



## Vitamin D Deficiency in Adults with Musculoskeletal Pain

### Kas İskelet Sistemi Ağrısı Olan Yetişkinlerde D Vitamini Yetersizliği

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### Summary

**Objective:** The aim of this study was to determine whether vitamin D deficiency in patients with musculoskeletal pain who were admitted to our hospital and to establish the difference between vitamin D levels according to gender and age groups.

**Materials and Methods:** Among 28.702 patients, 857 (3%) patients whose vitamin D levels were studied were included in the study. Serum 25(OH) D level was determined by liquid chromatography-mass spectrometry (LC-MS). The patients were divided into three groups according to 25(OH) D level as; Group 1: >30 µg/L (sufficient), group 2: 10-30 µg/L (moderate insufficient), and group 3: <10 µg/L (severe insufficient).

**Results:** The mean age of the patients were 49.1±14.5 (18-87) years and the mean serum vitamin D levels of patients admitted to our hospital were found 15.3±10.3 µg/L. The 25(OH) vitamin D levels of 91% (780) patients were below normal limits. In 44.2% (379) of the patients, 25(OH) D level was <10 µg/L and severe deficiency were found. Vitamin D levels were lower in females than those in males. Secondary hyperparathyroidism was detected in 17% (146) of the patients.

**Conclusion:** Vitamin D deficiency, which is still an important world-wide medical problem despite all preventive measures, is commonly seen in our country and affects especially female population.

**Keywords:** Vitamin D deficiency, parathyroid hormone, age, gender

### Öz

**Amaç:** Bu çalışmamızın amacı hastanemize kas iskelet sistemi ağrısı ile başvuran hastalarda D vitamini eksikliği olup olmadığını belirlemek ve yaş ile cinsiyete göre D vitamini düzeyleri arasındaki farkı tespit etmektir.

**Gereç ve Yöntem:** Çalışmaya 28,702 hastadan D vitamini düzeyi çalışılmış olan toplam 857 (%3) hasta dahil edildi. Serum 25(OH) D düzeyi likit kromatografi kütle spektrometresi (LK-KS) ile ölçüldü. Hastalar 25(OH) D vitamini düzeyine göre üç gruba ayrıldı. Grup 1: >30 µg/L (yeterli), grup 2: 10-30 µg/L (ılımlı yetersiz) ve grup 3: <10 µg/L (şiddetli yetersiz) yer aldı.

**Bulgular:** Hastaların yaş ortalaması 49,1±14,5 (18-87) yıl ve D vitamini düzeyi ortalaması 15,3±10,3 µg/L bulundu. D vitamini düzeyi hastaların %91'inde (780) normalin altındaydı. Hastaların %44,2'sinde (379) şiddetli yetersizlik tespit edildi ve 25(OH) D düzeyi <10 µg/L'nin altındaydı. D vitamini düzeyleri kadınlarda erkeklerden daha düşüktü. Sekonder hiperparatiroidi %17 (146) hastada gözlemlendi.

**Sonuç:** D vitamini eksikliği alınan tüm koruyucu önlemlere rağmen dünya çapında önemli bir sağlık problemidir, ülkemizde yaygın olarak görülür ve özellikle kadınları etkiler.

**Anahtar kelimeler:** D vitamini eksikliği, paratiroid hormon, yaş, cinsiyet

### Introduction

Vitamin D regulates calcium and phosphorus metabolism via its physiological effects over bowels, kidneys, and parathyroid gland (1-5). Under normal circumstances, 90-95% of vitamin D present in human body is synthesized in the skin by the effect of sunlight. Vitamin D from food is not of much significance if it is not particularly supplemented. Thus, sunlight is the main

source of vitamin D, and if it is utilized enough, vitamin D supplements are not required (6,7). 25(OH) D is one of the major metabolites of vitamin D in circulation. The reason why 25(OH) D is measured is that half-life of 25(OH) D is 2-3 weeks, whereas that of 1,25-dihydroxy vitamin D is 4-6 hours (8-10). Vitamin D deficiency is a worldwide common health problem. Vitamin D deficiency and insufficiency affect most of the men and women at all age groups in many geographic regions. This

situation results from limited exposure to sunlight together with insufficient dietary support containing little calcium intake (11). Vitamin D deficiency causes decline in serum calcium levels by decreasing its absorption from bowels, leading to compensatory parathyroid hormone (PTH) secretion. Thus, secondary hyperparathyroidism causes mobilization of calcium from bone and reduction in bone mineral density (BMD). Despite all preventive measures, vitamin D deficiency leads to medical problems in many countries, especially in elderly (12-14). Deficiency of vitamin D has been reported in patients with many types of musculoskeletal pain (15). Muscle weakness in severe vitamin D deficiency could also be caused by secondary hyperparathyroidism and resultant hypophosphatemia (16,17). The objective of this study was to determine mean vitamin D, calcium, phosphorus, alkaline phosphatase (ALP) and PTH levels of the patients admitting to the outpatient clinic with musculoskeletal pain and to observe differences among gender and factors due to differences in vitamin D levels.

### Materials and Methods

A total of 857 patients with musculoskeletal pain at different regions of skeletal system diagnosed as low back pain, fibromyalgia, artralgia, osteoarthritis, widespread pain, lombar disc herniation, servical disc herniation among 28.702 patients admitted to an outpatient clinic in Atatürk Training and Research Hospital were included in this cross-sectional, retrospective study. Age, gender, vitamin D levels, calcium, phosphorus, ALP and PTH levels were recorded retrospectively from patients' files. 25(OH) D was determined by liquid chromatography-mass spectrometry (LC-MS) on an Applied biosystems (USA). Calcium measurements were studied by Roche Cobas c 701 method using a BAPTA (Germany). Phosphorus measurements were studied by Roche Cobas c 701 method using a phosphomolybdate-UV. PTH was determined by Roche Cobas e 601 method using a electrochemiluminescence method (ECLIA). ALP was determined by Roche Cobas c 701 method using PNPP (p-nitro phenylphosphate). Patients were divided into three groups: Vitamin D levels: >30 µg/L was considered as sufficient, 10-30 µg/L as moderate insufficient, and <10 µg/L as severe insufficient (14). Parameters that may be relevant were compared with vitamin D levels. PTH levels above 67 pg/mL were defined as secondary hyperparathyroidism.

Our exclusion criteria included pregnancy or breast feeding at the time of study, sign of rickets, significant renal, hepatic, or thyroid dysfunctions or any other major systemic diseases, including malignancy, diabetes mellitus and metabolic bone diseases.

### Statistical Analysis

Statistical Package for Social Sciences (SPSS) 17.0 software package was used for statistical analysis. In addition to descriptive statistical analysis, comparison between the two groups was performed with Mann-Whitney U test for independent samples and with Spearman correlation analysis for relationship between the parameters. P value <0.05 was accepted as statistically significant.

### Results

Retrospective screening showed that 62.9% (18,078) of the patients admitted to our outpatient clinic were females and 37.1% (1.0624) were males. A total of 857 patients who were considered to have vitamin D deficiency and checked for serum 25(OH) D, PTH, calcium, phosphorus, and ALP levels were included in the study. Vitamin D levels were checked in 4.2% (773) of female and 0.9% (84) of male patients. The mean vitamin D level of the patients was 15.3±10.3 µg/L and the mean age of the patients was 49.1±14.5 (18-87) years. Table 1 shows demographical and laboratory findings of the patients who were considered to have vitamin D deficiency. The mean serum vitamin D level was found to be significantly lower in females than that in males (p=0.004). Table 2 shows 25(OH) D, PTH, calcium, phosphorus, and ALP levels of male and female patients. Patients were grouped according to vitamin D levels and gender (Table 3), and it can be clearly seen that

**Table 1. Demographical and clinical findings**

n=857	Mean ± SD (min-max)
Age (years)	49.1±14.5 (18-87)
25(OH) D (µg/L)	15.3±10.3 (5.3-84)
Calcium (mg/dL)	9.6±0.5 (7.6-15.6)
Phosphorus (g/dL)	3.55±0.5 (1.8-5.7)
ALP (µg/L)	77.1±24.9 (31-197)
Parathormone (pg/mL)	54.5±26.4 (9.6-199)

ALP: Alkaline phosphatase, SD: Standard deviation

**Table 2. Comparison of demographical and clinical findings according to gender**

Mean ± SD (min-max)	Female	Male	p
Age (years)	49.5±14.7 (18-87)	45.4±16.1 (20-82)	0.004*
25(OH) D (µg/L)	15.0±10.2 (5.3-84)	17.3±11.2 (6.6-74.2)	0.004*
Calcium (mg/dL)	9.6±0.5 (7.6-15.6)	9.8±0.5 (8.6-10.8)	0.112
Phosphorus (mg/dL)	3.57±0.5 (1.8-5.7)	3.37±0.5 (2.2-4.4)	0.026*
ALP (µg/L)	76.9±25.2 (31-197)	79.7±22.6 (42-143)	0.304
Parathormone (pg/mL)	55.5±26.9 (9.6-199)	45.9±19.8 (15-132)	0.004*

ALP: Alkaline phosphatase, SD: Standard deviation

91% (780) of them were below normal limits. In 44.2% (379) of these patients, the serum 25(OH) D level was <10 µg/L and severe insufficiency was detected. Severe insufficiency was seen in 47.1% of the female patients while it was seen in 27.4% of the male patients who were checked for vitamin D levels. Secondary hyperparathyroidism was detected in 17% (146) of the patients. There was no significant relationship between vitamin D level and age, calcium, phosphorus, ALP, and PTH levels of the patients (p>0.05).

## Discussion

Vitamin D deficiency should be taken into consideration in the differential diagnosis of patients with musculoskeletal pain and rectify is reported to be an important component in the treatment of these patients (18).

The objective of this study was to determine whether there is vitamin D deficiency in patients with musculoskeletal pain admitted to our hospital and to establish the difference between vitamin D levels according to gender and age groups. Reports from many different countries show that D hypovitaminosis is a world-wide problem and a major health issue (19,20). The usage of different threshold levels in studies complicates the evaluation of vitamin D deficiency and insufficiency. Vitamin D deficiency or insufficiency prevalence changes between 7% and 80% depending on the defined threshold (21). When serum 25(OH) D is higher than 30 ng/mL, the condition is considered as the normal vitamin D level (8-11). In our study, the mean serum 25(OH) D level of the patients was 15.3 ng/mL, which is very low. In 91% of the patients included in the study, the vitamin D level was below 30 ng/mL. In 44.2% (379) of the patients, the 25(OH) D level was below 10 µg/L and severe deficiency was detected. Kurt et al. (22) reported that the vitamin D level was below normal limits in 70% of the patients who were admitted to the osteoporosis clinic, and the mean vitamin D level was 26.13±18.62 µg/L in their study. Other studies have shown that vitamin D deficiency and insufficiency found in patients with musculoskeletal pain (23,24).

Insufficient vitamin D levels are associated with old age, female gender (25-28). The mean serum vitamin D level was found to be significantly lower in females than in males, while phosphorus and PTH levels were significantly higher in females than in males. Severe insufficiency was seen in 47.1% of the

female patients and was seen in 27.4% of the male patients who were checked for vitamin D levels. Likewise, other studies have also reported vitamin D deficiency being more common in females than in males (22,29,30). In our study, there was no correlation between vitamin D levels and age.

Vitamin D insufficiency due to decrease in active transport of calcium from bowels leads to reduction in ionized calcium concentration in circulation and increase in PTH secretion. PTH normalizes circulating ionized calcium concentration by mobilizing calcium from skeleton and other target tissues. Rise in PTH increases bone resorption and bone loss. Sahota et al. (31) detected 39% of vitamin D insufficiency (≤12 ng/mL) prevalence in their study in England, which included 421 osteoporotic postmenopausal women with the mean age of 71.2 years. Secondary hyperparathyroidism was detected in 33% of the patients with vitamin D insufficiency.

In our study group, severe vitamin D insufficiency was detected in 44.2% (379) and secondary hyperparathyroidism in 17% (146) patients. No significant relationship was found between vitamin D levels and age, calcium, phosphorus, ALP, and PTH levels of the patients. Singh et al. (32) found no relationship between serum calcium, albumin, phosphate, ALP levels and vitamin D deficiency in their study. There are studies showing negative correlation between 25(OH) D and PTH concentration (33,34). Recent studies reported that vitamin D deficiency is related to musculoskeletal symptoms. The present study had some limitations. First of all, it is a retrospective study, so we did not have any knowledge about the degree of sun exposure and vitamin D intakes of our patients. Another limitation of this study was that we compared vitamin D values of the participants with respect to gender despite the fact that most of them were women. Further studies are needed to investigate the role of vitamin D in patients with musculoskeletal pain.

## Conclusion

Although Turkey is a Mediterranean country, we demonstrated that 25(OH) D levels are low in Turkey. In our country, the importance of provision and consumption of vitamin D supported food and utilization of sunlight, especially for the population that is at risk, must be underlined.

## Author Contributions

*Ethics Committee Approval: April 2013, Informed Consent: Consent form was filled out by all participants Ankara Atatürk Training and Research Hospital, Concept: Sevgi Gümüş Atalay, Design: Fatma Fidan, Data Collection or Processing: Roni Atalay, Analysis or Interpretation: Berat Meryem Alkan, Literature Search: Sevgi Gümüş Atalay, Writing: Sevgi Gümüş Atalay, Peer-review: External and Internal peer-reviewed, Conflict of Interest: The authors reported no conflict of interest related to this article, Financial Disclosure: The authors declared that this study has received no financial support.*

**Table 3. Comparison of vitamin D levels according to gender**

Vitamin D (µg/L)	Female n (%)	Male n (%)	Total n (%)
>30 (sufficient)	60 (7.8)	17 (20.2)	77 (9)
10-30 (moderate insufficient)	357 (46.2)	44 (52.4)	401 (46.8)
<10 (severe insufficient)	356 (46.1)	23 (27.4)	379 (44.2)

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