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The impact of vitamin D and vitamin B12 on bone mineral density and musculoskeletal pain in patients with osteoporosis

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Abstract

Osteoporosis is a major cause of bone fragility and musculoskeletal pain, conditions that substantially reduce quality of life. Vitamin D plays a central role in calcium homeostasis and bone mineralization, while Vitamin B12 deficiency has been associated with impaired bone health and neuromuscular symptoms. However, their combined impact on Bone Mineral Density (BMD) and pain remains incompletely understood. We conducted a cross-sectional study at the Rheumatology Clinic of the University Clinical Center of Kosova (January 2022–August 2024). A total of 136 patients (aged 18-75 years) with chronic musculoskeletal pain underwent Dual-Energy X-Ray Absorptiometry (DEXA) to assess BMD in the lumbar spine and femoral neck. Serum 25-hydroxyvitamin D and Vitamin B12 levels were measured, and pain intensity was evaluated using the Visual Analog Scale (VAS). Osteoporosis was highly prevalent, affecting 59.6% of patients in the right femur, 65.4% in the left femur, and all patients in the spine. Patients with lower Vitamin D levels reported significantly higher pain scores ($r = -0.55$, $p<0.01$), while elevated Vitamin B12 levels showed a positive correlation with pain ($r=0.59$, $p<0.01$). BMD values in all skeletal sites were negatively correlated with pain severity, with the strongest association observed in the spine ($r = -0.73$, $p<0.01$). Vitamin D deficiency was strongly associated with both lower BMD and greater musculoskeletal pain, whereas Vitamin B12 variations showed complex correlations requiring further study. Early detection of osteoporosis and systematic monitoring of vitamin status may support more effective management of pain and bone health in affected patients.

Key words: osteoporosis, vitamin D, vitamin B12, spine, femur, BMD, musculoskeletal pain.

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Introduction

Musculoskeletal (MSK) disorders encompass conditions causing discomfort to severe damage in motor organs, muscles, tendons, bones, cartilage, ligaments, and nerves. Common disorders include Rheumatoid Arthritis (RA), Osteoarthritis (OA), Low Back Pain (LBP), Neck Pain (NP), and gout, with others classified as "other MSK disorders".[1] Chronic MSK pain persists or recurs for over three months, leading to emotional distress and functional impairment.[2] Pain is classified as secondary if linked to a specific disease or process or as primary chronic pain when no direct cause is identified. The latter includes diverse disorders with chronic inflammation or structural changes due to infection, crystal deposition, or auto inflammatory mechanisms.[3] Osteoporosis is characterized by reduced Bone Mineral Density (BMD) and deterioration of bone microarchitecture, which significantly increases fracture risk. Dual-Energy X-Ray Absorptiometry (DEXA) is the gold standard for measuring BMD, and reduced values are closely linked to musculoskeletal pain and functional decline BMD is a test that measures the strength of the bone and is often used to determine the prevalence of osteoporosis, which is a disease that causes bones to grow brittle and weak and makes fractures more common.[4] A safe and non-invasive way to diagnose osteoporosis and assess a person's risk of developing the disease in the future is through Bone Mineral Density (BMD) screening. Low BMD, manifested during osteopenia and osteoporosis, is most linked to musculoskeletal pain given the pre-existing weakness of bones, and the resulting pressure on muscles and tissue.[5] Generally, as people get older the value of BMD drops, especially in postmenopausal women, so bone health plays a significant role in chronic pain conditions.[6] Among nutritional factors, Vitamin D plays a critical role in bone metabolism by regulating calcium and phosphorus absorption, promoting mineralization, and supporting muscle function. Its deficiency is common worldwide and has been strongly associated with osteoporosis and MSK pain. Fat-soluble vitamin D3 is vital for controlling calcium and phosphorus levels, which is important for bone health.[7] It also helps in boosting calci-

um absorption[8], increasing insulin sensitivity,[9] skeletal growth,[10] optimal muscle function, peak bone mass, bone mineral density, encouraging bone mineralization, and having an immunoregulatory role.[11] Because of its involvement in the support of bone and muscles, Vitamin D3 is among the elements that need to be considered regarding musculoskeletal pain.

Vitamin B12 is a water-soluble vitamin mainly involved in the support of the nervous system and the formation of red blood cells.[12] Its deficit is associated with neurological abnormalities, such as peripheral neuropathy that is characterized by numbness and tingling as well as weakness of muscles.[13] New research has also established that Vitamin B12 deficiency is also a causative factor for MSK pain since the nutrient affects muscle and nerve formation.[14]

This study aimed to investigate the relationship between Vitamin D and Vitamin B12 levels, bone mineral density, and musculoskeletal pain in patients attending a rheumatology clinic. By identifying potential correlations, the study seeks to provide insights into metabolic factors influencing osteoporosis progression and pain, thereby informing strategies for prevention and management.

Materials and Methods

Study design

The present study was planned as a cross-sectional study aimed to investigate the correlation between BMD, Vitamin D3, and Vitamin B12 in patients with musculoskeletal pain. The study was carried out for 32 months (January 2022 to August 2024), at the Rheumatology Clinic, University Clinical Center of Kosova. The main rationale for the study was to test the hypothesis that low levels of Vitamin D3, Vitamin B12, and abnormal BMD are related to the presence and intensity of musculoskeletal pain in the patient sample.

Participants

The study participants were selected from both male and female patients, using a standard inclusion criterion of between 18 and 75 years of age, attending the Rheumatology Clinic with musculoskeletal pain complaints. The inclusion criteria that need to be met to participate in the study was self-reported previous musculoskeletal pain that has persisted for over 3 months before this study started. Thus, conditions that may independently affect bone mineral density or vitamin status such as having chronic kidney disease, malignancies, chronic liver disease, and long-term steroid or bisphosphonate therapy, were excluded so that the results cannot be affected by interference from other factors.

In total 136 patients were included in the study. All the participants gave their informed consent before their participation, and the ethical clearance (1101/2022 IRB) was provided by the Institutional Review Board of the University Clinical Center of Kosova, Rheumatology Clinic. All procedures complied with the ethical principles of the Declaration of Helsinki.

The sociodemographic characteristics presented in Table 1, indicate that most of the patients had attained at least basic education levels and were either employed or students. This high proportion of married participants can also be attributed to the social support in the study population.

Data collection

Clinical assessment and laboratory investigations were part of data collection. All individuals completed a thorough clinical evaluation based on personal and family history and a standard clinical examination.

Bone mineral density measurement

Bone mineral density was measured using dual-energy X-ray absorptiometry (DEXA; Hologic Discovery, USA) the gold standard method of assessing bone density.[15] Measurements were obtained from the lumbar spine (L1–L4) and femoral neck. Results were expressed as T-scores, with values between –1.0 and –2.5 indicating osteopenia and ≤ –2.5 indicating osteoporosis.[16] These classifications were made to compare the results of bone density to musculoskeletal pains being experienced.

Serum vitamin D3 levels

Venous blood samples were collected from each participant to determine serum 25-hydroxyvitamin D [25(OH)D], considered the best biomarker for Vitamin D3. Results lower than 20 ng/mL were considered as deficient, 20–30 ng/mL inadequate and above 30 ng/mL sufficient.

Serum vitamin B12 levels

Serum Vitamin B12 levels were determined by the Chemiluminescent Microparticle Immunoassay (CMIA). In the present study, Vitamin B12 deficiency was considered with concentration below 200 pg/ mL, while concentrations between 200-300 pg/mL were considered as borderline deficiency and concentrations more than 300 pg/ mL were taken as normal, more than 900 could be considered toxic.

Pain assessment

Musculoskeletal pain intensity was evaluated by Applying Visual Analog Scale (VAS).[17] Before and after the program all participants were asked to self-report their pain on the numeric rating scale from 0 to 10, where 0 means no pain and 10 stands for the worst pain. This made it possible to establish a patient rated intensity of pain which was then used to measure its relationship with BMD, Vitamin D3 and Vitamin B12.

Statistical analysis

Descriptive statistics (mean, standard deviation, frequencies, and percentages) were used to characterize the sample. The prevalence of osteopenia and osteoporosis was calculated for each skeletal site. Pearson correlation analyses were performed to assess relationships between Vitamin D, Vitamin B12, BMD, and pain scores. All tests were two-sided, and statistical significance was set at $p < 0.01$. Analyses were conducted using SPSS software version 25 (IBM, USA).

Table 1. Demographic characteristics of patients.

Data	Number of patients	%	
Educational status	Primary school	25	18.38
	High school	89	65.44
	University	22	16.18
Marital status	Single	5	3.68
	Married	115	84.56
	Widowed	16	11.76
Occupation	Unemployed	55	40.44
	Employed	60	44.12
	Retired	21	15.44

Results

Musculoskeletal assessment

A total of 136 patients participated in the study. Their average age was 58.43±9.4 years. The mean Body Mass Index (BMI) was 27.5±4.9 kg/m². Quantitative analysis of the health status, more specifically pain levels of the patients suggest that 41 of the patients were suffering from severe levels of pain, while 93 of them complained of moderate pain and 2 reported moderate pain only. These studies show moderate to severe pain levels among the participants and raised a possibility of the relationship with the subjects' bone conditions.

BMD scores and relationship of osteoporosis and osteopenia with pain level

Table 2 show results of the prevalence of osteoporosis and osteopenia in patients with musculoskeletal pain based on BMD measurements. The quantification of the BMD for the right hip demonstrated that patients were diagnosed with osteopenia and osteoporosis: 52 and 81 patients respectively. In this region, only 3 patients were presented with normal BMD. The same could be said about the left hip; 43 patients have osteopenia, 89 patients have osteoporosis, and 4 patients have normal BMD. A total of total of 40 patients had osteopenia in both left and right femora.

With regards to the total spine involvement, all 136 patients are seen to be related with osteoporosis having T score T-score ≤ -2.5, and no patients were found to have normal spine BMD levels.

Osteoporosis can still be diagnosed if the T-scores in the femoral areas (hip) fall below or equals -2.5 even if spine scores are higher than -2.5. A patient can have osteoporosis on the femur bones and yet not have it on the spine of their back. Such a case was found in only three patients. The variation is attributed to the factors like, Turnover rates of bones and regional patterns of bone loss. It is likely that in some individuals the hip may be more involved than the spine.

When examining the correlation between osteoporosis and pain, among 40 patients with osteopenia in both femora and the spine, most reported moderate to severe pain, with vitamin B12 levels ranging from marginal to toxic (840-915 pg/mL). Among 45 osteoporosis patients across all three regions, 28 reported severe pain and 17 moderate pain (Figure 1). This group also showed vitamin D disorders, with 33 having severe deficiency and 12 suboptimal levels. Of the 29 with osteoporosis in both femora and spine, all had low vitamin B12, 8 had inadequate levels, and 3 had toxic levels (Figure 1). These findings suggest vitamin deficiencies may contribute to osteoporosis severity and pain.

Table 3 shows the correlation between vitamin D3, vitamin B12, and the VAS score for low back pain. Correlation analyses demonstrated a significant negative association between Vitamin D levels and pain severity ($r=-0.55$, $p<0.01$). In contrast, Vitamin B12 levels showed a positive correlation with pain ($r=0.59$, $p<0.01$). BMD values in the spine and femoral regions were also negatively correlated with pain, with the strongest relationship observed for the spine ($r = -0.73$, $p<0.01$). These findings suggest that lower BMD and Vitamin D deficiency are linked with higher musculoskeletal pain, while the role of Vitamin B12 requires further investigation

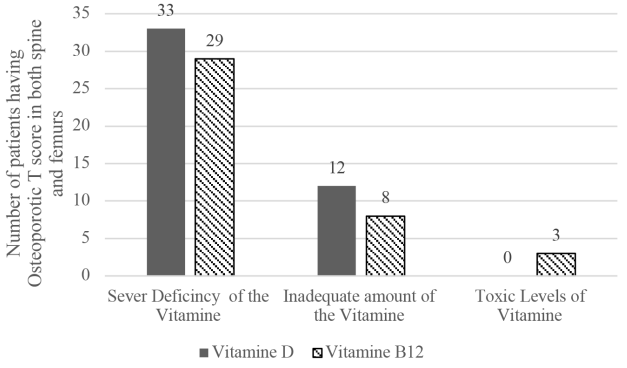

Figure 1. Vitamin deficiencies and toxicity in 45 patients with osteoporotic t-scores in both spine and femur.

Table 2. Prevalence of osteoporosis and osteopenia in patients with musculoskeletal pain based on BMD measurements.

Bone region	Patients with T- score ≤ - 2.5 (osteoporosis)	Frequency (%)	Patients with T score (-1 and -2.5) (Osteopenia)	Frequency (%)
Right femur	81	59.56	82	38.24
Left femur	89	65.44	43	31.62
Total spine	136	100	0	0
All three regions	45	33.09	40	29.41

Table 3. Correlation between Vitamin D3, B12 and VAS score.

	r	Sig.	Interpretation
Vitamin D3*Pain	-.554**	.000**	Negative correlation
Vitamin B12*Pain	.591**	.000**	Positive correlation
Left femur*Pain	-.410**	.000**	Negative correlation
Right femur*Pain	-.500**	.000**	Negative correlation
Total Spine*Pain	-.734**	.000**	Negative correlation

*Significant at .01 level.

Discussion

The purpose of the present study was to investigate the correlation of BMD, Vitamin D, and Vitamin B12 levels in patients with musculoskeletal pain. Data which was obtained from one hundred and thirty-six patients was quite useful in determining how nutrient deficiencies in these vitamins are related to the progression of osteoporosis in the spine, left femur, and right femur besides pain level. These findings have important implications in the context of the relationships between vitamin deficits, bone density, and musculoskeletal pain in patients with osteoporosis.

The risk of osteoporosis was identified in most of the study participants, whose BMD levels were low across the groups. More concretely, 81 osteoporosis patients were detected in the right femur, 89 in the left femur and a surprising 120 in the total spine. These findings are in support with other studies pointing to spine as being a major site for osteoporotic fracture leading to worsening of back pain.[18] The scores especially in spine implies that bone fragmentation in that area could be adding a lot of pain to these patients.

Another area of interest in the study was on the correlation between BMD and degrees of pain. Among 42 patients with osteoporosis at all three regions, spine, left femur and right femur, pain severity was severe in 26 patients while 16 patients complained of moderate pain only. suggests, therefore, the trend observed in this study concerning low BMD and the increased risk for fractures and the consequent pain as captured elsewhere.[19] As expected with this patient population, this study also indicates that bone density is lower, specifically in weight-bearing areas such as the femur and spine, which correlate with the patients' identified pain sites.

Deficiency of vitamin D was established as a problem among patients experiencing musculoskeletal pain and osteoporosis. To be specific, 31 patients who indicated osteoporosis at all three regions had severe Vitamin D deficiency and 12 others had inadequate Vitamin D levels. This is in accordance with the established part of Vitamin D in the bone system since its deficiency affects the ability of the body to absorb calcium which is vital for the bones hence leading to formation of osteoporosis.[20] Many of them conclusively defined Vitamin D deficiency as being directly linked with increased musculoskeletal pain within the elderly and within patients with chronic diseases such as osteoporosis. Such a state seen in this study underscores the importance of early treatment like Vitamin D supplementation to decrease pain and optimize bone health for the patients.

Furthermore, in this cross-sectional work the author explored the participants' Vitamin B12 status and its relation to osteoporosis and pain. The 43 patients who had osteopenia in both the left and right femurs, some patients had toxic level of Vitamin B12 of between 840-915 pg/mL while others lacked adequate Vitamin B12 level. In addition, thirty percent of the 42 confirmatory osteoporosis patients of all the three regions lacked normal levels of Vitamin B12 while the others had hyper levels. Due to such staggered changes in the pattern, further research must be done to pin down the exact process through which Vitamin B12 operates in the framework of bone metabolism. While it has always been associated with neurological disorders,[21] it has been hypothesized that Vitamin B12 may have effects on the skeletal system that are linked to collagen synthesis and osteoblast activity.[22] Some of the patients have high toxic levels of Vitamin B12, which might be related to supplementation thus, the need to monitor people taking supplements to avoid some of the effects. Our results are supported by the study of He *et al.*,[23] where the overdose of vitamin D led to increased fractures incidence. The fact that the conditions of patient with severe osteoporosis and pain worsen when there are both Vitamin D and Vitamin B12 deficiency brings several questions to clinician. A significant loss of bone density in osteoporosis patients with spine, left femur, right femur densities included those with deficiency in one or both vitamins. Perhaps, these vitamin deficiencies work synergistically with each other to increase bone resorption and pain. The low vitamin levels may have impaired bone remodeling[7] and the low level of vitamin B12 might have negatively affected bone density as well as skeletal stability.[24] This could partly explain why more patients with osteoporosis in all the three regions complained of increased pain than the patients with osteopenia or normal BMD. The results indicate that more vigilant follow up and prescribed vitamin supplementation may be required especially in relation to controlling pain and containing bone loss.

The clinician implications of these findings are enormous. First, running Vitamin D and B12 blood tests in persons with musculoskeletal discomfort and potential osteoporosis is vital. Secondly and relatedly, intervention strategies must consider possible vitamin deficiencies in the children, as well as the possible negative consequences of supplying the children with more vitamins than is necessary. Two of the most common supplements are Vitamin D and Vitamin B12, which should be taken in moderation to prevent worsening of bone or pain diseases. Thirdly, the link between osteoporosis and pain is positive high significantly supporting the idea that osteoporosis treatment should include pain control strategies. Our findings support the growing recognition that nutritional status plays a central role in bone health and pain perception. From a clinical perspective, incorporating Vitamin D and B12 testing into the evaluation of patients with musculoskeletal complaints may facilitate earlier diagnosis of osteoporosis and more targeted management strategies. However, supplementation should be carefully monitored to avoid imbalances and ensure effectiveness. This study has some limitations. Its cross-sectional design prevents establishing causation between BMD, vitamins, and pain. Better-controlled longitudinal studies could provide stronger evidence on how vitamin level variations affect bone density and pain over time. Additionally, factors like calcium levels, physical activity, and genetics, beyond Vitamin D and B12, may have influenced the results. The study explores the relationship between BMD, Vitamin D, B12, and musculoskeletal pain, emphasizing the need for accurate diagnosis and appropriate treatment. For osteoporosis, vitamin supplementation is crucial for improving bone health and reducing pain. Further research is needed to clarify these connections and optimize vitamin administration alongside other therapies.

Conclusions

Osteoporosis was highly prevalent among patients with musculoskeletal pain in this study. Lower Vitamin D levels were significantly associated with reduced bone mineral density and greater pain intensity, underscoring the importance of adequate vitamin D status in maintaining skeletal integrity. Variations in Vitamin B12 levels also correlated with pain and bone health, although the mechanisms remain uncertain and warrant further research. These findings emphasize the need for early screening of osteoporosis and vitamin levels, as well as targeted supplementation strategies to improve bone health and alleviate pain in patients at risk.

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Ethics approval: the Ethics Committee of Institutional Review Board of the University Clinical Center of Kosova, Rheumatology Clinic approved this study (1101/2022 IRB). The study is conformed with the Helsinki Declaration of 1964, as revised in 2013, concerning human and animal rights.

Informed consent: all patients participating in this study signed a written informed consent form for participating in this study.

Patient consent for publication: written informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

Availability of data and materials: all data generated or analyzed during this study are included in this published article.