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How Common is Fibromyalgia in Patients with Hypothyroidism?

Hipotiroidili Hastalarda Fibromiyalji Sıklığı

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ABSTRACT

Objectives: Fibromyalgia (FM) is the most common cause of chronic generalized musculoskeletal pain. The etiology and the pathophysiology are still not clear but there are some studies that elucidate relationship between FM and thyroid diseases. The aim of this study was to determine the frequency of FM in patients with hypothyroidism.

Methods: This is a cross-sectional, single-center, and prospective study from Bakırkoy Dr Sadi Konuk Training and Research Hospital. A total of 180 patients – who were applied to internal medicine outpatient clinics – included in the study and the patients who described the generalized musculoskeletal pain were consulted to the physical medicine and rehabilitation outpatient clinics. Demographic data, laboratory findings, presence of thyroid disease, and FM were noted. Patients were evaluated with Beck Depression Questionnaire (BDQ) and FM Impact Questionnaire (FIQ) for FM patients.

Results: About 39.4% (n=71) of the patients had FM and 60.6% (n=109) of them did not have FM. There was a positive correlation between FIQ score and age at diagnosis and disease duration. As the age at diagnosis and duration of disease increased, the FIQ score increased by 37.3% and 25.7%, respectively. In addition, as BDQ increased, the FIQ score increased by 44.8%.

Conclusion: Signs and symptoms of hypothyroidism are similar to signs and symptoms of FM, and approximately 40% of patients with hypothyroidism could have FM concomitantly. Hence, the presence of a diagnosis of hypothyroidism should not cause us to miss the diagnosis of FM in these patients. Therefore, all patients with hypothyroidism should also be examined for FM.

Keywords: Fibromyalgia; hyperthyroidism; hypothyroidism; pain; thyroid diseases.

ÖZET

Amaç: Fibromiyalji, kronik yaygın kas-iskelet sistemi ağrısının en sık nedenidir. Etyoloji ve patofizyoloji henüz netlik kazanmamıştır. Ancak fibromiyalji ile tiroid hastalıkları arasındaki ilişkiyi aydınlatan bazı çalışmalar mevcuttur. Bu nedenle bu çalışmada, hipotiroidili hastalarda fibromiyalji sıklığının belirlenmesi amaçlanmıştır.

Yöntem: Bu çalışma, tek merkezli kesitsel, prospektif bir çalışmadır. Çalışmaya dahiliye polikliniğine başvuran hipotiroidi tanılı 180 hasta dahil edildi. Ağrılı hastalar fiziksel tıp ve rehabilitasyon polikliniğinde değerlendirildi, tanı konulan fibromiyalji hastalarının demografik verileri, laboratuvar bulguları kaydedildi. Hastalar, Beck Depresyon Anketi (BDA) ve Fibromiyalji Etki Anketi (FEA) ile değerlendirildi.

Bulgular: Hipotiroidili hastaların %39,4'ünde (n=71) fibromiyalji saptanırken, %60,6'sında (n=109) fibromiyalji mevcut değildi. FEA skoru ile tanı yaşı ve hastalık süresi arasında pozitif bir korelasyon vardı. Tanı yaşı ve hastalık süresi arttıkça FEA skoru sırasıyla %37,3 ve %25,7 oranında artış gösterdi. Ayrıca BDA skoru arttıkça FEA skoru %44,8 oranında artış gösterdi.

Sonuç: Hipotiroidizmin belirti ve semptomları fibromiyalji belirti ve semptomlarına benzer ve hipotiroidili hastaların yaklaşık %40'ında eş zamanlı fibromiyalji tanısı mevcut olabilir. Dolayısıyla hipotiroidi tanısının varlığı bu hastalarda fibromiyalji tanısının gözden kaçmasına neden olmamalıdır. Bu nedenle hipotiroidili tüm hastalar fibromiyalji açısından da değerlendirilmelidir.

Anahtar sözcükler: Ağrı; fibromiyalji; hipertiroidizm; hipotiroidizm; tiroid hastalıkları.

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Fibromyalgia (FM) is the most common cause of chronic generalized musculoskeletal pain and it is generally accompanied by the other symptoms such as cognitive disturbance, fatigue, and multiple somatic and psychiatric symptoms. The etiology and the pathophysiology are still not clear.[1,2] There is no evidence of inflammation in affected (muscles, tendons, and ligaments) tissues. The prevalence is approximately 2–3% and increases with age. It can affect both genders and all ages but it is more common in female, especially between the ages of 20 and 55 years.[3-6] Diagnostic criteria consist of detailed history, physical examination, and laboratory tests to exclude other causes of pain and fatigue. Due to difficulties in diagnosis, 2016 American College of Rheumatology (ACR) revised FM criteria is widely used as a standardized approach.[5]

Thyroid autoimmunity and thyroid disorders may contribute to FM. It is not clear how thyroid disorders contribute to FM development because there are limited number of studies in this field. However, according to an article published in 2012, the FM prevalence in autoimmune thyroid diseases has been reported to be between 30% and 40%.[7] Therefore, the view that there is an increase in FM prevalence of people with thyroid disease has pushed researchers to investigate the cause and some questions have arisen; Is there any relationship between increased inflammatory markers, thyroid antibodies, duration of thyroid disease, or other variables of the patients and how does it affect the risk of developing FM? Therefore, in this study, we aimed to determine the frequency of FM in patients with hypothyroidism and the variables that may affect this frequency.

Methods

This is a single-center, prospective, cross-sectional clinical study conducted at Bakirkoy Dr. Sadi Konuk Training and Research Hospital in between July 10, 2019, and March 30, 2020. Patients equal to or older than 18 years of age who were admitted to our hospital's internal medicine outpatient clinic for hypothyroidism or subclinical hypothyroidism were included in the study. Patients having an underlying disease such as malignancy, diabetes mellitus, rheumatic diseases, hypertension, atherosclerotic heart disease, major depression and using pregabalin, selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, and tricyclic antidepressant drugs were excluded from the study. Patients' age, gender, height, weight, body mass index (BMI), age at diagnosis, disease duration, laboratory findings, and FM status were recorded. A total of 180 patients included in the study and the patients who described the generalized musculoskeletal pain were consulted to the physical medicine and rehabilitation outpatient clinics. The study was approved by Ethical Committee of Bakirkoy Dr. Sadi Konuk Training and Research Hospital with 2019/13/10-8/07/2019. Informed consent was obtained from all participants. 2016 ACR revised criteria were used to diagnose FM and patients were divided into two groups according to whether or not they had FM (Group 1=FM positive and Group 2=FM negative). Patients having FM were evaluated with Beck Depression Questionnaire (BDQ) and FM Impact Questionnaire (FIQ). The relationship of the groups with the variables was evaluated.

Statistical analysis

Descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, and maximum) were used when evaluating the study data. Frequency and percentage values of categorical variables, and arithmetic mean and standard deviation values of quantitative variables are presented. Percentage distributions and frequency values are given for categorical data. In the relationship analysis, Kendall's tau-b relationship analysis, which is suitable for a continuous categorical data, was used. Independent sample t-test was used in group difference analysis. Significance was evaluated at the level of $p<0.05$.

Results

In our study, 180 patients who admitted to our outpatient clinic and newly diagnosed or with a known diagnosis of hypothyroidism or subclinical hypothyroidism were evaluated for FM. The study population was consisted of 166 women (92.2%) and 14 men (7.8%). In all patients, 39.4% (n=71) of them had FM and 60.6% (n=109) did not have FM. Descriptive statistical information for some variables is given in Table 1.

FM was found in 41% (n=68) of the women and 21.4% (n=3) of the men. FM status by gender is shown in Table 2. When we compared Group 1 and Group 2 in terms of duration of hypothyroidism, BMI, Vitamin D, and hemoglobin levels, no significant difference was found ($p>0.05$ for all) (Table 3).

When we compared the groups of patients with and without FM, there was no significant difference between the groups in terms of thyroid autoantibodies (Table 4). BDQ and FIQ

Table 1. Descriptive data of patients

	Min	Max	Mean	SD
Age (year)	18.00	73.00	42.0944	10.06498
Height (cm)	145.00	191.00	161.9056	7.86243
Weight (kg)	39.00	121.00	73.6906	14.91778
BMI (kg/m^2)	17.10	42.60	28.0932	5.25345
Age at diagnosis	5.00	65.00	35.3966	10.59331
Duration of hypothyroidism (month)	1.00	396.00	81.7889	74.33000
TSH	0.02	129.00	6.7031	13.78093
fT4	0.13	83.00	1.7164	8.09463
fT3	2.09	4.54	3.3259	0.47193
Anti-TPO	0.10	1155.00	283.7374	355.90997
Anti-TG	0.10	2419.00	167.0174	485.89286
Hemoglobin	6.90	16.00	12.9522	1.31083
White blood cell count	3.99	13.85	7.2085	1.70956
Platelet count	106.00	532.00	279.8920	64.71277
Urea	8.80	42.50	24.8515	6.38890
Creatinine	.14	196.00	1.7828	14.85248
Glucose	72.80	160.00	93.3848	12.14042
AST	10.00	69.00	21.8497	7.95626
ALT	3.00	96.00	20.8098	14.54003
LDL	52.00	283.00	140.5753	42.04346
TG	41.00	713.00	135.5000	96.03336
HDL	25.00	111.50	52.0864	12.74231
Total cholesterol	<93.00	393.00	217.6923	54.07854
CRP	.00	15.00	3.3872	3.35855
Sedimentation	4.00	49.00	15.2667	9.45045
Creatinine kinase	29.00	385.00	101.3784	57.85407
Vitamin B12	70.00	1255.00	237.2139	145.79699
Vitamin D	4.90	96.00	19.5663	10.22354

Min: Minimum; Max: Maximum; SD: Standard deviation. BMI: Body mass index; TSH: Thyroid-stimulating hormone; fT3: Tri-iodothyronine; fT4: Thyroxine; Anti-TPO: Anti-thyroperoxidase antibodies; Anti-TG: Anti-thyroglobulin antibodies; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; LDL: Low-density lipoprotein; TG: Triglyceride; HDL: High-density lipoprotein; CRP: C-reactive protein.

Table 2. Fibromyalgia status by gender

			Fibromyalgia		Total
			Positive	Negative	
Gender	Female	n	98	68	166
		%	59.0%	41.0%	
	Male	n	11	3	14
		%	78.6%	21.4%	

were performed to 36 of 71 patients (50.7%) diagnosed with FM. Thirty-five patients declined to perform BDQ and FIQ questionnaire. When we compared BDQ and FIQ scores

Table 3. t-test difference analysis for some values in terms of fibromyalgia

	Fibromyalgia	n	Mean	SD	p-value
Duration of hypothyroidism (month)	Negative	109	76.22	7.01	0.352
	Positive	71	90.33	8.00	
BMI	Negative	109	27.62	5.47	0.261
	Positive	71	28.81	4.84	
Vitamin D	Negative	97	18.77	8.22	0.132
	Positive	63	20.79	12.67	
Hemoglobin	Negative	107	12.96	1.40	0.096
	Positive	69	12.92	1.15	

BMI: Body mass index. *Significant difference for 0.05.

with the variables separately; while there was no significant correlation between BDQ score and age, gender, disease duration, age at diagnosis, anti-TPO, anti-TG, Vitamin B12, and Vitamin D; only there was a positive correlation between FIQ score and age at diagnosis and disease duration, but no significant correlation was found with other variables. As the age at diagnosis and duration of disease increased, the FIQ score increased by 37.3% and 25.7%, respectively. Analysis of BDQ and FIQ scores with the variables is shown in Table 5. In addition, the relationship between BDQ and FIQ score was examined and found that as BDQ increased, the FIQ score increased by 44.8%.

Discussion

FM is a disease characterized by hyperalgesia and allodynia that causes chronic widespread non-articular musculoskeletal pain and generalized tenderness.[8] The pathogenesis of FM is not entirely elucidated, the current evidences are support the concept of central nervous system malfunction resulting in amplification of pain transmission and interpretation.[8] It has long been known that there are similarities between the symptoms of thyroid dysfunction and the clinical findings in FM.[9] The previous studies reported that there are problems in the production and utilization of thyroid hormones in FM patients.[10] Furthermore, studies recently reported that there was an association between thyroid autoimmunity and FM.[11-13] In a study conducted with 79 patients diagnosed with Hashimoto thyroiditis (HT) in 2017,[14] the presence of FM was evaluated, and the frequency of FM in these patients was 62%. In patients with HT and FM, anti-TPO levels and duration of the disease were significantly higher in patients

Table 4. Anti-TPO and Anti-TG Mann–Whitney U differences analysis in terms of fibromyalgia

	Fibromyalgia	n	Mean rank	Mann–Whitney U	p-value
Anti-TPO	Negative	104	84.32		
	Positive	66	87.36	3309.5	0,694
	Total	170			
Anti-TG	Negative	102	80.67		
	Positive	65	89.23	2975,0	0,262
	Total	167			

*Significant difference for 0.05. Anti-TPO: Anti-thyroperoxidase antibodies; Anti-TG: Anti-thyroglobulin antibodies.

Table 5. Relationship analysis of some variables with BDQ and FIQ score

Variables		Correlation coefficient (r)	p value
Age	BDQ	−0.237	0.164
	FIQ	−0.265	0.119
Gender	BDQ	−0.151	0.379
	FIQ	−0.194	0.256
Height	BDQ	−0.073	0.671
	FIQ	−0.050	0.774
Weight	BDQ	−0.160	0.350
	FIQ	−0.215	0.208
BMI	BDQ	−0.123	0.474
	FIQ	−0.187	0.274
Age at diagnosis	BDQ	−0.086	0.616
	FIQ	0.373	0.025*
Duration of hypothyroidism (month)	BDQ	−0.107	0.535
	FIQ	0.252	0.008*
Anti-TPO	BDQ	0.063	0.729
	FIQ	−0.090	0.618
Anti-TG	BDQ	−0.155	0.398
	FIQ	−0.044	0.809
Hemoglobin	BDQ	−0.071	0.689
	FIQ	−0.270	0.123
White blood cell count	BDQ	−0.307	0.077
	FIQ	−0.145	0.412
Platelet count	BDQ	0.054	0.763
	FIQ	−0.021	0.907
C-reactive protein	BDQ	−0.092	0.629
	FIQ	−0.161	0.396
Sedimentation	BDQ	−0.094	0.629
	FIQ	−0.028	0.886
Vitamin B12	BDQ	0.014	0.937
	FIQ	0.180	0.317
Vitamin D	BDQ	−0.097	0.610
	FIQ	−0.116	0.543

*Significant difference for 0.05. BMI: Body mass index; Anti-TPO: Anti-thyroperoxidase antibodies; Anti-TG: Anti-thyroglobulin antibodies.

with HT than those without FM. However, in that study, researchers did not observe a significant difference between groups for age, weight, height, and BMI. They also found a strong positive correlation between FIQ and disease duration, age, TSH, and anti-TPO. They performed multiple regression analysis and TPOAb was seen to be an independent risk factor in FM patients.

In our study, the frequency of FM in patients with hypothyroidism and/or subclinical hypothyroidism was found to be 39.4% and female (F)/male (M) ratio was 68/3 with female dominance. However, we could not find any significant difference between the presence of FM and thyroid antibodies, disease duration, BMI, and age at diagnosis.

In another cross-sectional study[15] with 500 HT patients and 310 age- and sex-matched control patients, patients were evaluated for non-specific rheumatic manifestations. It was determined that there were minimal differences in regard to rheumatic manifestations between the groups and the most common manifestations were polyarthralgias and myalgias/FM, and non-specific rheumatoid manifestations observed 3-fold more in HT patients. When comparing HT patients with and without rheumatological manifestations, the ratio of female/male was high (24:1 vs. 5:1) and with higher age at the time of diagnosis. In our study, the absence of a control group was a limitation, but similarly in our study, the ratio of female/male was high (F:M=68:3).

In the study conducted by Soy et al.,[16] the presence of rheumatic diseases was investigated in 65 autoimmune thyroid patients. Hypothyroidism was detected in 50 patients (77%), hyperthyroidism was detected in 12 patients (18%), and 3 patients (5%) were euthyroid. In all patients, 56 of the them were female, nine were male and 62% of the patients had various rheumatic diseases with the most common was 20% FM. In our study, the frequency of FM in patients with thyroid dysfunction was common with a rate of 39.4% and consistent with this study, female gender was higher.

It should be kept in mind that the signs and symptoms of hypothyroidism are similar to signs and symptoms of FM, and approximately 40% of patients with hypothyroidism could have FM concomitantly. Hence, the presence of a diagnosis of hypothyroidism should not cause us to miss the diagnosis of FM in these patients. Therefore, all patients with hypothyroidism should also be examined for FM.

Disclosures

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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