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# Association Between Vitamin D Status and Knee Osteoarthritis: A Case-Control Study

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## ABSTRACT

**Introduction:** Knee osteoarthritis (KOA) is a major cause of pain, disability, and reduced quality of life among older adults. Vitamin D plays an important role in musculoskeletal health and may influence cartilage metabolism, inflammation, and subchondral bone remodeling. However, the association between vitamin D deficiency and KOA remains controversial. This study aimed to evaluate the relationship between serum vitamin D status and knee osteoarthritis and to assess its association with radiographic disease severity.

**Materials and Methods:** A hospital-based case-control study was conducted in the Department of Orthopaedics of a tertiary care teaching hospital from July 2024 TO December 2025. A total of 80 participants were enrolled, including 40 patients with primary KOA (cases) diagnosed according to American College of Rheumatology criteria and 40 age- and sex-matched healthy controls without clinical or radiological evidence of knee osteoarthritis. Serum 25-hydroxyvitamin D [25(OH)D] levels were measured using chemiluminescent immunoassay and categorized as sufficient (>30 ng/mL), insufficient (20–29 ng/mL), or deficient (<20 ng/mL). Radiographic severity was assessed using the Kellgren–Lawrence grading system. Statistical analysis was performed using SPSS version 26.0, with $p<0.05$ considered significant.

**Results:** The mean serum vitamin D level was significantly lower in cases than controls (22.1 ± 6.3 ng/mL vs. 31.6 ± 7.4 ng/mL; $p<0.001$). Vitamin D deficiency was observed in 55.0% of cases compared with 12.5% of controls, whereas sufficient vitamin D levels were present in 20.0% and 60.0% of participants, respectively ($p<0.001$). Cases also had a significantly higher mean BMI than controls (29.1 ± 4.3 kg/m² vs. 26.7 ± 3.8 kg/m²; P=0.009). Vitamin D deficiency increased progressively with disease severity, occurring in 12.5% of Grade I, 44.4% of Grade II, and 92.9% of Grade III KOA patients ($p<0.001$). Individuals with vitamin D deficiency had significantly higher odds of KOA (OR=8.56; 95% CI: 2.70–27.15; $p<0.001$).

**Conclusion:** Vitamin D deficiency is significantly associated with the presence and radiographic severity of knee osteoarthritis. Routine assessment of vitamin D status may help identify individuals at increased risk and support comprehensive management strategies in patients with KOA.

***Keywords****: Osteoarthritis Knee; Vitamin D Deficiency; 25-Hydroxyvitamin D; Body Mass Index*

## INTRODUCTION

Knee osteoarthritis (KOA) is a leading cause of chronic pain, disability and reduced mobility among adults and older individuals worldwide. It is one of the important causes of impaired quality of life particularly in elder individuals. The global burden of osteoarthritis has risen substantially with increasing life expectancy, obesity, sedentary lifestyle with the knee being one of the most commonly affected joints.[1] KOA is no longer seen solely as a disease of mechanical "wear and tear" and it is now accepted as a multifactorial disorder involving cartilage degradation, subchondral bone remodeling,

synovial inflammation and metabolic influences. Because disease-modifying options remain limited, identifying modifiable biological factors that cause KOA is of considerable clinical as well as public health importance.[2]

Vitamin D is traditionally known for its role in calcium homeostasis, bone mineralization, and musculoskeletal function. Serum 25-hydroxyvitamin D [25(OH)D] is the accepted marker of vitamin D status and its deficiency is common across diverse populations. Vitamin D deficiency is particularly common among older adults, women, individuals with obesity, limited sunlight exposure, and secondary to low dietary intake.[3] Beyond skeletal health, vitamin D receptors are also expressed in chondrocytes, osteoblasts, synoviocytes and immune cells. Their presence in these locations suggest that vitamin D may influence joint tissue metabolism and inflammatory pathways. Deficiency may contribute to muscle weakness, impaired balance, altered joint loading and suboptimal subchondral bone quality. All these factors are relevant to the initiation and progression of KOA.[4]

From a biological perspective an association can exist between vitamin D deficiency and KOA. Vitamin D is known to modulate chondrocyte proliferation, extracellular matrix turnover and subchondral bone remodeling. Low vitamin D levels may also decrease quadriceps strength and increase pain sensitivity thereby aggravating functional limitation in cases with KOA. However, whether vitamin D deficiency is a causal contributor to knee osteoarthritis or a marker of poor general health or a consequence of reduced outdoor activity caused by knee pain remains uncertain and debatable. This uncertainty highlights the need for population-specific analytical studies that compare vitamin D status between individuals with KOA and appropriately selected healthy individuals with no knee pain or osteoarthritis.[5]

Several epidemiological studies have analysed the relationship between vitamin D status and KOA, however the findings of these studies remain inconsistent. Some observational studies have reported that low serum 25(OH)D levels are associated with increased knee pain, radiographic severity, cartilage loss and disease progression .[6] In contrast, other longitudinal and interventional studies have failed to demonstrate a consistent protective effect of adequate vitamin D levels on structural progression or clinical outcomes . These discrepancies may be due to differences in study design, different population characteristics and presence of confounding variables.

The existing evidence is limited by conflicting results and underrepresentation of many regional populations in whom both KOA and vitamin D deficiency are highly prevalent.[7] Therefore, this case-control study aims to assess the association between serum vitamin D status and knee osteoarthritis by comparing vitamin D levels among patients with KOA and healthy controls without knee pain. By addressing these knowledge gaps, this study aims to analyse whether vitamin D deficiency is significantly associated with KOA and also whether routine assessment of vitamin D status should be done in patients with knee osteoarthritis.

**MATERIALS AND METHODS: -**

This case-control study was conducted in the Department of Orthopaedics of a tertiary care hospital. The duration of study was 18 months extending from July 2024 to December 2025. The study included a total of 80 individuals out of which there were 40 patients diagnosed with knee osteoarthritis (cases) and 40 age- and sex-matched healthy individuals without knee pain or clinical evidence of knee osteoarthritis (controls). written informed consent was obtained from all participants. The diagnosis of knee osteoarthritis was established according to the American College of Rheumatology (ACR) criteria and supported by radiographic evaluation using the Kellgren–Lawrence grading system. Sample size was calculated using the formula for comparison of proportions in case-control studies. While calculating sample size a confidence level of 95%, power of 80% and anticipated difference in vitamin D deficiency prevalence between cases and controls was considered based on previous published literature. The minimum calculated sample size was 72 subjects; however, to improve statistical validity and to make up for drop out cases 80 participants were enrolled in the study.

Eligible cases as well as controls were recruited consecutively from the outpatient and inpatient orthopaedic department. Detailed demographic and clinical information, including age, gender, body mass index (BMI), occupation and duration of symptoms were asked and noted. Additionally, presence of comorbid illnesses and lifestyle characteristics was also collected using a structured proforma. All participants underwent comprehensive clinical examination. Patients in the case group were evaluated for knee pain, stiffness, functional limitation and physical findings suggestive of osteoarthritis. In osteoarthritis of knee group standard anteroposterior weight-bearing and lateral radiographs of the affected knee were obtained and severity of osteoarthritis was graded according to the Kellgren–Lawrence classification. Controls were selected from individuals attending routine health check-ups or relatives accompanying patients and were confirmed to have no clinical or radiological evidence of knee osteoarthritis.

Under aseptic precautions venous blood samples (5 mL) were drawn from all participants. Serum was separated and analyzed for 25-hydroxyvitamin D [25(OH)D] concentration using a standardized chemiluminescent immunoassay method. Vitamin D status was categorized according to established laboratory reference values: sufficient (>30 ng/mL), insufficient (20–29 ng/mL) and deficient (<20 ng/mL). The serum vitamin D levels of cases and controls were compared to determine the association between vitamin D status and knee osteoarthritis. In addition, the relationship between serum

vitamin D levels and radiographic severity of osteoarthritis was evaluated using Kellgren–Lawrence grades in individuals with osteoarthritis.

Data was entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) version 26.0. Continuous variables were expressed as mean ± standard deviation. categorical variables were presented as frequencies as well as percentages. The independent Student's t-test was used to compare continuous variables between cases and controls. Chi-square test or Fisher's exact test was applied to analyze categorical variables. Odds ratios (ORs) were calculated to assess association between vitamin D deficiency and knee osteoarthritis. A p-value $< 0.05$ was considered statistically significant.

**Inclusion Criteria**

**Cases**

- Patients aged ≥40 years.
- Patients diagnosed with primary knee osteoarthritis based on ACR clinical and radiological criteria.
- Patients willing to provide written informed consent.
- Patients with Kellgren–Lawrence Grade I–III osteoarthritis.

**Controls**

- Age- and sex-matched healthy individuals.
- No clinical symptoms or radiological evidence of knee osteoarthritis.
- Ready to give written and informed consent to be part of study.

**Exclusion Criteria**

- Secondary osteoarthritis due to trauma, inflammatory arthritis, or congenital disorders.
- Kellgren–Lawrence Grade IV osteoarthritis.
- History of rheumatoid arthritis, gout, ankylosing spondylitis, or other inflammatory joint diseases.
- Chronic kidney disease, chronic liver disease, malabsorption syndromes, or endocrine disorders affecting vitamin D metabolism.
- Current use of vitamin D supplementation, calcium supplementation, corticosteroids, anticonvulsants, or bisphosphonates within the previous six months.
- Patients with malignancy or severe systemic illness.
- Pregnant or lactating women.
- Individuals unwilling to participate in the study.

**RESULTS**

Females constituted the majority of participants, accounting for 24 (60.0%) cases and 22 (55.0%) controls. Males comprised 16 (40.0%) cases and 18 (45.0%) controls. The gender distribution of both the groups was comparable with no statistically significant difference (p=0.82).

| Gender | Cases (n=40) | Controls (n=40) | p-value |
|---|---|---|---|
| Male | 16 (40.0%) | 18 (45.0%) | 0.82 |
| Female | 24 (60.0%) | 22 (55.0%) | |
| **Total** | **40 (100%)** | **40 (100%)** | |

**Table 1: Gender Distribution Among Cases and Controls**

The highest proportion of participants belonged to the 60–69 years age group comprising 14 (35.0%) cases and 12 (30.0%) controls. The 40–49 years age group represented the smallest proportion, with 6 (15.0%) cases and 8 (20.0%) controls. The composition of age group was comparable in both the groups with no statistically significant difference (p = 0.872).

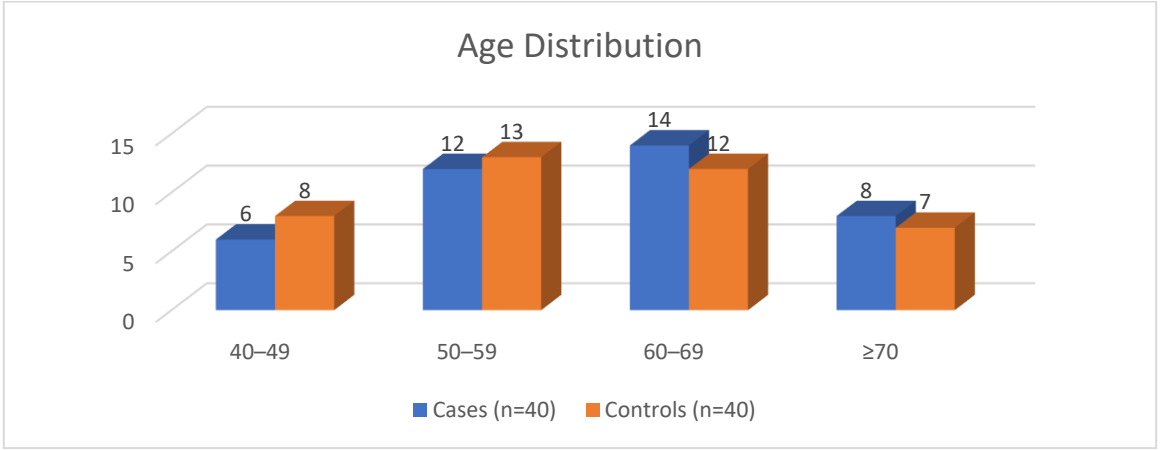


**Figure 1: Age Distribution Among Cases and Controls**

The analysis of the duration of symptoms and severity of osteoarthritis among the studied cases showed that the most common duration of symptoms was between 1–3 years (35.0%) followed by 6–12 months (30.0%), less than 6 months (20.0%) and more than 3 years (15.0%). Regarding the severity of osteoarthritis based on the Kellgren–Lawrence grading system, Grade II osteoarthritis was the most prevalent (45.0%), followed by Grade III (35.0%) and Grade I (20.0%) patients (Table 2, Figure 2).

| Variable | Cases (n=40) | Percentage |
|---|---|---|
| **Duration of Symptoms** | | |
| <6 months | 8 | 20.0% |
| 6–12 months | 12 | 30.0% |
| 1–3 years | 14 | 35.0% |
| >3 years | 6 | 15.0% |
| **Severity of Osteoarthritis (Kellgren-Lawrence Grade)** | | |
| Grade I | 8 | 20.0% |
| Grade II | 18 | 45.0% |
| Grade III | 14 | 35.0% |

**Table 2: Duration of Symptoms and Severity of Osteoarthritis Among Cases**


**Figure 2. Standing AP and lateral radiographs of both knees showing bilateral osteoarthritic changes characterized by medial joint space narrowing, marginal osteophytes, and subchondral sclerosis, consistent with knee osteoarthritis.**

The analysis of the body mass index (BMI) distribution showed that the majority of participants in both groups were overweight. Obesity (≥30 kg/m²) was observed in 13 (32.5%) cases compared to 7 (17.5%) controls. Normal BMI (<25 kg/m²) was recorded in 8 (20.0%) cases and 16 (40.0%) controls. The difference in BMI distribution between the two groups was statistically significant ($p < 0.05$) (Table 3).

| BMI (kg/m²) | Cases (n=40) | Controls (n=40) | p-value |
|---|---|---|---|
| Normal (<25) | 8 (20.0%) | 16 (40.0%) | **< 0.05** |
| Overweight (25–29.9) | 19 (47.5%) | 17 (42.5%) | |
| Obese (≥30) | 13 (32.5%) | 7 (17.5%) | |
| **Total** | **40 (100%)** | **40 (100%)** | |

**Table 3: Body Mass Index (BMI) Distribution Among Cases and Controls**

The analysis of the comparison of serum vitamin D levels between the studied cases and controls showed that vitamin D deficiency (<20 ng/mL) was present in 22 (55.0%) cases of osteoarthritis as compared to only 5 (12.5%) in controls. In contrast, sufficient vitamin D levels (>30 ng/mL) were observed in 24 (60.0%) controls and 8 (20.0%) cases. Vitamin D insufficiency (20–29 ng/mL) was noted in 10 (25.0%) cases and 11 (27.5%) controls. The difference in serum vitamin D status between cases and controls was statistically highly significant ($p < 0.001$) (Table 4).

| Vitamin D Status | Cases (n=40) | Controls (n=40) | p-value |
|---|---|---|---|
| Sufficient (>30 ng/mL) | 8 (20.0%) | 24 (60.0%) | **<0.001** |
| Insufficient (20–29 ng/mL) | 10 (25.0%) | 11 (27.5%) | |
| Deficient (<20 ng/mL) | 22 (55.0%) | 5 (12.5%) | |
| **Total** | **40 (100%)** | **40 (100%)** | |

**Table 4: Comparison of Serum Vitamin D Levels Between Cases and Controls**

The analysis of the association between vitamin D status and severity of osteoarthritis among the studied cases showed that vitamin D deficiency (<20 ng/mL) was most prevalent in patients with Grade III osteoarthritis, being observed in 13 (92.9%) patients, followed by 8 (44.4%) patients with Grade II and only 1 (12.5%) patient with Grade I osteoarthritis. The association between vitamin D status and osteoarthritis severity was statistically significant, as indicated by a p-value of ($p < 0.001$) (Table 5).

| Vitamin D Status | Grade I (n=8) | Grade II (n=18) | Grade III (n=14) | p-value |
|---|---|---|---|---|
| Sufficient (>30 ng/mL) | 5 (62.5%) | 3 (16.7%) | 0 (0.0%) | **<0.001** |
| Insufficient (20–29 ng/mL) | 2 (25.0%) | 7 (38.9%) | 1 (7.1%) | |
| Deficient (<20 ng/mL) | 1 (12.5%) | 8 (44.4%) | 13 (92.9%) | |
| **Total** | **8 (100%)** | **18 (100%)** | **14 (100%)** | |

**Table 5: Association Between Vitamin D Status and Severity of Osteoarthritis Among Cases**

The analysis of the comparison of mean clinical characteristics between the studied cases and controls showed that the mean age was 61.4 ± 8.9 years among cases and 59.8 ± 8.4 years among controls. The mean body mass index (BMI) was higher in cases (29.1 ± 4.3 kg/m²) compared to controls (26.7 ± 3.8 kg/m²). Similarly, a significant difference was seen in serum vitamin D levels with cases having a lower mean serum vitamin D concentration ( 22.1 ± 6.3 ng/mL) as compared to controls (31.6 ± 7.4 ng/mL). The differences in mean BMI ($p = 0.009$) and mean serum vitamin D levels ($p < 0.001$) was found to be statistically significant ($P<0.05$) (Table 6).

| Variable | Cases (n=40) Mean ± SD | Controls (n=40) Mean ± SD | p-value |
|---|---|---|---|
| Age (years) | 61.4 ± 8.9 | 59.8 ± 8.4 | 0.4108 |
| BMI (kg/m²) | 29.1 ± 4.3 | 26.7 ± 3.8 | 0.009 |
| Serum Vitamin D (ng/mL) | 22.1 ± 6.3 | 31.6 ± 7.4 | <0.001 |

**Table 6: Comparison of Mean Clinical Characteristics Between Cases and Controls**

The analysis of the odds ratio for the association between vitamin D deficiency and knee osteoarthritis among the studied participants showed that vitamin D deficiency (<20 ng/mL) was present in 22 (55.0%) cases compared to 5 (12.5%) controls. Vitamin D levels ≥20 ng/mL were found in 18 (45.0%) cases and 35 (87.5%) controls. The calculated odds ratio was 8.56 (95% CI: 2.70–27.15). This indicated that individuals with vitamin D deficiency had higher odds of having knee osteoarthritis as compared to those without deficiency. This association was found to be statistically highly significant ($p < 0.001$) (Table 7).

| Variable | Cases (n=40) | Controls (n=40) | Odds Ratio (95% CI) | p-value |
|---|---|---|---|---|

| | | | | |
|---|---|---|---|---|
| Vitamin D Deficient (<20 ng/mL) | 22 (55.0%) | 5 (12.5%) | 8.56 (2.70–27.15) | <0.001 |
| Not Deficient (≥20 ng/mL) | 18 (45.0%) | 35 (87.5%) | ------ | |

**Table 7: Odds Ratio for Association Between Vitamin D Deficiency and Knee Osteoarthritis**

## DISCUSSION

The present case-control study showed a significant association between low serum vitamin D levels and knee osteoarthritis (KOA). Patients with KOA were found to have substantially lower mean serum 25-hydroxyvitamin D concentrations than healthy controls. Furthermore, vitamin D deficiency was observed in more than half of the cases, whereas only a small proportion of controls were Vitamin D deficient. These findings support the hypothesis that vitamin D may play an important role in the pathogenesis as well as progression of osteoarthritis. The observed difference in vitamin D status between cases and controls is consistent with the findings reported by Heidari et al[8] and Muraki et al[9] Both of these authors showed an inverse relationship between serum vitamin D levels and symptomatic knee osteoarthritis. Heidari[8] reported a higher prevalence of vitamin D deficiency in patients with knee OA. This suggested that inadequate vitamin D status may contribute to Osteoarthritis susceptibility. Similarly, Muraki et al[9] observed that lower vitamin D concentrations were associated with increased prevalence of radiographic knee osteoarthritis and presence of knee pain. The marked difference in vitamin D levels observed in the current study further strengthens the growing body of evidence suggesting that vitamin D deficiency is not merely a coincidental finding but may represent an important metabolic factor associated with KOA.

Another important finding of the present study was the strong relationship between vitamin D deficiency and radiographic severity of osteoarthritis. The prevalence of deficiency increased progressively from Kellgren–Lawrence Grade I to Grade III disease, with nearly all Grade III patients exhibiting deficient vitamin D levels. This observation suggested role of vitamin D in disease progression rather than simply disease occurrence. Similar findings were reported by McAlindon et al[10] and Bergink et al[11]. McAlindon et al[10] demonstrated that lower vitamin D levels were associated with increased risk of radiographic progression and cartilage loss in knee osteoarthritis cases. Likewise, Bergink et al[11] found that individuals with lower vitamin D concentrations experienced greater progression of radiographic osteoarthritis over a period of time.

The current study also found that body mass index (BMI) was significantly higher among patients with KOA than among controls. Obesity is a well-recognized risk factor for osteoarthritis because of both mechanical loading and metabolic effects. These findings align with observations reported by Felson et al[12] and Sowers et al[13] who identified excess body weight as one of the strongest predictors of incident and progressive knee osteoarthritis. The higher mean BMI observed among cases in the present study therefore suggests that vitamin D deficiency and obesity may act synergistically in promoting osteoarthritis development and progression. Future studies employing multivariate analyses would be valuable to clarify the independent contribution of vitamin D deficiency after adjusting for obesity and other established risk factors.

The calculated odds ratio in the present study indicated that individuals with vitamin D deficiency had more than eightfold higher odds of having knee osteoarthritis than those with adequate vitamin D levels. This substantial increase in risk is comparable to findings reported by Zhang et al[14] and Cao et al[15] who reported significant associations between vitamin D deficiency and symptomatic knee osteoarthritis. These investigators proposed that vitamin D deficiency may influence pain perception. These studies also emphasized that vitamin D deficiency may lead to impaired quadriceps muscle function and reduced joint stability thereby altering biomechanical loading of the knee joint. Reverse causation remains possible, whereby patients with severe knee pain engage in less outdoor activity, resulting in reduced vitamin D synthesis. Therefore, prospective longitudinal studies are required to determine whether correcting vitamin D deficiency can reduce the incidence or progression of KOA.

The strengths of the present study include the use of age- and sex-matched controls, objective measurement of serum 25(OH)D concentrations and assessment of radiographic severity using the Kellgren–Lawrence grading system. Nevertheless, limitations included relatively small sample size, single-center design and inability to establish temporal causality. Despite these limitations, the study provides additional evidence supporting a significant association between vitamin D deficiency and both the presence and severity of knee osteoarthritis. Larger prospective studies will be helpful in determining whether correction of vitamin D deficiency can meaningfully influence long-term outcomes in patients with KOA.

## CONCLUSION

There was a significant association between vitamin D deficiency and knee osteoarthritis. Patients with knee osteoarthritis were found to have significantly lower serum vitamin D levels and a higher prevalence of vitamin D deficiency as compared to healthy controls. Moreover, vitamin D deficiency was also found to be strongly associated with greater radiographic severity of osteoarthritis. These findings suggest that inadequate vitamin D status may contribute to the occurrence as well as progression of knee osteoarthritis. These findings underline the potential value of routine vitamin D assessment in at-risk individuals.

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