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RESEARCH ARTICLE

Vitamin D Deficiency is Associated with Knee Osteoarthritis and is Implicated in the Osteoarthritis Severity

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ABSTRACT

Background: Levels of Vitamin D may impact the development and progression of knee osteoarthritis (OA), a disorder common in elderly people The aim of this study was to investigate the association between serum Vitamin D deficiency and knee OA.

Methods: One hundred twenty (40 male and 80 female) consecutive patients were recruited from the rheumatology outpatient clinic for the study. X-rays in two anterior-posterior and lateral views of the knees were performed for all patients. Staging of knee OA was done according to Kellgren-Lawrence criteria and divided into two groups; group A consisting of grades 1 and 2, and group B, consisting of grades 3 and 4. One hundred (30 male and 70 female) healthy individuals without clinical and radiographic signs of the disease were defined as a control group. Hematological and biochemical investigations, including measurement of 25-hydroxyvitamin D serum level, were performed for all participants. Pain intensity using a visual analog scale (VAS) and disease severity using the Western Ontario and McMaster Universities Arthritis Index was measured for all patients.

Results: The mean age of patients and controls were 60±3.5 and 54±2.6 years, respectively. Vitamin D levels of patients and controls were 13±3.3 and 32±2.5, respectively. More severe disease and diseases with prolonged duration were associated with a lower vitamin D level, and low vitamin D levels were associated with high VAS and WOMAC.

Conclusion: Vitamin D deficiency was associated with the development and the severity of knee OA as well as with the disease duration.

Keywords: vitamin D, osteoarthritis, knee, radiography

Introduction

Osteoarthritis (OA) is a common chronic disease characterized by a loss of articular cartilage and changes in the subchondral bone. The knee is one of the most commonly affected joints. [1]

In addition to the damage and loss of articular cartilage, there is remodeling of subarticular bone, osteophyte formation, ligamentous laxity, weakening of periarticular muscles, and, in some cases, synovial inflammation. Pain is the major clinical symptom in knee OA joint. [2]

Several environmental factors, including obesity, malalignment, trauma, or joint instability, have been associated with knee OA. [3] Vitamin D is considered a steroid hormone that has a central role in the metabolism of calcium, phosphorus, and bone mineralization. [4] This vitamin is associated with normal bone metabolism. [5] Literature documented that insufficient vitamin D levels have been associated with many chronic diseases, such as cardiovascular diseases, cancers, metabolic syndrome, autoimmune diseases, changes in cartilage composition, and the progression of knee OA. [4, 6] Several epidemiologic studies have demonstrated that low levels of vitamin D are associated with higher levels of knee pain, increased prevalence of osteoarthritis (OA), as well as the development and progression of knee OA. [6-9] Normal metabolism of bone and cartilage depends on the presence of vitamin D. Deficiency of vitamin D adversely affects calcium metabolism, osteoblastic activity, matrix ossification, bone density, and articular cartilage turnover. [10] Vitamin D deficiency may lead to osteoarthritis by reducing proteoglycan synthesis and accelerating metalloproteinase activity. [11] Given this correlation between OA and vitamin D deficiency, this study aimed to evaluate the association between knee OA and low concentrations of serum vitamin D, particularly in our locality, since the scanty reports regarding this issue.

Patients and methods

This case-control study was carried out in the outpatient departments of Rheumatology at Basra Teaching Hospital from January 2021 to July 2022. One hundred twenty (40 male and 80 female) consecutive patients with knee OA attending the outpatient and One hundred (30 male and 70 female) healthy individuals from the general population without clinical and radiographic signs of the disease were defined as controls recruited for the study. All the patients underwent x-rays in two anterior-posterior and side views of the knees. Staging of knee OA was done according to Kellgren-Lawrence criteria [12] and divided into two groups; group A consisting of grades 1 and 2, and group B consisting of grades 3 and 4. Hematological and biochemical investigations, including measurement of 25-hydroxyvitamin D serum level, were performed for all participants. Pain intensity using a visual analog scale (VAS) and disease severity using the Western Ontario and McMaster Universities Arthritis Index (WOMAC) [13] were measured for all patients. Vitamin D levels less than 20 ng/ml were considered as vitamin D deficiency.

Ethical considerations

The study was conducted in accordance with the principles of the Declaration of Helsinki, and verbal consent was obtained from all participants prior to their involvement.

Statistical analysis

SPSS Software version 25.0 was used for data analysis. Percentages and mean were used to present the data in tables. Comparison of study groups was carried out using chi-square and Fisher's exact test for categorical data; and Student's t-test for continuous data. A P-value of < 0.05 was considered statistically significant.

Results

The mean age of patients and controls were 60 ± 3.5 and 54 ± 2.6 years, respectively. Vitamin D levels of patients and controls were 13 ± 3.3 and 32 ± 2.5, respectively; the difference was statistically significant ($P= 0.002$), as shown in Table 1. Group B (grades 3 and 4) was associated with a lower level of vitamin D than group A (grades 1 and 2); the difference was statistically significant ($P= 0.002$), as shown in Table 2. Patients with prolonged disease duration (> 10 years) were associated with a lower vitamin D level than those with disease duration of less than ten years; the difference was statistically significant ($P= 0.003$), as shown in Table 3. Low vitamin D levels were associated with high VAS and WOMAC ($P<0.05$), as shown in Table 4.

Table 1: Demographic characteristics and vitamin D levels in knee OA patients and controls

Characteristics	Patient	Controls	P value
Total No.	120	100	
Men	40	30	
Women	80	70	
Age (mean± SD)	60±3.5	54±1.6	
Disease duration(mean± SD)	10±2.4		
BMI(mean± SD)	27±2.6	25±1.3	
Vitamin D level (mean± SD)	13±3.3	32±2.5	0.002

BMI: body mass index

Table 2: Vitamin D levels according to the grade of knee OA

	Group A	Group B	P value
Vitamin D level (mean± SD)	17	9	0.002

Table 3: Vitamin D levels according to the disease duration

Disease duration Vitamin D level (mean± SD)	Group A	Group B
≤ 10 years	20	16
>10 years	11	8
P value	0.003	0.003

Table 4: VAS and WOMAC according to vitamin D level

Vitamin D level	VAS	WOMAC
≤ 15 ng/ml	5	23
>15 ng/ml	9	45
P value	<0.05	<0.05

VAS: visual analog scale, WOMAC: Western Ontario and McMaster Universities Arthritis Index

Discussion

Osteoarthritis is the most common form of arthritis, characterized by cartilage destruction and loss that results in functional failure. [14] Vitamin D is a hormone that affects bone metabolism and non-bony tissues. The relationship between vitamin D and knee OA has been studied previously. Several studies support the effect of vitamin D deficiency on knee OA progression, whereas no association was reported in other studies. [6, 10, 14,15] There is evidence that vitamin D deficiency may play a role in osteoarthritis pathogenesis. Results from studies of the correlation between low blood concentrations of vitamin D and knee OA are conflicting. Heidari [6] reported an increased prevalence of vitamin D deficiency and its crucial association between this deficiency and knee OA in patients less than 60 years of age. Ding et al. [16] concluded from radiographs and magnetic resonance imaging that optimal vitamin D concentration was associated with knee pain and reduced knee cartilage loss. Therefore vitamin D supplementation could alleviate knee OA pain. Supplementation of vitamin D for six months decreased protein damage, minimized pain (VAS), improved quality of life, improved hand grip strength and physical performance in OA patients, and improved lower extremity functions. [17,18] However, Sanghi et al. [19] confirm a reason for the positive impact of vitamin D; only OA patients with insufficiency of vitamin D are the group most likely to benefit from supplementation. Vitamin D stimulates chondrocytes to produce proteoglycan proteins. Metalloproteinase activity increased in low vitamin D concentration, resulting in reduced proteoglycan matrix proteins synthesis, cartilage degeneration, and loss. [11] In this study, we demonstrated that knee OA had been associated with vitamin D deficiency, especially in severe and long-lasting OA. Our observations were consistent with those of Bergink et al., who showed that low vitamin D consumption increases the radiographic progression of knee OA, especially when the patient's bone mineral density (BMD) is low. Therefore, he states that; improving vitamin D levels in patients may have a protective role against the occurrence and progression of OA, especially in those patients with low BMD. [9] The same result was demonstrated by McAlindon et al., who found a significant relationship between low serum vitamin D levels and OA deterioration, and those with more advanced OA had lower

vitamin D levels. [8] In contrast, Al-Jarallah et al. and Felson et al. did not establish any relationship between vitamin D levels and the radiographic grade of knee OA. [10, 15] The association between vitamin D deficiency and different causes of musculoskeletal pain, such as fibromyalgia, low back pain, and knee and hip OA, has been well documented. In agreement with Hasan Anari et al. [20], who showed that most patients with vitamin D deficiency were in grade three and above, we demonstrated lower levels of vitamin D were associated with grades 3 and 4 of knee OA. In this study, the prolonged disease duration of knee OA was found to be associated with lower vitamin D levels. In agreement with other studies, our study showed an increased pain sensitivity and poor function were associated with lower vitamin D levels, especially in advanced knee OA. Vitamin D exerts anatomic, hormonal, neurological, and immunological influences on pain, potentially playing an essential role in the etiology and maintenance of chronic pain states and associated comorbidities. [21-23] One limitation of our study is that it is not an interventional study and involves a small number of participants. More expanded with a high number of participants interventional studies are needed to establish the exact correlation between vitamin D deficiency and the development and severity of knee osteoarthritis.

Conclusion

Vitamin D deficiency was associated with the development of knee OA. The severity of knee OA and the disease duration are associated with lower levels of vitamin D. vitamin D supplementation may improve knee OA.

Author contributions

AM and AH conceived, designed, collected, analyzed, and interpreted the patient data of the study and wrote the manuscript. AA and ZK advised on the design of the study. Collected, analyzed, and interpreted the patient data and wrote the manuscript. Both authors read and approved the final manuscript.

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Conflicts of interest

The authors declare no conflict of interest.

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