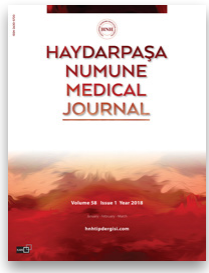
HAYDARPAŞA NUMUNE MEDICAL JOURNAL

DOI: 10.14744/hnhj.2019.78941
Haydarpasa Numune Med J 2021;61(2):172–176



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ORIGINAL ARTICLE

The Effect of Fibromyalgia on Bone Mineral Density in Patients with Hypothyroidism

Yaşar Keskin[1], Teoman Aydın[1], Berna Ürkmez[2], Özgür Taşpınar[3], Ahmet Adil Çamlı[4], Huriye Şenay Kızıltan[5], Ali Hikmet Eriş[5], Ahmet Serdar Mutluer[6]

[1]Department of Physical Medicine and Rehabilitation, Bezmialem Vakif University Faculty of Medicine, Istanbul, Turkey
[2]Department of Physical Medicine and Rehabilitation, University of Health Sciences, Hamidiye Faculty of Medicine, Haydarpaşa Numune Health Application and Research Center, Istanbul, Turkey
[3]Department of Physical Medicine and Rehabilitation, Istinye University,Faculty of Medicine, Istanbul, Turkey
[4]Department of Internal Medicine, Bezmialem Vakif University Faculty of Medicine, Istanbul, Turkey
[5]Department of Radiation Oncology, Bezmialem Vakif University Faculty of Medicine, Istanbul, Turkey
[6]Faculty of Medicine, Bezmialem Vakif University, Istanbul, Turkey

Abstract

Introduction: The aim of this study was to investigate whether the presence of fibromyalgia affects the bone mineral density (BMD) in hypothyroid patients.

Methods: Our study consisted of three groups, including 30 patients with hypothyroidism and FMS, 30 patients with hypothyroidism, and 27 healthy volunteers. Lumbar vertebrae and left proximal femur BMD measurements of groups were performed by dual-energy X-ray absorptiometry. Groups were compared in terms of BMD.

Results: Lumbar spinal total T score and lumbar spinal total BMD were significantly different between healthy volunteers and the other two groups. However, no significant difference was found between the groups in terms of age, gender, body mass index, smoking and alcohol use habits, erythrocyte sedimentation rate, C-reactive protein, thyroid-stimulating hormone, fT3, fT4, and 25-OH Vitamin D.

Discussion and Conclusion: BMD was lower in patients with hypothyroidism and in patients with both fibromyalgia and hypothyroidism compared with healthy individuals. However, there was no difference in BMD between patients with both fibromyalgia and hypothyroidism and only with hypothyroidism.

Keywords: Bone mineral density; fibromyalgia; hypothyroidism.

Fibromyalgia syndrome (FMS) is a common rheumatic disease characterized by chronic widespread pain and reduced pain threshold, with hyperalgesia and allodynia. Additional symptoms include fatigue, depression, anxiety, sleep disturbance, headache, migraine, variable bowel habits, diffuse abdominal pain, and urinary frequency [1]. The etiology and mechanisms of fibromyalgia are not fully understood; neuroendocrine dysfunctions as well as central pain mechanisms and central sensitization appear to be the most important factors. Despite the presence of extensive musculoskeletal pain, physical examination, laboratory findings, and radiological examinations are normal.

Correspondence (İletişim): Yaşar Keskin, M.D. Bezmialem Vakif Universitesi, Tip Fakultesi, Fiziksel Tip ve Rehabilitasyon Anabilim Dali, 34093 İstanbul, Turkey
Phone (Telefon): +90 544 787 66 44 **E-mail (E-posta):** ykeskin42@hotmail.com
Submitted Date (Başvuru Tarihi): 11.02.2019 **Accepted Date (Kabul Tarihi):** 27.05.2019

The disease mostly occurs in women between 20 and 50 years of age. The estimated prevalence of fibromyalgia in the general population is between 2.9 and 4.7% [2].

Osteoporosis in fibromyalgia patients may be a problem due to sedentary lifestyle and insufficient body condition. Studies have reported that sedentary life may be a risk factor for the development of osteoporosis because of accompanying problems such as depression in patients with FMS [3].

Vitamin D deficiency leads to symptoms related to musculoskeletal system, resulting in confusion with some musculoskeletal disorders [4]. In the recent studies, it has been reported that osteomalacia may occur with symptoms and findings mimicking diseases such as FMS, polymyalgia rheumatics, ankylosing spondylitis, rheumatoid arthritis, multiple myeloma (MM), and metastatic bone disease [5]. Danish women with FMS symptoms have been reported to have Vitamin D deficiency and osteomalacia in the majority [6].

In many studies, it has been reported that thyroid hormones are necessary in physiological doses for healthy development and maturation of bone. The presence of a number of risk factors for osteopenia due to thyroid hormones has been demonstrated. These; hyperthyroidism, advanced age, menopause, and total thyroidectomy in a long-term clinical manifestation. Thyroid function should be closely monitored while investigating the causes in patients with osteoporosis [7].

Our aim in this study was to investigate whether fibromyalgia affects bone mineral density (BMD) negatively in hypothyroid patients.

Materials and Methods

Patients

Randomize, prospective, controlled; patients between the ages of 25 and 65 were diagnosed with hypothyroidism by the Internal Medicine Department of Bezmialem Vakif University and patients were directed to Physical Therapy and Rehabilitation Clinic of Bezmialem Vakif University. The diagnosis of fibromyalgia was established according to the alternative diagnostic criteria of the American College of Rheumatology Fibromyalgia 2013 [8]. Patients were divided into groups with FMS and without FMS. The cases were included in the study as 30 patients with hypothyroidism and FMS, 30 patients with only hypothyroidism, and 27 healthy volunteer control groups (Fig. 1).

Those with an associated disorder that could affect bone metabolism (hypogonadism, hyperthyroidism, hyperparathyroidism, MM, diabetes mellitus, etc.), history of medication known to cause osteoporosis (glucocorticoids, methotrexate, diuretics, aluminum- and magnesium-containing anti-acid, etc.), history of previous surgery and premature menopause, as well as those who were immobile for an extended period, who had spinal surgery or any fracture, and smokers and alcohol users were not included in the study. Informed written consent was obtained from all participants.

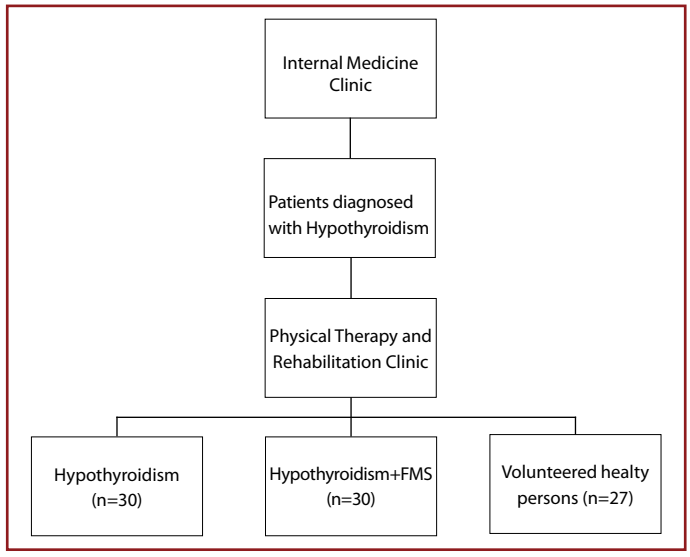

Figure 1. Patient participation chart.

Evaluation and Measurement Parameters

Patients were evaluated for BMD. Lumbar vertebra BMD (L1-L4 anterior-posterior projection) and left proximal femur (neck and total score) were measured with dual-energy X-ray absorptiometry (DXA) (DPX-LUNAR®) to determine the differences. BMD data are expressed in g/cm^2 and standard deviation scores (Z and T scores) are calculated. As a result of the BMD measurement made; T scores between –1 and –2.5 were defined as osteopenia and those less than –2.5 and as osteoporosis (WHO Working Group, 1994). The number of standard deviations above or below the mean reference value that matched age and sex was reported as Z scores [9].

Serum free T3, free T4 (sT4), and thyroid-stimulating hormone (TSH) levels were measured in the patients and control group. Patients with increased TSH levels and patients with lower sT4 levels were considered clinically hypothyroid, thyroid hormone normal TSH values were subclinical hypothyroid patients, and these patients were included in the study.

Patients and control group filled out the form with age, height, body mass index (BMI), duration of illness, alcohol and cigarette, postmenopausal period status, and blood values were measured. In the measured blood values; erythrocyte sedimentation rate (ESR), serum C-reactive protein (mg/dL) (CRP) level, and 25-OH Vitamin D (25OH-D) levels were measured. The ESR was measured through the Westergren method (mm/h) and the serum CRP level was determined with the help of nephelometry (mg/dL).

All the recruited subjects signed informed consent forms before participating in the study and the approval of the local Ethics Committee was obtained. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2013.

Statistical Analysis

The calculations were performed using the Statistical Package for the Social Sciences (SPSS) for Windows software version 16.0 (SPSS Inc., Chicago, IL, USA). The Kolmogorov–Smirnov test was used to confirm that data within the ranges of normal distribution in both groups. A non-parametric test was employed for the variables outside the normal distribution. The comparison of the data between the groups was carried out through the Kruskal–Wallis test and Mann–Whitney U-test. Statistical significance was based on a value of $p<0.05$ with a 95% confidence interval.

Results

The demographic and clinical characteristics of groups' subjects are presented in Table 1. Among the groups, no significant difference was found in terms of age, sex, BMI, postmenopausal period status, smoking habits, alcohol habits, ESR, CRP, TSH, fT3, fT4, and 25OH-D.

No statistically significant difference was found between the groups in terms of median values of lumbar BMD, lumbar T and Z scores, proximal femur BMD, proximal femur T and Z scores and total femur BMD, and total femur T and Z scores (Table 2).

When the patients with hypothyroidism and patients with hypothyroidism and fibromyalgia were compared with healthy volunteers, there was a significant difference between lumbar spinal total T score and lumbar spinal total BMD values ($p<0.05$).

Discussion

FMS has been reported to be a risk factor for low BMD [10,11]. Hypothyroidism has been shown to cause low BMD in some studies [12,13]. In our study, BMD of patients with hypothyroidism and both hypothyroidism and fibromyalgia was compared. There was no significant difference between patients' lumbar spine BMD, proximal femur neck BMD, total femur BMD, total femur T and Z scores, lumbar spine T and Z scores, and femur neck T and Z scores.

Thyroid disorders are one of the major common disorders which may affect the bone density thyroid hormones have

Table 1. Comparison of demographic, clinical characteristics, and laboratory parameters of the groups

	Hypothyroidism (n=30)	Hypothyroidism and FMS (n=30)	Healthy volunteer (n=27)	p*
Sex, n (%)	27 females (90)	26 females (87)	24 females (90)	>0.05
Age (year)	47.53±5.46	46.00±8.75	45.20±5.75	>0.05
Hypothyroid disease duration (year)	1.56±0.85	2.2±1.45	-	>0.05
Body mass index (kg/m^2)	27.13±3.34	28.77±3.88	26.40±4.22	>0.05
Patients with postmenopausal period, n (%)	5 (16)	4 (13)	3 (11)	>0.05
Smoking status, n (%)	4 (13)	5 (16)	3 (11)	>0.05
Alcohol, n (%)	1 (3)	1 (3)	1 (3)	>0.05
ESR (mm/h)	17.72±13.26	15.46±9.31	16.22±11.54	>0.05
CRP (mg/l)	0.28±0.24	0.29±0.23	0.20±0.22	>0.05
25OH-D (ng/ml)	33.23±16.14	36.48 ±12.18	34.46±11.01	>0.05
TSH (mIU/ml)	2.05±1.52	1.86±1.39	1.93±1.22	>0.05
fT3 (pg/mL)	4.39±0.69	4.59±0.42	4.46±0.31	>0.05
fT4 (ng/dL)	1.44±0.25	1.40±0.26	1.46±0.21	>0.05

*Kruskal–Wallis test; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; TSH: Thyroid stimulating hormone; fT3: Free triiodothyronine; fT4: Free thyroxine; FMS: Fibromyalgia syndrome.

Table 2. BMD, Z and T scores of patients and control groups

	Hypothyroidism (n=30) (mean±SD)	Hypothyroidism-FMS (n=30) (mean±SD)	Healthy volunteer (n=27) (mean±SD)	p*
Lumbar total T score	–0.5733±1.094†	–0.5033±1.480§	0.3370±1.674	<0.05
Femur total T score	–1.9533±9.149	0.0833±1.483	0.0922±1.785	>0.05
Femur neck T score	–0.2867±1.025	–0.500±1.449	–0.2590±1.247	>0.05
Lumbar total BMD	1.0770±1.332†	1.0809±0.1841§	1.1890±0.205	<0.05
Femur total BMD	0.9712±0.1413	1.0082±0.1810	1.503±0.2076	>0.05
Femur neck BMD	0.9402±1.206	0.9546±0.1752	0.9802±0.1508	>0.05
Lumbar total Z score	–0.1800±1.021	0.900±1.4181	0.922±1.595	>0.05
Femur total Z score	0.0933±1.197	0.4167±1.382	0.1481±1.787	>0.05
Femur neck Z score	0.3333±0.962	0.4267±1.305	–0.1519±1.218	>0.05

*Kruskal–Wallis test; †,§Mann–Whitney U-test: †Significant difference between hypothyroidism and healthy volunteer; §significant difference between hypothyroidism-FMS and healthy volunteer. SD: Standard deviation; FMS: Fibromyalgia syndrome; BMD: Bone mineral density.

been shown to have effects on osteoclasts directly. In a study of 16.249 patients, both hyperthyroidism and hypothyroidism found a high risk of bone fracture. In adult patients with hypothyroidism, bone density is increased, but bone quality is low, so it may lead to an increased risk of fracture in these patients [15]. In the study of Lee et al.[16] (413 female patients), the mean age was 52.2 + 6.6 years and serum TSH, fT4 level, and BMD of femur neck were measured by DXA method. In the study, subclinical hyperthyroidism and hypothyroidism were reported to decrease BMD of the femur neck [16]. In our study, BMD was lower in hypothyroid patients than in healthy volunteers. These BMD decreases were statistically significant, especially in the lumbar region. Yang et al.[17] in their systematic review and meta-analysis, subclinical hyperthyroidism and subclinical hypothyroidism were found to be associated with increased risk of fracture, while there was no correlation between BMD change and subclinical hypothyroidism. Although evidence has been associated with subclinical hyperthyroidism associated with decreased BMD, there has been no evidence of a definite association between subclinical hypothyroidism and low BMD risk.[17] In our study, the DEXA measurements of our patients in the hypothyroid group were seen as osteopenic. Lumbar total t score and lumbar BMD values were significantly lower in hypothyroid patients.

Conclusion

In a meta-analysis conducted in 2017, 12 studies with 695 fibromyalgia patients and 784 controls were selected. In conclusion, meta-analysis showed that BMD was significantly lower in Caucasian and fibromyalgia patients in the female population. This result suggests that FMS may be a risk factor for osteoporosis; this shows that it contributes to the development of low BMD or osteoporosis [18]. In another meta-analysis conducted in 2017, reduced BMD of lumbar vertex was found in the patients with fibromyalgia compared with patients with fibromyalgia and normal subjects [19].

The majority of patients with fibromyalgia do not exercise regularly and have low physical fitness. This suggests that fibromyalgia patients are at risk for osteoporosis. The data on the incidence of osteoporosis in fibromyalgia patients are contradictory. Some studies have reported low BMD in FMS, while others have suggested no such relationship. Jensen et al.[21] in one study, he reported a tendency to lower BMD in the hip rather than the lumbar spine in premenopausal fibromyalgia patients. Al-Allaf et al.[20] detected decreased BMD of the mid-distal radius, which correlated with cortical bone; however, they observed no differences in BMD of the other regions.

Studies have shown that FMS is associated with D-vitamin deficiency [22]. However, there are contradictions between the studies on this subject. De Rezende Pena et al.[23] in a cross-sectional study, they evaluated the differences in the concentration of 25 (OH) D-vitamins between 87 fibromyalgia patients and 92 healthy volunteers and reported no statistical difference between them. Studies show that large differences in ethnic, cultural, and nutritional habits are factors affecting D-vitamin status [23]. Moreover, researchers do not have previous D-vitamin supplementation in participants, data on previous blood levels are not available in most studies [24]. Additional parameters related to heterogeneity are evident, including differences in the criteria used for D-vitamin deficiency, small study samples, and the absence of control groups. Therefore, the relation-

ship between D-vitamin and fibromyalgia is unclear [25]. In our study, there was no statistically significant difference in D-vitamin content between patients with fibromyalgia and those with hypothyroidism only with hypothyroidism.

As a result, BMDs in hypothyroid patients with hypothyroidism and fibromyalgia are lower than healthy individuals. However, there was no difference in BMD between hypothyroid patients with fibromyalgia and those with hypothyroidism. A clear consensus on the status of osteoporosis in patients with fibromyalgia and hypothyroidism is not yet available in the literature. Further studies are needed to elucidate this issue.

Ethics Committee Approval: Bezmialem Vakif University Ethics Committee (Approval date/no: 25.03.2015/7-6).

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: T.A.; Design: Y.K., A.A.Ç.; Data Collection or Processing: B.Ü., A.S.M., A.H.E.; Analysis or Interpretation: B.Ü., H.Ş.K.; Literature Search: H.Ş.K., Ö.T.; Writing: Y.K., Ö.T.

Conflict of Interest: None declared.

Financial Disclosure: The authors declared that this study received no financial support.

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