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Research Article

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THE FREQUENCY OF FIBROMYALGIA IN FEMALE PATIENTS WITH IMPAIRED FASTING BLOOD GLUCOSE: CROSS-SECTIONAL STUDY

BOZULMUŞ AÇLIK GLUKOZU OLAN KADIN HASTALARDA FİBROMİYALJİ SIKLIĞI: KESİTSEL ÇALIŞMA

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Öz

Amaç: Bozulmuş açlık glukozu olan kadınlarda fibromiyalji sıklığını değerlendirmek.

Materyal ve Metot: Dahiliye polikliniğine nonspesifik nedenlerle başvuran kadınlar arasından, rutin muayenesinde açlık kan şekeri düzeyi 100-126 olanlar çalışma grubunu (Grup 1) ve açlık kan şekeri değeri 100'den küçük olanlar kontrol grubunu oluşturdu (Grup 2). Bozulmuş açlık glukozu (BAG) olan hastalara (Grup 1) oral glukoz tolerans testi (OGTT) yaptırıldı ve 2. Saat OGTT değeri 140'ın altında olan hastalar çalışmaya dahil edildi. Fibromiyalji Etki Anketi (FIQ) kullanılarak fonksiyonel durum değerlendirildi. Fibromiyalji tanısı için ağrı yerleşim skoru (AYS) ve semptom etkilenme skorlaması (SES) değerlendirildi.

Bulgular: Ortalama yaş Grup 1'de 48.99 ± 7.50 (n = 73) ve Grup 2'de 47.84 ± 7.92 idi (n = 73), aralarında anlamlı fark yoktu. Ortalama VKİ (vücut kitle indeksi) Grup 1'de 30.41 ± 5.01, Grup 2'de 28.00 ± 4.61 idi, aradaki fark anlamlıydı ($p < 0.05$). Gruplar mesleki durum, eğitim yılı, medeni durum bakımından benzerdi. Grup 1'deki hastaların% 26'sına, Grup 2'deki hastaların% 11'ine fibromiyalji tanısı kondu ve aradaki fark anlamlıydı ($p < 0.001$). Ortalama FIQ Grup 1'de 44.27 ± 21.98 ve Grup 2'de 24.95 ± 21.49 idi, aradaki fark anlamlıydı ($p < 0.001$). Glukoz düzeyi, AYS ($r = 0.368$, $p < 0.001$), SES ($r = 0.322$ $p < 0.001$) ve FIQ ($r = 0.287$, $p < 0.001$) ile ilişkiliydi.

Sonuç: Fibromiyalji, bozulmuş açlık glukozu bozuk olan kadın hastalarda, açlık glukoz düzeyi normal olanlara göre daha yaygındır. Glukoz düzeyi AYS, SES ve fonksiyonellik ile ilişkilidir. Klinik bir hastalık olmasa da bozulmuş açlık glukozu sadece diyabet gelişimi için bir risk faktörü değil aynı zamanda kadınlarda fibromiyalji için bir risk faktörüdür.

Anahtar Kelimeler: Fibromiyalji, bozulmuş açlık glukozu, fibromiyalji etki anketi.

Abstract

Objectives: To assess the frequency of fibromyalgia among women with impaired fasting glucose.

Materials and Methods: The sample was selected from the female patients who applied to the Internal Medicine clinic and whose fasting blood glucose level were 100-126 in their routine examination (Group1) and patients whose fasting blood glucose were less than 100 constituted the control group (Group2). Oral glucose tolerance test (OGTT) has been applied to patients with impaired fasting glucose (IFG) and whose 2nd hour OGTT levels were under 140 has been included. Functional status was assessed by using the Fibromyalgia Impact Questionnaire (FIQ). Pain Location Inventory (PLI), and Symptom Impact Questionnaire (SIQR) were evaluated for the diagnosis of fibromyalgia.

Results: Mean age was 48.99±7.50 in Group1 (n=73) and 47.84±7.92 in Group2 (n=73) with no significant difference between them. Mean BMI (body mass index) was 30.41±5.01 in Group1 and 28.00±4.61in Group2, this difference was significant ($p<0.05$). 26% of the patients in Group1, 11% of the patients in Group2 were diagnosed with fibromyalgia and difference was highly significant ($p<0.001$). Mean FIQ was 44.27±21.98 in Group1 and 24.95±21.49 in Group2, this difference was also significant ($p<0.001$). Glucose level was associated with PLI ($r=0.368$, $p<0.001$), SIQR ($r=0.322$ $p<0.001$) and FIQ ($r= 0.287$, $p<0.001$).

Conclusion: Fibromyalgia is more prevalent in female patients with IFG than in patients with normal fasting glucose levels. Glucose level is associated with both PLI, SIQR and functionality. Although not a clinical disease, IFG is not only a risk factor for development of diabetes but also a risk factor for fibromyalgia in women.

Keywords: fibromyalgia, impaired fasting glucose, fibromyalgia impact questionnaire.

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Introduction

Fibromyalgia (FM) is a painful syndrome characterized by chronically widespread musculoskeletal pain, stiffness, and multiple tender points.[1] Pain is a characteristic feature of FM; in addition, this disease is usually associated with depression, fatigue, sleep disturbance, and disability.[2]

The etiology and pathogenesis of this disease is unknown, and no single factor causes all the symptoms of FM.[3] From the viewpoint of metabolic etiology, it can be said that patients with FM are often overweight or obese and have diabetes mellitus (DM) and metabolic syndrome.[4,5,6] Diabetes Mellitus is a chronic metabolic disease in which the organism cannot benefit from carbohydrates, fats and proteins sufficiently because of deficiencies in insulin or insulin-induced defects.[7] Although pathogenesis is not fully understood, musculoskeletal problems are common in DM patients.[5] FM is one of these musculoskeletal problems.[7] Also fibromyalgia is reportedly more common in diabetic patients; further, it is interesting to note that FM-related findings are observed in patients with poor diabetes control.[8] Chronic pain and DM may have common biological background factors, such as high levels of bradykinin and interleukin-6 as well as upregulation of kinin receptors [B1 or B2 receptors]. Cytokines acting through B1 and B2 receptors also play a role in FM pathogenesis as well as in DM.[9,10] Studies suggest that chronic pain is more common in individuals with impaired fasting glucose or DM than in those without glucose metabolism disorders .[5,8] Impaired fasting glucose (IFG) is the stage between normal glucose homeostasis and diabetic h hyperglycaemia [fasting plasma glucose is higher than 100 mg/dL but lower than 126 mg/dL] that reflects impaired glucose regulation under basal conditions.[11] Individuals with IFG show evidence of early beta-cell insufficiency and they can be described as prediabetic.[12] To the best of our knowledge, the frequency of FM has not been investigated among individuals with IFG. Thus, we aimed to evaluate the frequency of FM in IFG patients.

Materials and Methods

This cross-sectional study was conducted between January 2016 and December 2016. Patients agreed for study participation by providing written consent as per the requirement of the local ethics committee (Gaziosmanpasa University, approval date July 2015, number 125). The experimental group subjects were selected from female patients who visited were referred to the internal medicine outpatient clinic for suspicion of diabetes and whose fasting blood glucose level was between 100 mg/dL and 126 mg/dL; the control group subjects were selected from the same group whose fasting blood glucose level was < 100 mg/dL. Patients with type 2 diabetes, a severe systemic disease (chronic kidney disease, liver disease etc.), psychiatric disease, hypothyroidism or hyperthyroidism, or any connective tissue disease were not included in the study. In addition, patients who used medications that influenced the FM symptoms, such as analgesics, antidepressants,

and anticonvulsive medications, were also excluded. Male patients were not included in our study, since fibromyalgia mainly affected women.[8]

Patients who applied to the internal medicine outpatient clinic for non-specific reasons were included in the study based on routine laboratory test results patients referred from the internal medicine clinic were examined by the same investigator (Ayla Cagliyan Turk) without knowing fasting blood glucose levels.

Experimental group subjects with IFG (Group 1) underwent an oral glucose tolerance test (OGTT), and patients with levels > 140 mg/dL at the 2 nd hour were excluded because they were diagnosed with "impaired glucose tolerance".[13] Total 73 patients who met the study's inclusion criteria were included; 6 patients were excluded because they had impaired glucose tolerance and 3 because of diabetes. The control group (Group 2) comprised 73 patients whose fasting blood glucose level was < 100 mg/dL and who agreed to participate in the study.

Implementation of OGTT: The patient was seated in a quiet room after 10-12 hour of overnight fasting, and blood samples were drawn. Thereafter, 75 g glucose solution dissolved in 300 mL of water was administered within 5 minutes. Two hours later, another blood sample was drawn. During the test, the patient was allowed to remain at rest, not eating, and not smoking.

The FM diagnosis was established according to 2013 Alternative Diagnostic Criteria following an examination by the Physical Medicine and Rehabilitation Specialist.[14] "2013 Alternative Diagnostic Criteria." was published by Bennet et al in 2013, for evaluating more areas in terms of the pain being questioned and grading the patients' symptoms in a wider range. For this purpose, Pain Location Inventory (PLI) and Symptom Impact Questionnaire (SIQR) were developed. Patients with symptoms and pain of at least 3 months, Pain Location Inventory (PLI) ≥ 17 and Symptom Impact Questionnaire (SIQR) score ≥ 21 are considered as FM. The pain localization inventory questions the constant feeling of pain in the past 7 days for each of the 28 areas defined in the body. Each point is accepted as one point. SIQR questions pain, energy, stiffness, sleep, depression, memory problems, anxiety, sensitivity to touch, balance problems, and sensitivity to loud sound, bright light, smell and cold. Each item is scored between 0-10. 10 separate scores are collected. The total score will be between 0 and 100. This total score is divided by 2 to get the SIQR score.[14]

Age (years), height (cm), weight (kg), body mass index (BMI) (kg/m^2), education status, occupation, marital status, regularity of exercise (2-3 days/week was accepted as regular exercise[15]), and number of tender points were recorded. In addition, their fasting glucose level (mg/dL) and 2-hour oral glucose tolerance test OGTT results were recorded from the laboratory examinations.

The functional status was assessed using the Fibromyalgia Impact Questionnaire (FIQ).[16] The reliability of the validity of the questionnaire was adapted by Sarmer et al.[17] This scale measures 10 different features, including

physical function, wellbeing, missing work, difficulty in performing professional duties at the workplace, pain, fatigue, morning fatigue, stiffness, anxiety, and depression. Except for the ability to feel good, low scores indicated healing or a lower effect of the disease. The FIQ was filled by the patients themselves. The maximum possible score for each subhead is 10; thus, the maximum possible total score is 100. While an average FM patient gets 50 points, more severely affected FM patients usually score > 70 points. FIQ was applied to both the patient group and the control group.

Statistical analyses

Continuous quantitative variables are expressed in terms of mean and standard deviation values. Mann-Whitney U Test was used for data that comprised independent measures and were not normally distributed. Spearman Correlation test was used for analyzing the correlation between the non-normality variables. All data analyses were performed using Statistical Package for the Social Sciences (SPSS) 21 package program. Group sample sizes of 31 and 31 achieve 99% power to detect a difference of 7,1 between the null hypothesis that both group means are 12,9 and the alternative hypothesis that the mean of group 2 is 5,8 with estimated group standard deviations of 6,8 and 5,9 and with a significance level [alpha] of 0,05000 using a two-sided Mann-Whitney test assuming that the actual distribution is uniform. Probability of $p < 0.05$ was accepted as significant. Power analysis was performed by G Power 3.

Results

Total 146 patients were included in the study. IFG (Group 1) was present in 73 patients, and the control group (Group 2) comprised 73 patients. The demographic data of the groups showed no differences in the education level, occupation, marital status, and exercise levels ($P > 0.05$) of the two groups. Moreover, a significantly higher proportion of Group 1 patients (26%, n = 19) than Group 2 patients (11%, n = 8) were diagnosed with FM as per the 2013 Alternative Diagnostic Criteria ($P < 0.05$).

The mean age of the patients in Group 1 (n = 73) was not significantly different from that of those in Group 2 [n = 73] [48.99 ± 7.50 years vs. 47.84 ± 7.92 years; $P > 0.05$]. A comparison of the BMI value, fasting glucose level, PLI, SIQR and FIQ averages of the groups are shown in Table 1. All values were significantly higher in Group 1 than in Group 2 (Table 1). The mean 2nd hour OGTT was 108.07 ± 21.86 mg/dL in Group 1.

When two groups were compared according to FIQ scores Group 1 had significantly higher scores than Group 2 in all subgroups ($p < 0.001$) (Table 2).

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Table 1. Comparisons of groups by baseline data

	Group 1 n = 73 Mean±SD	Group 2 n = 73 Mean±SD	Minimum-maximum	P
Age (years)	48.99 ± 7.50	47.84 ± 7.92	30-65	0.153
BMI (gr/m2)	30.41 ± 5.01	28.00 ± 4.61	18.73-45.72	< 0.001
Primary school graduates (%)	71.2	63		> 0.05
Housewife (%)	76.7	72.6		> 0.05
Regularly exercise (%)	20.5	24.7		> 0.05
Fasting glucose level (mg/dl)	106.92 ± 6.01	89.41 ± 6.15	72-124	< 0.001
Pain Location Inventory	12.90 ± 6.76	5.78 ± 5.90	0-29	< 0.001
Symptom Impact Questionnaire	20.84 ± 9.51	12.40 ± 8.41	0-43	< 0.001
Fibromyalgia Impact Questionnaire	44.27 ± 21.98	24.95 ± 21.49	0-95.25	< 0.001
Fibromyalgia rate % (n)	26 (n=19)	11 (n=8)		0.019

Mann-Whitney U Test, Group 1: Patients with Impaired Fasting Glucose, Group 2: Patients with Normal Fasting Glucose
Data are presented as mean ± standard deviation, SD: standard deviation

Table 2. Comparing the Groups According to FIQ Subgroups

	Group 1 n = 73 Mean±SD	Group 2 n = 73 Mean±SD	Minimum-maximum	P
Glucose (mg/dl)	106.92 ± 6.01	89.41 ± 6.15	72-124	< 0.001
FIQ- Physical Disability	3.14 ±1 .97	1.81 ±-1.46	0-9.08	< 0.001
FIQ- Feeling good	5.78 ± 3.34	3.11 ± 3.35	0-10	< 0.001
FIQ-Work days	3.51 ± 3.12	1.86 ± 2.99	0-10	< 0.001
FIQ-Working ability	4.22 ± 2.84	2.00 ± 2.66	0-10	< 0.001
FIQ-Pain	5.38 ± 2.51	2.93 ± 2.80	0-10	< 0.001
FIQ-Fatigue	5.26 ± 3.06	3.27 ± 2.71	0-10	< 0.001
FIQ-Feeling rested	4.48 ± 3.40	2.74 ± 2.74	0-10	0.002
FIQ- Stiffness	2.48 ± 2.71	1.15 ± 1.94	0-10	0.001
FIQ-Anxiety	4.88 ± 2.89	2.73 ± 2.86	0-10	< 0.001
FIQ- Depression	4.88 ± 3.06	2.70 ± 2.56	0-10	< 0.001

Mann-Whitney U Test, Group 1: Patients with Impaired Fasting Glucose, Group 2: Patients with Normal Fasting Glucose
Data are presented as mean ± standard deviation, SD: standard deviation

There was a significant positive correlation between the fasting glucose level and the pain location inventory (r = 0.386 P < 0.001), symptom score (r = 0.322 P < 0.001) and FIQ (r = 0.287 P < 0.001) in the whole group analyses. There was a significant positive correlation between the glucose level and FIQ subgroup scores (Table 3).

Table 3. Correlations between fasting glucose level and some variables in Group 1

Variables	Fasting glucose level (mg/dl)	
	r	p
Age	0.185	0.026*
Body Mass Index	0.251	0.002**
Pain location Inventory	0.386	<0.001**
Symptom Impact Questionnaire	0.322	<0.001**
Fibromyalgia Impact Questionnaire (average)	0.287	<0.001**
Physical disability	0.271	0.001**
Feelings of well-being	0.235	<0.001**
Work days	0.210	0.011*
Working ability	0.321	<0.001**
Pain	0.288	<0.001**
Stiffness	0.206	0.013*
Anxiety	0.269	0.001**
Depression	0.266	0.001**

Spearman rank correlation tests *p < 0.05 **p < 0.01

Discussion

Although previous studies have demonstrated the association between DM, impaired glucose tolerance with FM and chronic pain, our study is the first to show the relationship between IFG and FM. In our study, we found that the frequency of FM was significantly higher in women with IFG than in those without IFG.

Further, the fasting glucose level was associated with age, BMI, pain location inventory, symptom impact questionnaire and the FIQ averages. In addition, physical disability, feeling of well-being, work days, working ability, fatigue, pain, stiffness, anxiety and depression, and fasting glucose level were correlated in the FIQ subgroups, and the scores of all subgroups of FIQ in the IFG group were significantly higher.

The pathophysiology of FM syndrome is unclear; however, environmental, psychological, and genetic factors have been identified as being potential causal elements. With regard to the disease pathogenesis, current theories include central sensitization and hypothalamic-pituitary-adrenal axis dysregulation.[18]

The incidence of fibromyalgia in diabetic patients was reported to be 17%-23%. It is not fully understood why the frequency of FM is increased in diabetic patients. It can be thought that increased oxidative stress plays a role in both diseases.[19,20] In our study, we found FM rate in female IFG patients as 26% similar to DM patients.

In the studies conducted by Wolak et al., in which both women and men with 137 Type 2 DM were taken, the study group was compared with 139 age and gender compatible volunteers without diabetes.[21] Although there was no difference in the FM frequency between the male subjects in both the groups, diabetic men had more tender points than the non-diabetic men. Moreover, pain thresholds at the related points were significantly lower in the diabetic men than in the non-diabetic men. Diabetic women had a significantly higher prevalence of FM than the non-diabetic women [23.3% versus. 10.6%]. However, there were no significant differences between the two groups of women with respect to the number of tender points and pain threshold. In all the diabetic subjects, the number of tender points was directly correlated to the duration of diabetes. In our study, the rate of FM was significantly higher in the IFG group. The fasting glucose level was correlated with the number of tender points (PLI).

Shown in previous a study the HbA1c levels of diabetic patients with FM were significantly higher than those of the diabetic patients without FM.[8] Similarly, the number of tender points; pain scores and the prevalence of sleep disorders, fatigue, and headache were higher in diabetic patient group. Yanmaz et al. reported that there was no relationship between FM and glycosyl hemoglobin [HbA1c] and glycosylated hemoglobin [HbA1c] levels with age, height, weight, disease duration and fasting blood glucose levels in diabetic patients.[5] In our study, patients with IFG had higer frequency of FM than the control group, and the glucose level was related to the pain location inventory, symptom impact questionnaire, physical capacity, work days, working ability, and stiffness, anxiety and depression

Krein et al. conducted on 993 patients with diabetes, 60% subjects were found to have chronic pain.[22] Patients with chronic pain generally have a worse diabetic disability, and these patients face greater challenges in following a recommended exercise and meal plan.[22] Chronic widespread pain is a common condition not only in diabetics, but also in people with impaired glucose tolerance. In a study conducted by Mantyselka et al. on 480 patients that investigated daily chronic pain, impaired glucose tolerance, and diabetes, the prevalence of chronic pain was 21% in all patients. The prevalence was 18% in patients with normal plasma glucose levels and 38% in those with high plasma glucose levels. In this study, high plasma glucose level was defined as 109.90 mg / dl and above and high glucose levels and diabetes were associated with daily chronic pain.[23] In our study, impaired fasting glucose has been shown to be associated with pain.

All these clinical data may indicate that patients with abnormal glucose levels exhibit significant clinical manifestations. Those with mild glucose metabolism disorders and obvious diabetes should be screened for general, chronic pain conditions, not only for diabetic neuropathy. In a similar manner, individuals with persistent chronic pain may benefit from screening for leading conditions, such as diabetes and impaired glucose tolerance or impaired fasting glucose. Treatment of chronic pain is challenging, especially in patients with a chronic illness such as diabetes who take multiple medications. Blood glucose regulation in diabetic

patients can reduce pain. Normalizing blood glucose levels in patients with IFG also may reduce pain. However, the answer to this question can be demonstrated by prospective studies.

The most notable limitation of this study is that patients and control groups included patients admitted to the hospital. Because of the ease of access to the patients, the selection was made from the population coming to the hospital. This may have led to high rates of illness.

In conclusion, our study has demonstrated in female patients with IFG, the frequency of FM is more frequent than that in patients with a normal fasting blood glucose level. There is a significant relationship between the glucose level and the pain location inventory, symptom impact questionnaire and functional status due to FM. There is a disturbance in the functional capacity owing to FM in IFG patients. Physical capacity, work days, working ability, fatigue, pain and stiffness are associated; at the same time, anxiety and depression develop due to the abnormal glucose levels.

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