How Common is Fibromyalgia in Patients with Hypothyroidism?

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Abstract

**Background:** Fibromyalgia (FM) is the most common cause of chronic generalized musculoskeletal pain and it is generally accompanied by the other nonspecific common symptoms. The etiology and the pathophysiology is still not clear but also there are some studies that show a relationship between FM and thyroid diseases. So, 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 cross-sectional, single center and prospective study. 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. We have evaluated demographic data, laboratory, presence of thyroid disease and FM, and Beck Depression Questionnaire (BDQ) and FM Impact Questionnaire (FIQ) for FM patients.

**Results:** 39.4% (n = 71) of the patients had FM and 60.6% (n = 109) of them did not. 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 is similar to signs and symptoms of FM, and approximately 40% of patients with hypothyroidism could have FM concomittantly. Therefore, all patients with hypothyroidism should also be examined for FM.

Introduction

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, multiple somatic and psychiatric symptoms. The etiology and the pathophysiology is still not clear (1,2). There is no evidence of inflammation in affected (muscles, tendons, ligaments) tissues. The prevalence is approximately 2 to 3 percent and increases with age. It can affect both gender and all ages but it is more common in female, especially between ages of 20-55 years (3-6). Diagnostic criteria consist of detailed anamnesis, 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 fibromyalgia 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. But 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 fibromyalgia in patients with hypothyroidism and the variables that may affect this frequency.

**Materials And Methods**

This is a a single center, prospective, cross-sectional clinical study conducted at Bakirkoy Dr. Sadi Konuk Training and Research Hospital in between 10/07/2019 and 30/03/2020. 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 (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs) 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). Written informed consent was obtained from all the participants. 2016 ACR revised criteria was used to diagnose FM and patients were divided into two groups according to whether or not they had FM (group 1 = FM positive, group 2 = FM negative). Patients having FM were evaluated with Beck Depression Questionnaire (BDQ) and Fibromyalgia Impact Questionnaire (FIQ). The relationship of the groups with the variables were evaluated.

**Statistical analysis:**

Descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, maximum) were used when evaluating the study data. Frequency and percentage values of categorical variables, 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 outpatients 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 was given in Table 1.
Table 1
Descriptive Data of Patients

|                         | Minimum | Maximum | Mean     | Std. Deviation |
|-------------------------|---------|---------|----------|----------------|
| 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/m²)             | 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        |

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
|                         | Minimum | Maximum | Mean   | Std. Deviation |
|-------------------------|---------|---------|--------|----------------|
| Sedimentation           | 4.00    | 49.00   | 15.2667| 9.45045        |
| Creatine 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       |

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

FM was found in 41% (n = 68) of the women and 21.4% (n = 3) of the men. FM status by gender was 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 were found (p > 0.05 for all) (Table 3).

| Gender | Fibromyalgia | Total |
|--------|--------------|-------|
|        | Positive     | Negative |       |
| Female | N 98         | 68     | 166   |
|        | % 59.0%      | 41.0%  |       |
| Male   | N 11         | 3      | 14    |
|        | % 78.6%      | 21.4%  |       |
Table 3

| Fibromyalgia | N   | Mean | Std. Deviation | p   |
|--------------|-----|------|----------------|-----|
| 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

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 were performed to 36 of 71 patients (%50.7) diagnosed with FM. 35 patients declined to perform BDQ and FIQ questionare. When we compared BDQ and FIQ scores with the variables separately; while there was no significant corelation 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 corelation between FIQ score and age at diagnosis and disease duration, but no significant corelation 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 were 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%.
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   |           |                |         |

Anti TPO: *Anti*-thyroperoxidase antibodies, Anti TG: *Anti*-thyroglobulin antibodies

* Significant difference for 0.05
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   |

BMI: Body Mass Index, Anti TPO: Anti-thyroperoxidase antibodies, Anti TG: Anti-thyroglobulin antibodies  
* Significant difference for 0.05
| Variables                          | Correlation coefficient (r) | P value |
|-----------------------------------|----------------------------|---------|
| 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   |

BMI: Body Mass Index, Anti TPO: Anti-thyroperoxidase antibodies, Anti TG: Anti-thyroglobulin antibodies

* Significant difference for 0.05

**Discussion**

FM is a disease characterized by hyperalgesia and allodynia that causes chronic widespread nonarticular 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) Previous studies reported that there are problems in the production and utilization of thyroid hormones in FM patients. (10) Also, studies recently reported that there was an association between thyroid autoimmunity and FM. (11, 12, 13) In a study conducted with 79 patients diagnosed with hashimato 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 with HT than those without FM. But 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, 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. But we could not find any significant difference between presence of FM and thyroid antibodies, disease duration, body mass index, age at diagnosis.
In another cross-sectional study (15) with 500 hashimoto thyroiditis 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/fibromyalgia, and non-specific rheumatoid manifestations observed threefold 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%) was euthyroid. In all patients, 56 of the them were female, 9 were male and 62% of the patients had various rheumatic disease with the most common was (20%) fibromyalgia. In our study the frequency of fibromyalgia in patients with thyroid disfunciton was common with a rate of %39.4 and consistent with this study female gender was higher.

**Conclusion**

It should be kept in mind that the signs and symptoms of hypothyroidism is similar to signs and symptoms of FM, and approximately 40% of patients with hypothyroidism could have FM concomittantly. So 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.

**Declarations**

**Funding:**

None

**Conflicts of interest/Competing interests:**

The author reports no conflicts of interest in this work.

**Ethics approval:**

The study was approved by Ethical Committee of Bakirkoy Dr. Sadi Konuk Training and Research Hospital with the number of 2019/13/10-8/07/2019.

**Availability of data and material:**
Correspondence and requests for data and materials should be addressed to the corresponding author.

**Code availability:**

Not applicable.

**Authors' contributions:**

All authors contributed to research design, data collection, statistical evaluation, writing, source research and submission to the journal.

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