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Does Hypermobility Syndrome Affect Bone Density?

Hipermobilite Sendromu Kemik Yoğunluğunu Etkiler mi?

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Abstract

Objective: This study aimed to examine whether benign joint hypermobility syndrome (BJHS) affects bone mineral density (BMD).

Materials and Methods: A cross-sectional controlled design was used. Seventy-two participants were enrolled: 36 patients diagnosed with BJHS (group 1) and 36 healthy individuals (group 2). Participants aged ≥18 years were included. BJHS was diagnosed according to Beighton criteria with a score ≥4. Individuals with secondary osteoporosis, inflammatory rheumatic disease, systemic illness, pregnancy, liver or kidney failure, spinal or hip fractures, metal implants, or the use of medications affecting bone metabolism were excluded. BMD of the lumbar spine and femur was measured by dual-energy X-ray absorptiometry and reported as absolute values and T and Z-scores.

Results: Group 1 and group 2 had mean ages of 29.74±7.97 and 32.02±7.73 years, and mean body mass index (BMI) values of 23.51±2.84 and 24.76±3.17, respectively. No significant differences were found between groups regarding age, sex, BMI, or biochemical parameters. All T and Z-scores were significantly lower in BJHS patients compared with healthy controls ($p<0.05$).

Conclusion: Patients with BJHS demonstrated reduced BMD, suggesting that hypermobility may negatively affect bone structure. Individuals with BJHS should be assessed for osteopenia or osteoporosis as part of routine evaluation.

Keywords: Joint hypermobility, benign joint hypermobility syndrome, bone density, dual-energy X-ray absorptiometry

Öz

Amaç: Bu çalışmanın amacı, benign eklem hipermobilite sendromunun (BJHS) kemik mineral yoğunluğunu (KMY) etkileyip etkilemediğini incelemektir.

Gereç ve Yöntem: Çalışma kesitsel kontrollü tasarımda yürütüldü. Toplam 72 katılımcı değerlendirildi: BJHS tanısı alan 36 hasta (grup 1) ve 36 sağlıklı birey (grup 2). Çalışmaya ≥18 yaş bireyler dahil edildi. BJHS tanısı, Beighton kriterlerine göre ≥4 puan ile doğrulandı. Sekonder osteoporoz, enflamatuvar romatizmal hastalık, sistemik hastalık, gebelik, karaciğer veya böbrek yetmezliği, omurga veya kalça kırığı öyküsü, metal implant varlığı ve kemik metabolizmasını etkileyen ilaç kullanımı dışlama kriterlerini oluşturdu. Lomber omurga ve femur KMY ölçümleri çift enerjili X-ışını absorbsiyometrisi ile yapıldı ve mutlak değerler ile T ve Z-skorları olarak raporlandı.

Bulgular: Grup 1 ve grup 2'nin sırasıyla ortalama yaşları 29,74±7,97 ve 32,02±7,73 yıl, vücut kitle indeksi (VKİ) değerleri 23,51±2,84 ve 24,76±3,17 idi. Yaş, cinsiyet, VKİ ve biyokimyasal parametreler açısından gruplar arasında anlamlı fark saptanmadı. Tüm T ve Z-skorlarının BJHS grubunda sağlıklı kontrollere kıyasla anlamlı düzeyde daha düşük olduğu belirlendi ($p<0,05$).

Sonuç: BJHS'li hastalarda KMY'nin azalmış olması, hipermobilitenin kemik yapısını olumsuz etkileyebileceğini düşündürmektedir. Bu nedenle BJHS'li bireylerin rutin değerlendirme kapsamında osteopeni veya osteoporoz açısından taranması önerilir.

Anahtar kelimeler: Eklem hipermobilitesi, benign eklem hipermobilite sendromu, kemik yoğunluğu, çift enerjili X-ışını absorbsiyometrisi

Introduction

Joint hypermobility is defined as the ability of a joint to move "beyond normal limits along physiological axes" (1). Benign joint hypermobility syndrome (BJHS) is characterized by an increase in general joint laxity, defined as joints having a range of motion above normal without any diagnosis of systemic rheumatological disease. The prevalence of BJHS varies according to gender and age, being more common in young women and decreasing in frequency with age. Although the pathophysiology of BJHS is not fully understood, it is considered a systemic abnormality of collagen (2,3).

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It is reported that proprioception is decreased in patients with BJHS, making joints more susceptible to trauma (4-6). The increase in joint laxity and decrease in proprioception in BJHS lead to balance disorders and increased risk of falling in patients (7). Clinical findings in BJHS are characterized by chronic pain, fatigue, and decreased physical activities. These clinical findings cause patients to maintain a sedentary lifestyle, leading to a reduction in load on bones and resulting in secondary deterioration of bone parameters (8-12). Additionally, the decrease in tendon stiffness of patients leads to a reduction in muscle strength and force transmission, creating a negative effect on bone structure (13,14). BJHS increases the risk of fractures in patients due to both the negative effects of BJHS on bone structure and the increased risk of falling. Therefore, it is important to evaluate the bone structure of patients with BJHS (15).

Studies evaluating the bone structure of BJHS patients have reported decreased bone mineral density (BMD), while some recent studies have reported no change in BMD (16-21). While previous studies have primarily evaluated dual energy X-ray absorptiometry (DEXA) derived Z-scores from either lumbar or femoral regions, often focusing on premenopausal or postmenopausal women and including patients with hypermobile Ehlers-Danlos syndrome (hEDS), the present study adopts a broader methodological approach (2,16,17,19). By including adults aged 18 years and older of both sexes diagnosed with BJHS, assessing both lumbar and femoral regions, and evaluating both T-scores and Z-scores, this study aims to provide more comprehensive and generalizable evidence regarding the relationship between joint hypermobility and BMD.

The aim of our study is to investigate the relationship between BJHS and BMD.

Materials and Methods

Study Participants and Design

This cross-sectional controlled study was reviewed and approved by the Clinical Research Ethics Committee of Balıkesir University (decision number: 2024/39, date: 26.04.2024), and written informed consent was obtained from all participants. The study was also conducted in accordance with the principles of the Declaration of Helsinki.

A total of 72 participants were included in the study, comprising 36 patients diagnosed with BJHS at the outpatient clinic of Physical Medicine and Rehabilitation at Balıkesir University Health Practice and Research Hospital, and 36 healthy participants to form the control group. In the study, patients diagnosed with BJHS were designated as group 1, while the control group consisting of healthy participants was designated as group 2. The study included individuals aged 18 and over, patients diagnosed with BJHS according to Beighton diagnostic criteria, patients with a Beighton score ≥4, and healthy participants without any known disease. All female participants were premenopausal, and no patients with natural or surgically induced menopause were included. Those who were pregnant, had secondary osteoporosis, had inflammatory rheumatic diseases, had fractures or metal implants in the back, waist and hip region, had liver and kidney failure, had systemic diseases and were using drugs that affected bone metabolism were excluded from the study.

The Beighton criteria (a 0-9 point scale) were used to assess the hypermobility of the participants included in the study (22). The Beighton criteria consist of five maneuvers: passive dorsiflexion of the fifth finger ≥90°, passive apposition of the thumb to the forearm, hyperextension of the elbows and knees ≥10°, and touching the floor with the palmar surface of the hand while keeping the knees fully extended. The first 4 maneuvers are evaluated for both extremities and each is scored as 0 or 1 point. According to the Beighton score, the total score ranges from 0 (inability to perform any of these maneuvers) to 9 (ability to perform all of these maneuvers). The Beighton score was calculated based on the results of the clinical examination of these maneuvers, and patients with a total score of ≥4 were included in the study.

Interventions

Sociodemographic characteristics, age, gender, occupation, marital status and systemic diseases of the participants who met the study inclusion criteria were recorded. Participants' body weights were measured using an MC-780 Tanita™ device (Tokyo, Japan) with a capacity of 150 kg and sensitivity of 0.1 kg, while height was measured using a non-stretch measuring tape in accordance with the method. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2).

BMD measurements were obtained at the lumbar spine (L1-L4 and L2-L4) and proximal femur (femoral neck, trochanter, and Ward's triangle) using DEXA device. BMD measurements were performed at the Department of Radiology, Balıkesir University Faculty of Medicine, using a GE Healthcare Lunar DXA device (General Electric Company, Coventry, United Kingdom). To minimize inter-device and inter-operator variability, all scans were performed at a single center using the same DEXA device by the same experienced technician. The results were reported as absolute BMDs (in grams per square centimeter) and as T and Z-scores. BMD classifications were based on World Health Organization criteria, whereby T-scores—reflecting the number of standard deviations from the mean BMD of a young adult reference population—were defined as normal (≥-1.0), osteopenic (between -1.0 and -2.5), or osteoporotic (≤-2.5) (23). Demographic information, physical examinations, evaluation of test results, and data collection for all participants were conducted by the same physical medicine and rehabilitation specialist. BMD measurements, aspartate aminotransferase, alanine aminotransferase, creatinine, urea, calcium, phosphorus, alkaline phosphatase, thyroid-stimulating hormone, free thyroxine, parathyroid hormone, and cholecalciferol values were recorded from participants' files.

Statistical Analysis

Data analysis was conducted using IBM SPSS Statistics version 25.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics for continuous variables were presented as mean, standard deviation, minimum, median, and maximum values. The normality of data distribution was evaluated using analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk tests). Group comparisons were performed using the independent samples t-test for normally distributed variables and the Mann-Whitney U test for non-normally distributed variables. As Beighton scores did not show a normal distribution, the association between Beighton scores and BMD T-scores was assessed using Spearman's rank correlation analysis. All tests were two-tailed, and statistical significance was set at $p<0.05$. The required sample size was calculated as 72 participants based on an effect size of 0.60, a type I error rate (α) of 0.05, and a statistical power (1-β) of 80%. Sample size estimation was performed using G*Power software version 3.1.9.7 (24).

Results

The gender distribution of participants in the study was 31 females and 5 males in group 1, 32 females and 4 males in group 2. The mean age was 29.74±7.97 in group 1 and 32.02±7.73 in group 2, while the mean BMI was 23.51±2.84 in group 1 and 24.76±3.17 in group 2 (Table 1). In the study, the mean serum cholecalciferol (ng/mL) values were 19.53±6.78 in group 1 and 20.92±7.87 in group 2. Blood biochemistry parameters including calcium, phosphorus, alkaline phosphatase, TSH, free T4, and parathormone values were within normal ranges for both groups. There were no statistically significant differences between the groups in terms of age, gender, BMI, and blood biochemistry parameter values ($p>0.05$) (Table 1).

In the study, one patient in group 1 diagnosed with BJHS exhibited BMD values within the osteoporotic range, whereas no participants in the control group met the criteria for osteoporosis. Low bone density was defined as the presence of osteopenia or osteoporosis in at least two skeletal regions based on T-score assessments. According to this definition, 16 patients (~45%) in group 1 were classified as having low bone density, compared with 4 patients (~12%) in the control group. This difference between groups was statistically significant ($p<0.05$) (Table 1). All BMD t and z scores obtained by DEXA from both the lumbar spine and femoral regions were significantly lower in patients with BJHS in group 1 compared with the control group ($p<0.05$) (Table 2).

In the BJHS group (n=36), the Beighton score demonstrated statistically significant negative correlations with BMD T-scores across multiple skeletal sites. Specifically, moderate inverse correlations were identified at the total femur (Spearman's ρ=-0.493, p=0.002), femoral neck (ρ=-0.539, p=0.001), lumbar spine L2-L4 (ρ=-0.528, p=0.001), and total lumbar spine (ρ=-0.492, p=0.002) (Table 3).

Table 1. Subjects' characteristics

	Hypermobility group (n=36)	Control group (n=36)	p-value
Gender (female/male)	31/5	32/4	
Age (year)	29.74±7.97	32.02±7.73	0.228
Body height (m)	1.63±0.07	1.64±0.08	0.928
Body weight (kg)	64.61±9.44	66.82±10.54	0.411
BMI (kg/m^2)	23.51±2.84	24.76±3.17	0.603
Calcium (mg/dL)	9.50±0.27	9.51±0.35	0.821
Phosphorus (mg/dL)	3.59±0.48	3.60±0.47	0.941
Alkaline phosphatase (IU/L)	72.37±22.64	64.20±20.95	0.122
TSH (mIU/L)	1.85±0.81	1.78±0.83	0.705
Thyroxine (T4), free (ng/dL)	2.90±3.49	2.35±1.96	0.226
PTH (pg/mL)	59.03±36.45	63.09±25.20	0.590
Cholecalciferol (ng/mL)	19.53±6.78	20.92±7.87	0.432
Osteopenic patients (n)	16	4	
Osteoporotic patients (n)	1	0	
Patients with low bone mass (n)	17	4	

BMI: Body mass index, TSH: Thyroid-stimulating hormone, PTH: Parathormone, m: Meter, kg: Kilogram, ng: Nanogram, pg: Picogram, L: Liter, dL: Deciliter, mL: Milliliter, IU: International unit, mIU: National-international unit, *: p<0.05; significant difference between groups

Table 2. BMD parameters in both groups

BMD	Hypermobility group (n= 36)	Control group (n= 36)	p-value
Lumbar L2-L4 t	-0.75±0.80	0.13±0.97	<0.001*
Lumbar L2-L4 z	-0.72±0.79	0.11±0.95	<0.001*
Lumbar L1-L4 t	-0.74±0.76	0.13±0.95	<0.001*
Lumbar L1-L4 z	-0.71±0.75	0.10±0.93	<0.001*
Femoral neck t	-0.64±0.87	0.09±1.11	0.003*
Femoral neck z	-0.62±0.79	0.21±1.12	0.001*
Femoral total t	-0.70±0.80	0.15±1.09	<0.001*
Femoral total z	-0.66±0.74	0.24±1.04	<0.001*

BMD: Bone mineral density, *: p<0.05; significant difference between groups

Table 3. Spearman correlation between Beighton score and BMD T-scores in the BJHS group

BMD parameter (T-score)	Spearman's ρ	p-value
Femoral neck t	-0.539	0.001
Femoral total t	-0.493	0.002
Lumbar L2-L4 t	-0.528	0.001
Lumbar total (L1-L4) t	-0.492	0.002

BJHS: Benign joint hypermobility syndrome, BMD: Bone mineral density. Values are Spearman's rank correlation coefficients (two-tailed), p<0.05 considered statistically significant

Discussion

In our study, we found that BMD decreased in both the lumbar spine and femoral regions of patients with BJHS. While studies evaluating BMD in BJHS patients have reported decreased BMD in patients with hypermobility, recent results also indicate no change in BMD (2,8,12,16,17,19).

Mishra et al. (19) evaluated BMD in their study investigating the extra-articular features of BJHS. The study was conducted with 58 BJHS patients and a control group of 30 healthy participants matched for age and gender. BMD measurements were taken from the lumbar spine (L1-L4) and femoral region using DEXA, and Z-scores were recorded. The study results showed that BMD decreased in both the lumbar spine and femoral regions of BJHS patients, although not at a statistically significant level. Gulbahar et al. (2) evaluated BMD in premenopausal women with BJHS in their study (2). The study included a total of 48 participants: 25 patients diagnosed with BJHS and 23 healthy controls matched for age and gender. Participants' BMD measurements were obtained from the lumbar spine (L1-L4) and femoral region (neck, trochanter, and Ward's triangle) using DEXA, and T and Z-scores were recorded. Their study found that both lumbar spine and femoral region T and Z-scores were lower in the BJHS group compared to the control group (p<0.05). Additionally, the risk of bone mass reduction in the hypermobility group was found to increase by 1.8 times. Our study is methodologically different from these studies because Mishra et al. (19) evaluated only Z-scores in BMD measurement and Gulbahar et al. (2) selected premenopausal women. However, despite these differences, the finding of decreased BMD values in the lumbar spine and femur region in individuals with hypermobility in both studies supports our results.

Dolan et al. (17) investigated whether hypermobility was associated with a tendency towards osteoporosis in the normally aging population. The study included 716 postmenopausal women aged 53 to 72 years. In the hypermobility assessment, 79 subjects had a Beighton score >1/9, and 82 had a Contompasis score >22. Only a participant had BJHS (Beighton score 4/9). Therefore, the study used the Contompasis score and considered subjects with localized hypermobility as hypermobile. In the hypermobile group, total hip BMD was found to be 3% higher compared to controls. However, it was noted that the physical activity scores of the hypermobile group were also higher than the controls. Dolan et al.'s (17) study differs from ours in that it was conducted on postmenopausal women over 50 years old and there were differences in physical activity levels. Contrary to our study results, the higher hip BMD values of participants with hypermobility in the study by Dolan et al. (17) may be due to the higher physical activity levels of hypermobile subjects.

In 2017, new diagnostic criteria for joint hypermobility were developed by the Ehlers-Danlos Society. According to these criteria, patients with hypermobility were classified as hEDS or hypermobility spectrum disorders (HSD) (1,12,25). In this classification, BJHS is included within the HSD classification. However, the term BJHS is still widely used and generally indicates the presence of hypermobility (21).

Recent studies on hypermobility have been conducted on patients diagnosed with hEDS and HSD. In these studies, DiFrancisco-Donoghue et al. (16) found that Z-scores obtained

by DEXA from the lumbar spine and both femur regions of patients with hypermobility were statistically significantly lower compared to the control group ($p<0.05$). In the study by Coussens et al. (8,12), no significant difference was found between groups in BMDmeasurement values obtained by DEXA in patients with hypermobility. However, in the results obtained by peripheral quantitative computed tomography (pQCT), it was found that patients with hypermobility had decreased cortical bone mineral content and thickness, decreased trabecular bone mass and density, and a higher fracture prevalence ($p<0.05$) (8,12). Unlike our study, these studies were conducted on female participants. The detection of decreased BMD values in DiFrancisco-Donoghue et al.'s (16) study is similar to our study results. On the other hand, the lack of significant change in BMD measurement values in Coussens et al.'s (8,12) study does not support our study results. Unlike our study, in Coussens et al.'s (8,12) studies, DEXA measurements were obtained from different body regions, and area BMD measurement scores were used instead of T or Z-scores for bone density measurement. Therefore, the fact that the results of the studies by Coussens et al. (8,12) and our study do not support each other may be due to differences in methodological methods. Nevertheless, the results of these studies show that the bone structure of patients with hypermobility is negatively affected.

Study Limitations

This study has certain limitations. Physical activity level, daily calcium and vitamin D intake, and lifestyle-related factors known to affect BMD were not systematically assessed, which may have resulted in residual confounding. In addition, reproductive and hormonal variables such as age at menarche, pregnancy and breastfeeding history, as well as smoking, alcohol consumption, prior fracture history, and family history of osteoporosis were not evaluated. Although sex distribution differed slightly between groups, the difference was not statistically significant, and no sex-stratified analyses were performed. These limitations should be considered when interpreting the findings. Future studies with larger sample sizes and comprehensive assessment of confounding factors are warranted.

Conclusion

In conclusion, the findings of this study suggest that bone structure may be adversely affected in patients with joint hypermobility, as reflected by lower BMD values. Individuals with BJHS appear to be at increased risk for reduced bone mass, potentially predisposing them to osteopenia, osteoporosis, and fracture. Accordingly, assessment of BMD using DEXA, given its clinical accessibility and cost-effectiveness, may be considered a useful tool for the evaluation and follow-up of bone health in this patient population.

Ethics

Ethics Committee Approval: This cross-sectional controlled study was reviewed and approved by the Clinical Research Ethics Committee of Balıkesir University (decision number: 2024/39, date: 26.04.2024).

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

Footnotes

Authorship Contributions

Concept: B.U., N.Ş., Design: B.U., N.Ş., Data Collection or Processing: B.U., N.Ş., Analysis or Interpretation: B.U., N.Ş., Literature Search: B.U., N.Ş., Writing: B.U., N.Ş.

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

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