# Semptomatik diz osteoartritinde vitamin D düzeyi: klinik ve radyolojik parametrelerle ilişkisi

# Vitamin D status in symptomatic knee osteoarthritis: association with clinical and radiological parameters

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***Özet***

***Amaç:*** *45-60 yaş arası kadınlarda D vitamini eksikliği ile diz osteoartriti arasındaki ilişkiyi belirlemeyi amaçladık.*

***Gereç ve yöntem:*** *Çalışmada diz osteoartritli 110 kadın hasta yer aldı. Hastalar vitamin D seviyesine göre iki gruba ayrıldı: 1. grup düşük D vitamini seviyesine sahip (< 20 ng/ml) 65 hasta ve 2. grup ise normal D vitamini seviyesine sahip (≥20 ng/ml) 45 hastayı içerdi. Osteoartritin şiddeti Kellgren-Lawrence (KL) derecelendirme skalası ile değerlendirildi. Ağrı, tutukluk ve fonksiyonel durum Western Ontario and McMasters Üniversiteleri Osteoartrit İndeksi (WOMAC) ile ölçüldü.*

***Bulgular:*** *Vitamin D eksikliği oranı % 59,09 idi. Ortalama vitamin D seviyesi 1. grupta 9,09 ±3,82; 2. grupta 27,84 ±6,42 idi. Vitamin D düzeyi 1. grupta anlamlı derecede düşüktü (p=0,00). K/L evre 1 (%28,89) ve K/L evre 2 (%64,44) sıklıkla grup 2'de daha fazla iken, evre 3 (%38,46) ve evre 4 (%15,38) grup 1'de fazla bulundu. 1. grup, 2. gruba göre anlamlı derecede yüksek radyografik evrelere sahipti (p=0,00). 1. gruptaki hastaların WOMAC skorları anlamlı derecede yüksekti (p=0,00). K/L skorları, VAS-ağrı ve WOMAC skorları ile korele bulundu (p=0,00). K/L skorları vücut kitle indeksi (VKİ) ile anlamlı korelasyon göstermedi (p=0, 82).*

***Sonuç:*** *Vitamin D eksikliği ağrı, tutukluk, fonksiyonel ve radyolojik durum açısından diz osteoartriti ile ilişkilidir.*

***Anahtar Kelimeler:*** *D vitamini eksikliği, osteoartrit, diz*

***Türkçe kısa makale başlığı:*** *Diz osteoartritinde vitamin D düzeyi*

***Abstract***

***Objective:*** *We aimed to examine the relationship between vitamin D deficiency and knee osteoarthritis in women aged 45-60.*

***Methods:*** *110 female patients with knee osteoarthritis were included. Patients were divided into two groups according to vitamin D level: group 1 included 65 patients with low vitamin D (< 20 ng/ml), and group 2 included 45 patients with vitamin D in normal ranges (≥20 ng/ml). Severity of osteoarthritis was evaluated by Kellgren-Lawrence (KL). Pain, stiffness and functional status were measured by Western Ontario and McMasters Universities Osteoarthritis Index (WOMAC).*

***Results:*** *Rate of vitamin D deficiency was 59.09%. Mean vitamin D level was 9.09±3.82 in group 1 and 27.84±6.42 in group 2. Vitamin D was significantly lower in group 1 (p=0.00). K/L grade 1(28.89%) and 2(64.44%) were most frequently found in group 2, whereas grade 3(38.46%) and 4(15.38%) were found in group 1. Group1 had significantly higher radiographic grades than group 2 (p=0.00). Patients in group 1 scored significantly higher in WOMAC (p=0.00). K/L scores were correlated with VAS-pain and WOMAC scores (p=0.00). K/L scores showed no significant correlation with body mass index (BMI) (p=0.82).*

***Conclusion:*** *Vitamin D deficiency is associated with knee OA in terms of pain, stiffness, functional and radiological status.*

***Key words:*** *vitamin D deficiency, osteoarthritis, knee*

***İngilizce kısa makale başlığı:*** *Vitamin D status in knee osteoarthritis*

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**Introduction**

Osteoarthritis (OA) is the most common form of arthritis, and knee is one of the most frequently involved joint (1). Altered joint loading due to obesity, malalignment, trauma or joint instability have been found to be associated with knee OA (2).

Vitamin D has multiple biological effects on cartilage, bone and muscle functions. Since OA affects all joint structures, including articular cartilage, bone and periarticular muscle, vitamin D has beneficial effects on these joint structures in OA. Moreover, low vitamin D may lead to vascular smooth muscle cell proliferation, endothelial cell dysfunction, vascular dysfunction, and increased inflammation; all of these may play roles in etiology of OA (3).

The aim of this study was to examine the relationship between vitamin D deficiency, and radiographical and clinical parameters of knee osteoarthritis.

**Methods**

110 women (aged 45-65 years) fulfilling the diagnostic criteria of the American College of Rheumatology (ACR) for classification of knee OA (4) who were admitted to our outpatient clinic between December 2013 and February 2014 were consecutively enrolled in the study. The serum levels of vitamin D of the patients were assessed by using Enzyme Linked Immunosorbent Assay (ELISA). Vitamin D levels less than 20 ng/ml were considered as deficient. The patients were divided into two groups according to the level of vitamin D: group 1 consisted of 65 patients with low vitamin D level (< 20 ng/ml), and group 2 consisted of 45 patients with vitamin D level in normal ranges (≥20 ng/ml).

Patient information regarding age, body mass index (BMI), and disease duration was recorded. Anteroposterior and lateral knee radiographs were taken during weight-bearing. The severity and grade of osteoarthritis were evaluated by using Kellgren-Lawrence (K/L) grading scale: grade 1, doubtful narrowing of joint space and possible osteophytic lipping; grade 2, definite osteophytes and possible narrowing of joint space; grade 3, moderate multiple osteophytes, definite narrowing of joint space, some sclerosis, and possible deformity of bone contour, and grade 4: large osteophytes, marked narrowing of joint space, severe sclerosis, and definite deformity of bone contours (5, 6). The severity of pain, stiffness and functional status were assessed by using Western Ontario and McMasters Universities Index of Osteoarthritis (WOMAC). WOMAC includes three subgroups. WOMAC A is used for evaluating the knee pain. Total subscore ranges between 0 and 20. Stiffness is assessed using the stiffness subscale of the WOMAC (WOMAC B) which includes two items with total subscore of zero to eight. WOMAC C includes 17 items. Patients are asked to rate the degree of difficulty related to functional activities using a 5-point numeric scale (0: none, 1: mild, 2: moderate, 3: severe, 4: extreme) with a total subscore ranging from 0 to 68 (7). 10 cm Visual Analog Scale-Pain (VAS-pain) was used for determining level of pain (8). The subjects with inflammatory arthritis, osteonecrosis, metabolic bone diseases, neoplasms, paresis, neuropathy, history of knee trauma or knee surgery, and history of intra-articular injections and physical therapy in the preceding six months were excluded.

Participants were informed about the study, and their written informed consent was taken. The study was approved by the Medical Research Ethics Committee of Kocaeli Training and Research Hospital. It conforms to the provisions of the World Medical Association's Declaration of Helsinki.

**Statistical analyses**

Data were presented by descriptive analysis with mean ± standard deviation (SD). Scores of the above-mentioned scales were obtained for statistical analyses. Depending on these values, the level of the linear relation between these scales was evaluated by correlation analysis. The presence of correlation between these scales was evaluated by Pearson's correlation coefficient. Independent samples t test was used to compare the differences between two groups for continuous variables. Chi-square test was used for categorical variables.

Statistical Package for the Social Sciences-15.0 (SPSS-15.0) software for Windows® was used for statistical analyses. Statistical significance and the confidence interval was set at p<0,05 and 99%, respectively.

**Results**

The study included a total of 110 female patients with knee osteoarthritis. Mean age was 54.45±4.78 [45-63] (median 53) in group 1 and 55.18±5.18 [45-64] (median 55) in group 2. Mean BMI in group 1 and group 2 was 28.83±4.12 [20, 4-39] (median 29) and 28.67±3.57 [21.5-35] (median 28), respectively. There was no statistically significant difference between groups in terms of age and BMI (p>0.05) (Table 1).

The rate of vitamin D deficiency was 59.09%. Mean level of vitamin D was 9.09 ±3.82 [4-19] (median 8) in group 1 and 27.84 ±6.42 [19-50] (median 27) in group 2. Level of vitamin D was significantly lower in group 1 (p=0.00) (Table 1).

Mean VAS-pain score was 6.52±1.44 [1-10] (median 7) in group 1 and 3.6±1.85 [1-9] (median 3) in group 2. VAS-pain score was significantly higher in group 1 (p=0.00) (Table 1).

Mean score was 14.87±3.40 [4-20] (median 15) in group 1, 6.89±3.97 [2-20] (median 6) in group 2 for WOMAC A, 4.11±2.13 [0-8] (median 4) in group 1, 1.58±1.73 [0-7] (median 1) in group 2 for WOMAC B, 46.35±18.27 [4-68] (median 52) in group 1, 16.00±16.31 [1-58] (median 9) in group 2 for WOMAC C and 63.89±21.93 [8-91] (median 68) in group 1, 24.04±19.89 [6-82] (median 17) in group 2 for WOMAC TOTAL. Patients in group 1 scored significantly higher in WOMAC A, B, C, and WOMAC TOTAL (p=0.00) (Table 1).

**Table 1. Demographic and clinical data of the patients with knee osteoarthritis**

| | Group 1 (n=65) | Group 2 (n=45) | P value |
|---|---|---|---|
| **Age (year)** | 54.45±4.78 | 55.18±5.18 | 0.86 |
| **BMI (kg/m2)** | 28.83±4.12 | 28.67±3.57 | 0.85 |
| **VAS-pain (cm)** | 6.52±1.44 | 3.6±1.85 | 0.00* |
| **Vitamin D (ng/ml)** | 9.09±3.82 | 27.84±6.42 | 0.00* |
| **WOMAC A** | 14.87±3.40 | 6.89±3.97 | 0.00* |
| **WOMAC B** | 4.11±2.13 | 1.58±1.73 | 0.00* |
| **WOMAC C** | 46.35±18.27 | 16.00±16.31 | 0.00* |
| **WOMAC TOTAL** | 63.89±21.93 | 24.04±19.89 | 0.00* |

***BMI:** Body mass index, **VAS-pain**: Visual analog scale-pain, **WOMAC:** Western Ontario and McMasters Universities Index of Osteoarthritis *P < 0.05 ( significant)*

K/L grades 1 (28.89%) and 2 (64.44%) were most frequently found in group 2, whereas grades 3 (38.46%) and 4 (15.38%) were found in group 1. Group 1 had significantly higher radiographic grades than group 2 when compared (p=0.00) (Table 2).

**Table 2. Radiological data of the patients with knee osteoarthritis**

| Kellgren/Lawrence | Group 1 (n=65) n(%) | Group 2 (n=45) n(%) | *P* value |
|---|---|---|---|
| Grade 1 | 2(3.08%) | 13(28.89 %) | 0.00 * |
| Grade 2 | 28(43.08 %) | 29(64.44 %) | |
| Grade 3 | 25(38.46 %) | 3(6.66%) | |
| Grade 4 | 10(15.38 %) | 0(%) | |

**P < 0.05 ( significant)*

K/L scores were strongly correlated with VAS-pain, WOMAC-A, WOMAC-B, WOMAC-C and WOMAC-TOTAL (r: 0.45, 0.57, 0.47, 0.54, and 0.56 respectively) (p=0.00) (Table 3).

K/L scores showed no significant correlation with BMI (p=0.82) (Table 3).

**Table 3. The association between clinical and radiological parameters**

| | | BMI | VAS-ağrı | WOMAC-A | WOMAC-B | WOMAC-C | WOMAC-Toplam |
|---|---|---|---|---|---|---|---|
| **Kellgren/ Lawrence** | r | 0.166 | 0.45 | 0.57 | 0.47 | 0.54 | 0.56 |
| | p | 0.82 | 0.00* | 0.00* | 0.00* | 0.00* | 0.00* |

*BMI: Body mass index, VAS-pain: Visual analog scale-pain, WOMAC: Western Ontario and McMasters Universities Index of Osteoarthritis*
**P < 0.05 ( significant)*

**Discussion**

The relationship between vitamin D deficiency and knee osteoarthritis is still unclear. The aim

of our study was to examine the relationship between vitamin D deficiency and knee osteoarthritis in terms of pain, functional status and radiological grading.

In our study, K/L radiographic grades 1 and 2 were most frequently found in group 2, whereas grades 3 (38.46%) and 4 (15.38%) were found in group 1. Group with vitamin D deficiency had higher radiographic grades, when compared with the other group. We reported that low level of vitamin D was associated with worsening of radiographic knee osteoarthritis. This was suggested in previous studies. Bergink et al. reported that low dietary vitamin D intake increased the development and worsening of knee OA, in the 'Rotterdam Study' (9). This finding was also suggested in 'Framingham Study', which showed low vitamin D might be associated with development of cartilage loss and progression of knee OA (10). In a recent study, it was demonstrated a significant positive association between serum vitamin D deficiency and symptoms of knee OA in the patients aged < 60 years (11). Similarly, Cao indicated moderate evidence showing that low levels of vitamin D were associated with increased progression of radiographic OA (3). On the other hand, Ding et al. concluded that serum vitamin D levels were related with decreased knee cartilage loss (12). In contrast to these studies, Felson indicated that vitamin D status was not related to the risk of joint space or cartilage loss in knee OA (13). Hunter et al. found that there was evidence of decreased vitamin D levels in patients with radiographic knee OA, but after adjusting for age, BMI and relatedness, the significant differences disappeared (14). While, Muraki found no significant association between radiographic knee OA and level of vitamin D (15). Also Al-Jarallah reported that the level of vitamin D was not associated with the severity of radiographical grading (16).

In our study, WOMAC scores were higher in patients with vitamin D deficiency. Patients with vitamin D deficiency scored significantly higher in knee pain, stiffness and functional status subgroups of WOMAC. This was concordant to the previous studies in the literature. Laslett et al. reported that moderate vitamin D deficiency was associated with knee pain, functional impairment and stiffness in older adults with knee osteoarthritis (17). However, Muraki suggested that vitamin D level tended to be associated with knee pain, without association with radiographic knee OA, indicating that the association of vitamin D level with knee pain may be independent of radiographic knee OA (15).

Evaluation of clinical parameters is important as radiological assessment in the diagnosis and management of knee OA. Since radiological diagnosis of knee OA without clinical symptoms like pain, stiffness, and functional limitation may lead to unnecessary drug use in older adults, it is important to determine the relationship between clinical variables and radiographic findings. We found that radiographic severity which was measured by K/L grading was associated with increasing pain, stiffness and functional limitation. Mermerci et al. also concluded that severity of radiographic knee osteoarthritis was highly related with pain severity (1). McAlindon et al. reported an increase in frequency of disability with worsening of radiographic knee osteoarthritis (18). Duncan et al. indicated a relationship between the degree of radiographic change and the severity of knee pain and functional limitation (19). In contrast to these studies, Cubukcu et al. reported that radiological findings did not correlate with the severity of pain and functional impairment as assessed by WOMAC (20). Zhai also concluded that knee pain in older adults was not associated with radiographic knee OA (21).

In previous studies, BMI was reported to be associated with radiographic knee osteoarthritis (22-25). Obesity may act through the direct effect of body weight on load and also through the influence of other factors that mediate the mechanical impact of excess body weight at the knee. Varus malalignment by focusing body weight forces medially may be a medicating factor between obesity and knee osteoarthritis (26). On the

contrarily, we found no association between BMI and radiographic knee osteoarthritis.

In the present study, the rate of vitamin D deficiency was reported as 59.09% in Turkish female patients with knee osteoarthritis. Ding et al. reported the rate of vitamin D deficiency in Tasmanian patients with knee osteoarthritis as 45% (12). In a study performed on the patients with knee OA, the prevalence of vitamin D deficiency was found as 39.8% (11). It was more frequent in our series. There may be two reasons for more frequent vitamin D deficiency in our patients. The first one was the season in which study was performed. The patients were assessed in winter months (either in December or January or February). Second, all of our patients were women and the majority of Turkish women wear traditional clothes causing inadequate exposure to sunlight and vitamin D deficiency.

There were some limitations in our study. The first one was relatively small number of subjects. The second one was its cross-sectional design rather than longitudinal follow- up.

This study has demonstrated a significant association between vitamin D deficiency and knee OA in terms of pain, stiffness, functional status and radiological grading. Vitamin D supplementation may be useful for clinical symptoms like pain, stiffness and functional impairment instead of analgesics which have potential side effects in elderly patients with knee OA.

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