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Fibromyalgia Syndrome in Patients with Type 2 Diabetes Mellitus

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Abstract

BACKGROUND/AIMS: This study aimed to assess the frequency of fibromyalgia syndrome (FMS) in patients with type 2 diabetes mellitus (DM). Additionally, we aimed to evaluate the association of pain severity with glycemic control of DM.

MATERIALS AND METHODS: Patients with type 2 DM who were being followed up in an endocrinology clinic were included in this study. FMS was diagnosed according to the 2010 criteria set by the American College of Rheumatology. The patients' pain during the morning and sleep was evaluated by the Visual Analog Scale (VAS). Fasting blood glucose and hemoglobin A1c (HbA1c) levels were measured to assess the glycemic control of DM. Their quality of life was assessed with the Health Assessment Questionnaire (HAQ).

RESULTS: Ninety-four patients (62 female, 32 male; mean age of 56.5±10.1 years) with type 2 DM and 40 healthy controls (26 female, 14 male; mean age of 52.3±10.1 years) were enrolled in this study. FMS was diagnosed in 19.1% of the diabetic patients and 7.5% of the control group ($p=0.120$). No significant difference was observed between the HbA1c levels of the type 2 DM patients with or without FMS ($p=0.814$). There was a weak negative correlation between VAS day and night scores and HbA1c levels in the diabetic patients ($r=-0.20$, $p<0.01$; $r=-0.27$, $p<0.01$, respectively). HAQ scores were higher in the diabetic patients with FMS when compared with those patients without FMS ($p<0.01$).

CONCLUSION: FMS frequency (using 2010 ACR criteria) was higher in those patients with type 2 DM compared to the healthy controls. Furthermore, good metabolic control of DM decreased daily pain among the diabetic patients and increase their quality of life.

Keywords: Fibromyalgia, diabetes mellitus, pain, prevalence

INTRODUCTION

Fibromyalgia syndrome (FMS) is a chronic condition with widespread pain. Other symptoms include fatigue, sleeping disorders, memory problems, altered sensory perceptions, bowel or bladder problems, and depression.[1,2] FMS has a prevalence of 0.2-6.6% in the general population, 2.4-6.8% in females, 0.5-1.6% in males, and 0.6-15% in special populations (healthcare workers, medical students, low socioeconomic levels, serious train crash survivors, Caucasians and Turks, the elderly, textile workers and primary care center users).[3] FMS and its associated medical comorbidities can significantly increase society's economic burden and result in work loss due to temporary or permanent disability.[4-6] FMS prevalence is found to be higher in specific populations such as inflammatory bowel disease, chronic hepatitis C, hyperprolactinemia and hemodialysis patients and diabetes mellitus.[7] Diabetes mellitus (DM) type 2 is also a chronic disease, mainly characterized by sensorial abnormalities which can mimic the

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symptoms of FMS.[8] The prevalence of fibromyalgia has been shown to be higher in type 2 diabetic patients than in the healthy population in several previous studies.[8-10] Previous studies have used the ACR 1990 diagnostic criteria (88.4% sensitivity and 81.1% specificity)[11] and found a wide range of FMS prevalence rates in type 2 DM.[8-12] According to one study, the 2010 criteria were found to be three times more diagnostic than the 1990 ACR criteria.[13,14] As far as we are aware, there was no consideration of the FMS's health effects in the diabetic population in the previous studies. Therefore, we performed this study to assess FMS frequency in patients with type 2 DM, using the ACR 2010 criteria set. The secondary endpoint was to evaluate the association of pain severity in FMS with the glycemic control of DM and to evaluate health-related quality of life in these patient groups.

MATERIALS AND METHODS

Patients and Study Design

This study was designed as a cross-sectional case-controlled study conducted between January, 2016 and January, 2019. Patients with type 2 DM who were being followed up in the endocrinology clinic were enrolled. Diabetic patients diagnosed more than six months previously, both those on oral anti-diabetic and insulin treatments, were included in this study. Those patients with anemia, hyperthyroidism, hypothyroidism, malignancy, pregnancy, pre-existing inflammatory rheumatologic diseases, abnormal neurological findings (such as allodynia, hyperalgesia, altered deep tendon reflexes), or the presence of diabetic wounds were excluded. Additionally, any patients on analgesics, anti-convulsants, or antidepressant medications were excluded since these could alter the degree of pain. Healthy volunteers from the hospital staff were recruited into this study as controls.

Data Collection

After the patients' history was taken, a single researcher made physical examinations. Complete blood count, blood biochemistry, erythrocyte sedimentation rate, C-reactive protein, urinalysis, rheumatoid factor, and thyroid-stimulating hormone were studied for differential diagnosis. The patients' glycated hemoglobin A1c (HbA1c) levels measured on admission or within the previous two months were accepted as valid. Their current pain severity was investigated, and all patients and control group members filled out a questionnaire measuring their health-related quality of life. Written informed consent was obtained from all subjects. Ethical approval was taken from Çukurova University's Faculty of Medicine Local Ethical Committee (protocol number: 46, date: 02.10.2015).

Outcome Measures

The patients' pain during the morning and night was evaluated by a 10 cm linear Visual analog scale (VAS). Respondents mark the location on a 10 cm line corresponding to their current degree of pain.

Fasting blood glucose and HbA1c levels were measured to assess the disease control of DM. HbA1c levels were measured with high-performance liquid chromatography. Fasting blood glucose levels <100 mg/dL and HbA1c levels <6.5% were accepted as good glycemic control (according to the EASD criterion).[15]

The quality of life was assessed with the Health Assessment Questionnaire (HAQ). Each question is scored between 0-3, and the total scores can range from 0 to 60; higher scores indicate worse function and more significant disability.

Statistical Analysis

For statistical analysis, the SPSS 22 program was used. The analysis was performed using non-parametric tests. Student's t-test, Mann-Whitney U, chi-square, and Fisher's exact test were used for comparisons where appropriate. For correlation analysis, Pearson's correlation analysis was used. A value of p less than 0.05 was accepted as statistically significant.

RESULTS

Ninety-four patients (62 female, 32 male) with type 2 DM and 40 healthy controls (26 female, 14 male) were included in this study. The mean age of the diabetic patients and the healthy controls were statistically similar (56.5±10.1 years vs. 52.3±10.1 years; p=0.458). The mean age of the patients with and without FMS within the diabetic group were statistically similar (55.0±7.0) years vs. 55.3±10.8 years; p=0.907). The demographic and clinical characteristics of the subjects are given in Table 1.

Table 1. Sociodemographic features and laboratory parameters of the study patients

Variables	Type 2 DM (n=94)	FMS (+) (n=18)	FMS (-) (n=76)	Control (n=40)
Age (mean ± SD), years	56.56±10.14	55.04±7.09	55.33±10.81	52.30±10.15
Gender (female) n (%)*	62 (65.9)	15 (83.3)	47 (61.8)	26 (65)
Duration of disease (months, mean ± SD)	94.91±70.90	72.66±67.40	65.53±74.84	-
BMI	29.36±4.40	24.31±4.25	28.8±4.31	25.08±4.67
Current smoker, (%)	13.5	11.1	14.4	15.0
ESR	15.05±10.51	13.4±11.98	9.97±11.0	-
CRP	0.85±3.23	0.47±0.37	0.62±2.96	-
Fasting glucose	137.66±44.54	141.00±48.89	136.89±43.80	-
HbA1c	7.30±1.57	7.22±1.28	7.32±1.64	-
VAS morning*#	3.00±2.94	5.19±3.09	2.03±2.46	1.42±2.07
VAS night*#	2.52±2.70	4.80±3.17	1.64±2.08	1.25±1.87
HAQ score**#	1.48±1.94	4.21±2.01	1.23±1.80	0.65±1.25

#p<0.05, ##p<0.001 (patients with type 2 DM vs. control) *p<0.05, **p<0.001 (patients with FM vs. patients without).
DM: diabetes mellitus, FMS: fibromyalgia syndrome, SD: standard deviation, BMI: body mass index, ESR: erythrocyte sedimentation, CRP: C-reactive protein, HbA1c: hemoglobin A1c, VAS: visual analogue scale, HAQ: Health Assessment Questionnaire.

The prevalence of FMS was statistically similar in both the diabetic group and the control group (19.1% vs. 7.5%, p=0.120). The fasting blood glucose levels were statistically similar in those diabetic patients with or without FMS (141.00±48.89 mg/dL vs. 136.89±43.80 mg/dL; p=0.734).

HbA1c levels were statistically similar in the diabetic patients with or without FMS (7.22±1.28% vs. 7.32±1.64%; p=0.814). The duration of diabetes was similar in both patient groups with or without FMS (72.66±67.40 days vs. 65.53±74.84 days; p=0.709). The mean VAS morning scores were significantly higher in the diabetic patients than in the healthy controls (3.00±2.94 vs. 1.42±2.07; p=0.003). The mean VAS night scores were significantly higher in the diabetic patients than in the healthy controls (2.52±2.70 vs. 1.25±1.87; p=0.008).

There were weak negative correlations between VAS morning and VAS night scores with the fasting glucose levels in the diabetic patients (r=-0.24, p<0.01; r=-0.27, p<0.01, respectively). There were weak correlations between VAS morning and night scores with the HbA1c levels (r=-0.20, p<0.01; r=-0.27, p<0.01, respectively). The results of correlation analysis between the fasting glucose and HbA1c levels with other variables are shown in Table 2.

HAQ scores were higher, indicating worse quality of life in the diabetic subjects compared to the healthy controls (p=0.013). HAQ scores were statistically significantly higher in the diabetic patients with FMS than the patients without FMS (p<0.01). HAQ scores were higher in the control group's FMS patients compared to those subjects without FMS (p<0.001) (Table 1).

DISCUSSION

The prevalence of FMS in the general population varies between 0.2% and 6.6%.[3] In Turkey, the incidence is believed to be around 100,000 and gradually increasing.[16] In the present study, we have found a 19.1% frequency of FMS in diabetic patients according to the ACR 2010 diagnostic criteria. There are several studies investigating the prevalence of FMS in diabetic patients. The FMS prevalence in diabetic patients was found to be 9% in the study of Patucchi et al.[9] and 23.3% in the study of Wolak et al.[10] In the studies of Yanmaz et al.[8] and Tishler et al.[12] using the 1990 ACR criteria for diagnosis, FMS prevalence in diabetic patients was 18% and 17%, respectively. According to data from the clinical database of Clalit Health Services of Israel,[17] in which they evaluated the frequency of DM in FMS patients, the prevalence of DM was found to be 19.8% among 14,296 FMS patients, which was higher than the non-FMS controls.

Table 2. Correlation analysis of pain and health quality

	Fasting glucose (r, p)	HbA1c (r, p)
Age	-0.001, 0.990	-0.936, 0.229
BMI	0.148, 0.145	0.507, 0.663
Disease duration	0.269, 0.010	-0.739, 0.471
Smoking duration	0.054, 0.615	0.189, 0.879
ESR	0.057, 0.594	-0.852, 0.374
VAS morning	0.244, <0.010	0.200, <0.010
VAS night	0.270, <0.010	0.270, <0.010
VAS global	0.270, <0.010	0.224, 0.023
HAQ score	0.063, 0.558	-0.629, 0.567

BMI: body mass index, ESR: erythrocyte sedimentation rate, VAS: visual analogue scale, HAQ: Health Assessment Questionnaire, HbA1c: hemoglobin A1c.

The ACR 1990 diagnostic criteria were used to diagnose FMS in the studies mentioned above, which do not include the symptoms of FMS apart from pain.[11] The 2010 diagnostic criteria set for FMS includes both pain and the other somatic symptoms of FMS such as fatigue, sleep disturbances, stiffness, and cognitive impairment; therefore, these updated criteria view fibromyalgia as a systemic symptom-based disease, rather than a peripheral musculoskeletal disease with the pathology centered on the tender points. The ACR 2010 criteria correctly classify FMS as 88.1%[14] but include systemic symptoms, which may be an advantage for usage in the diabetic population where chronic painful conditions could overlap.[18,19] In the study of Yanmaz et al.[8], there were no healthy age and sex-matched control groups. Instead, they used rheumatoid arthritis patients as their control group, with these patients having a higher prevalence of FMS than the healthy population. In another study conducted by Tishler et al.[12], the FMS prevalence was higher in the diabetic population than in the healthy controls. In our study, the frequency of FMS in our diabetic patients was higher than in the control group, which corroborates the former studies' data. However, the difference did not reach a statistically significant level. There are some methodological differences between our study and the former studies. Our study solely included type 2 diabetic patients and used the ACR 2010 criteria for FMS diagnosis; therefore, we could not make an exact comparison with the previous studies.

We found no differences between the FMS positive and negative diabetic groups regarding their glycemic control, but there was a weak correlation between their pain levels and fasting glucose and HbA1c levels. Similar to our study, Yanmaz et al.[8] found no difference in fasting glucose and HbA1c levels between diabetic patients with or without FMS. However, contrary to this, Tishler et al.[12] found higher HbA1c levels in diabetic patients with FMS, and they also reported a positive correlation between the number of tender joints and HbA1c levels. According to a study by Hoff et al.[20], chronic widespread pain is 1.6 times more likely among patients with DM than those without DM. Although they could not show a clear-cut association between chronic widespread pain, non-fasting glucose and HbA1c levels; they observed a linear trend of decreasing prevalence of chronic non-widespread MSCs with increasing HbA1c. Hence, with the results of these former studies and the present study, we cannot conclude that there is a causal association between blood glucose control and the occurrence of FMS. Diabetes is a leading cause of neuropathy in patients, and diabetic neuropathy mainly manifests as pain. One of our study's major limitations was that we could not objectively exclude neuropathic pain in the diabetic patients. In our study, we believe that pain severity measured with VAS could reflect both "neuropathic pain" and "pain caused by fibromyalgia". Therefore, it is possible that the negative correlation between pain severity and glycemic control in this study may be mainly due to neuropathic pain.

The quality of life in diabetic patients was lower than in the healthy controls. Moreover, the health quality was lower in those patients with FMS in both the diabetic and control groups than in those patients without FMS. Health quality can be affected by several variables such as pain, sleep disturbances, and also the presence of macro-vascular and microvascular complications. It is not surprising that the diabetic population had a worse health quality result when compared with the healthy controls. However, it should be emphasized that the concomitant FMS presence had significant negative consequences for

the patients' quality of life according to the results of the present study, which confirms the importance of the accurate diagnosis of this disease.

Study Limitations

There were some limitations of our study. First, we have not used sophisticated methods such as EMG, or vascular angiography to evaluate the existence of peripheral neuropathy or ischemic neuropathy in our subjects. We cannot ignore that DM affects vascular reactivity[21] and induces diabetic neuropathy.[22] However, the ACR 2010 criteria include some specific clinical findings such as sleep disturbances, depression, anxiety balance, and memory problems which may support FMS syndrome rather than vascular changes. Also, the duration of diabetes mellitus, which is one of the most important variables in causing diabetic neuropathy, was found to be similar in type 2 DM patients with or without FMS. Secondly, our sample size was small. Third, since this study was a cross-sectional study, we could not evaluate the effect of treatment modalities of diabetes on the occurrence of FMS. Our study's strong points were that we used the 2010 ACR criteria for FMS, which include both pain and other systemic symptoms, so this is thought to be a more accurate tool to diagnose FMS in the diabetic patient group. In addition, we had a healthy control group for comparison. What's more, as far as we know, this is the first study to evaluate the influence of FMS on the health quality of the diabetic population.

CONCLUSION

In conclusion, consistent with similar studies, we found a high FMS prevalence rate (19.1%) in type 2 DM patients compared to the healthy controls (7.5%). However, no correlation was observed between metabolic control and the prevalence rate of FMS. Diabetic patients may have an increased prevalence of pain due to different etiologies. An early and accurate diagnosis of FMS may increase health quality in this patient group. Further studies with larger sample sizes, including an objective test to exclude peripheral neuropathy, would provide a more accurate identification of FMS syndrome in the diabetic population.

MAIN POINTS

- The FMS rate is higher in type 2 diabetes patients.
- There is no correlation between glycemic control and the prevalence of FMS.
- The health quality is lower in both diabetic patients and healthy controls with FMS when compared with those patients without FMS.

ETHICS

Ethics Committee Approval: Ethical approval was taken from Çukurova University's Faculty of Medicine Local Ethical Committee (approval number: 46, date: 02.10.2015).

Informed Consent: Written informed consent was obtained from all subjects.

Peer-review: Internally peer-reviewed.

Authorship Contributions

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

DISCLOSURES

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

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