overflow, and stress have been suggested to contribute to the development of MetS.[12,13]

In patients with rheumatic diseases, the presence of cytokines, along with increased risk for cardiovascular diseases, indicated a need to examine the prevalence of the MetS in these diseases.[12] Although the relationship between the many rheumatological diseases and MetS has been investigated and the prevalence of MetS in various rheumatic diseases has been reported between 14%-63%, the prevalence of MetS in patients with fibromyalgia has not been studied in the literature.[14,15] Since stress and neuroendocrinological mechanisms have been suggested in the etiology of both MetS and fibromyalgia, MetS may be commonly seen in patients with fibromyalgia. Providing knowledge of the risk of MetS in patients with fibromyalgia will be the first step for early diagnosis and management of this fatal metabolic condition. We aimed to evaluate the prevalence of MetS and whether there is an increase in MetS parameters in patients with primary fibromyalgia syndrome.

METHOD

Study Design and Population

This was a case-control study. The patient group included 35 female subjects aged 20-64 years who were diagnosed with fibromyalgia syndrome in Turgut Ozal University Medical Faculty Department of Rheumatology between January 2012 and January 2013. Besides, age-matched healthy controls were included in this study. All study subjects signed an informed consent form before participation.

Diagnosis of MetS

To diagnose MetS, we used the US National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATPIII) description.[11] According to NCEP-ATPIII, presence of at least three of the following criteria was accepted as diagnostic for MetS: central obesity (waist circumference ≥ 88 cm for females), dyslipidemia (triglyceride ≥150 mg/dL or high-density lipoprotein cholesterol (HDL-cholesterol) <50 mg/dL for females), blood pressure ≥130/85 mmHg, and fasting plasma glucose ≥110mg/dL.[11]

Parameters Evaluated

Age, anthropometric and laboratory characteristics of subjects were recorded. On physical examination, weight, height, waist and hip circumferences, and blood pressure were measured. Body mass index (BMI) was calculated as kg/m^2 using weight and height measurements. Waist and hip circumferences were measured while the patient was standing. Waist circumference was accepted as the narrowest distance between the lower point of the costal arch and spina iliaca anterior superior. Hip circumference was measured at trochanter major level covering the pubic bone in the front and gluteus maximus muscle at the back.

Laboratory parameters included fasting blood glucose, HDL-cholesterol, and triglyceride, all of which were measured spectrophotometrically with Roche Cobas C501 device. Fasting insulin level was determined by the electrochemoimmunoassay method (Roche Cobas 6000 module device). The homeostasis model assessment-insulin resistance (HOMA-IR) was calculated according to the formula: HOMA-IR=[fasting insulin (μ/mL)×fasting glucose (mg/dL)]/405. An increase in HOMA-IR values indicates an increase in insulin resistance. HOMA-IR >2.7 indicates insulin resistance.[16]

The exclusion criteria were inflammatory rheumatologic diseases (e.g., polymyositis), metabolic diseases (e.g., diabetes mellitus, hypothyroidism and Cushing disease), inflammatory muscle disease, coronary arterial disease, chronic infection, malignancy, and pregnancy.

Statistical Analysis

The SPSS software package for Windows (Statistical Package for Social Sciences, version 20.0, SPSS Inc., Chicago, IL, USA) was used for all analyses. The study data were summarized with descriptive statistics such as frequency, percentage, mean, standard deviation, median and interquartile range [IQR]. The normal distribution of data was tested using the Kolmogorov Smirnov test. The categorical variables of fibromyalgia and control groups were compared by Chi-square or Fisher's exact test. Independent sample Student t-test or Mann-Whitney U test was used for normally or non-normally distributed continuous study variables to compare with fibromyalgia group versus control groups, respectively. A p-value less than 0.05 was considered significant.

RESULTS

Thirty-five (54.6%) female patients with fibromyalgia and 29 (45.4%) age-matched healthy controls were included in this study. The clinical and laboratory characteristics of patients are summarized in Table 1.

Although MetS was more prevalent in fibromyalgia patients than the control group, the difference did not reach a statistically significant level (p=0.770). Similarly, there was no significant difference between fibromyalgia and control groups regarding the prevalence of insulin resistance (p=0.830). On the other hand, the prevalence of high waist

Table 1. The anthropometric measures and laboratory characteristics of patients in fibromyalgia and control group

	Fibromyalgia group (n=35)	Control group (n=29)	p
Age (years)	44.9±9.9	30.2±7.1	<0.001*
Body mass index (kg/m^2)	23.9±3.1	21.9±4.1	0.002*
Waist circumference (cm)	84.2±12.3	72.3±13.3	<0.001*
Hip circumference (cm)	102.7±7.3	96.9±7.1	0.002*
Systolic blood pressure (mmHg)	122.7±12.1	111.2±10.9	<0.001*
Diastolic blood pressure (mmHg)	73.2±12.7	62.5±6.6	<0.001*
Fasting blood glucose (mg/dL)	92.2±10.7	89.2±8.5	0.230*
Triglyceride (mg/dL)	89.7 [69.3]	83.4 [41.3]	0.085†
HDL cholesterol (mg/dL)	56.1±13.4	55.6±12.6	0.909*
HOMA-IR index	2.6 [1.4]	2.5 [1.4]	0.624†

HOMA-IR: Homeostasis model assessment-insulin resistance.
Data were given as mean±standard deviation and median [IQR].
*Student t test, †Mann-Whitney U test.

circumference was significantly higher in the fibromyalgia group than the control group (p<0.001). High blood pressure was also more prevalent in the fibromyalgia group than the control group (p=0.009). Dyslipidemia prevalence did not show a significant difference between groups (p=0.250). The prevalence of MetS and its components in fibromyalgia and control groups are summarized in Table 2.

DISCUSSION

Fibromyalgia is nine times more common in females than males, and its prevalence increases with age being highest in subjects over 60 years.[15,17–19] MetS, on the other hand, affects approximately 20% of the general population and 40% of those over 60 years.[20] One of the most important epidemiological studies of MetS in Turkey, Heart Disease and Risk Factors in Turkish Population (TEKHARF) study, indicated that the prevalence of MetS increased from 24.4% in 1990 to 36.2% in 2000 in Turkish population.[21] A recent prevalence study covering all regions of Turkey in 2013 reported the prevalence of MetS as 41.8% in the female population with a mean age of 45.5 years.[22] Given that the mean age of our study population was lower and the prevalence of MetS increases with age, the lower rate of MetS in our study population is not surprising. Although our study had a similar design in general with the prevalence study by Gundogan et al., the MetS diagnostic criteria was fasting blood glucose in our study instead of glycosylated hemoglobin (HbA1c) that was used in the study.[22]

Obese patients have an increased risk of rheumatic diseases. Similarly, in patients with fibromyalgia, the prevalence of obesity is approximately 40%, and overweight 30%. Obesity has also been reported to aggravate fibromyalgia symptoms.[23,24] However, the relationship between obesity and fibromyalgia is not very clear. Impaired physical activity, sleep disorders, cognitive disorders, thyroid dysfunction, hypothalamic-pituitary-adrenal axis dysfunction,

Table 2. The prevalence of MetS and its components in fibromyalgia and control groups

	Fibromyalgia group (n=35)	Control group (n=29)	p
MetS	7 (20.0%)	5 (17.2%)	0.770
Insulin resistance*	16 (45.7%)	14 (48.3%)	0.830
High waist circumference†	23 (65.7%)	6 (20.7%)	<0.001
High blood pressure‡	10 (28.6%)	1 (3.4%)	0.009
Dyslipidemia§	12 (34.3%)	14 (48.3%)	0.250

*HOMA-IR>2.7, †Waist circumference ≥88 cm, ‡Blood pressure ≥130/85 mmHg, §Triglyceride ≥150 mg/dL or HDL-cholesterol <50 mg/dL.
MetS: Metabolic syndrome.
Data were given as n (%).
Chi-square and Fischer's exact test.

metabolic and hormonal disorders, such as endogenous opioid system disorders, presence of more pain receptors in the fat tissue, high levels of proinflammatory cytokines and increased mechanical load have been charged for the relation between fibromyalgia and obesity.[23–26] On the basis of these proposed relationships, we aimed to evaluate the prevalence of MetS and its components in fibromyalgia patients.

In a previous study by Loevinger et al. comparing 109 fibromyalgia patients with 42 control subjects, MetS was found to be 5.56 times more frequent in the fibromyalgia group.[27] In our study, the prevalence of MetS was slightly higher in the fibromyalgia group than the control group without a statistically significant difference. Loevinger et al. also reported that waist circumference, high HbA1c levels, serum triglyceride levels, and systolic and diastolic blood pressures were significantly higher in fibromyalgia patients compared to the control group.[27] Unlike this study, we found that there was no significant relation between triglyceride and HDL-cholesterol levels and fibromyalgia, but BMI was higher in patients with fibromyalgia.

As mentioned above, the relationship between obesity and fibromyalgia is not very clear. We found higher BMI in patients with fibromyalgia compared to control. This is similar to the findings of a recently published study of 105 fibromyalgia and 61 control subjects, which also reports that fibromyalgia patients had significantly higher BMI than the control group.[28] Another recent study from Spain also reported that the mean BMI of 183 fibromyalgia patients was 27.3 kg/m^2, which was relatively higher than the control group.[29] Furthermore, Cordero et al. found that total cholesterol, low-density lipoprotein cholesterol, and triglyceride levels of patients with fibromyalgia were 57.9%, 63.4%, and 19.9% higher than the healthy control group, respectively.[29] In the present study, triglyceride levels, although higher in patients with fibromyalgia, did not show a statistically significant difference from the control group.

In a recent study from our country, the mean systolic blood pressure was measured as 136.7 mmHg and 133.9 mmHg, and diastolic blood pressure as 87.3 mmHg and 85.9 mmHg in fibromyalgia and control groups, respectively.[30] On the contrary, our findings showed that both systolic and diastolic blood pressures were significantly higher in the fibromyalgia group than the control group.

Similar to MetS, patients with diabetes mellitus had a higher risk of fibromyalgia than the general population due to stress, anxiety and depression that arose from chronic disease state.[25,26] Therefore, we evaluated fasting blood glucose levels in the context of our study, which primarily focused on MetS prevalence in fibromyalgia patients. Our results indicated that there was an insignificant slight increase in fasting blood glucose levels of fibromyalgia patients compared to the control group.

Although there are many studies investigating the association between MetS and inflammatory rheumatic diseases, such as rheumatoid arthritis and ankylosing spondylitis, to our knowledge, there is almost no study in the literature on the relationship between MetS and fibromyalgia.[31–33] The available studies are mostly limited to clinical and laboratory parameters separately of MetS in fibromyalgia.[27,29,30] To our knowledge, the present study is the first study to evaluate the prevalence of MetS in patients with fibromyalgia. However, it is not devoid of limitations. The main limitation of this study was its small sample size, which may be the underlying cause of not statistically significant differences between groups.

CONCLUSION

MetS and fibromyalgia are two common clinical conditions. In the previous studies, some parameters of MetS were found to be associated with fibromyalgia. In the present study, we showed that although statistically insignificant, metabolic prevalence increases in patients with fibromyalgia, while some MetS parameters, including waist circumference, and systolic and diastolic blood pressures, were significantly higher in patients with fibromyalgia. Therefore, we suggest that fibromyalgia patients may be under greater risk of MetS than the general population. For a definitive conclusion on the MetS and fibromyalgia, further large-scale studies are needed.

This study was presented as poster abstract during the 38th Türkiye Endokrinoloji ve Metabolizma Hastalıkları Kongresi & 2. Ulusal Lipid Sempozyumu on 11th-15th May 2016 in Cornelia Diamond Hotel, Belek, Antalya.

This study was derived from the first author's specialty thesis work.

Disclosures

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Ethics Committee Approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.Written con-

sent was obtained from the Local Ethics Committee of Turgut Ozal University Faculty of Medicine with the decision number 99950669/577 on 28.06.2013 for this study.

Authorship Contributions: Concept – H.K.K.; Design – H.K.K.; Supervision – H.K.K.; Materials – T.D.; Data collection &/or processing – T.D.; Analysis and/or interpretation – T.D., H.K.K.; Literature search – T.D., H.K.K.; Writing – T.D.; Critical review – H.K.K.

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