Althea Medical Journal
ISSN Online: 2337-4330
https://doi.org/10.15850/amj.v12n1.3723

Original Article

25-hydroxyvitamin D Serum Level and Risk of Knee Osteoarthritis in the Elderly

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Abstract

Background: Osteoarthritis (OA) is a degenerative joint disease that commonly affects the elderly, particularly in the knees. It may lead to chronic pain, physical limitations, depression, and significantly impact an individual's ability to participate in social, occupational, and community activities, ultimately reducing quality of life. Vitamin D has been suggested as a factor that may help reduce the risk of knee OA in older adults. This study aimed to investigate the relationship between serum 25-hydroxyvitamin D levels and the risk of knee OA among the elderly.

Methods: This cross-sectional study involved elderly residents of a nursing home in North Jakarta, Indonesia. Data was collected through interviews and physical examinations of both knees following the American Rheumatism Knee OA diagnostic criteria. Participants who met these criteria were classified as high-risk for knee OA. Blood samples were analyzed for 25-hydroxyvitamin D (25(OH)D) levels using an enzyme-linked immunosorbent assay (ELISA). Bivariate analysis was performed using the Chi-square test.

Results: Of the 48 participants, the majority were female (64.6%) and aged 70–79 years (47.9%). A total of 22.9% of participants were classified as 25(OH)D insufficient and 25% were deficient. Interestingly, 62.5% were at high risk of knee OA. There was a significant association between 25(OH)D levels and the risk of knee OA (p=0.031).

Conclusions: Serum 25(OH)D levels are significantly associated with the risk of knee OA in the elderly. Promoting daily outdoor activities and considering vitamin D supplementation may help reduce the risk of knee OA and improve bone health in this population.

Keywords: 25-hydroxyvitamin D, elderly, knee osteoarthritis

Althea Medical Journal.
2025;12(1):58–64

Received: March 1, 2024
Accepted: Novemver 16, 2024
Published: March 30, 2025

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Introduction

Osteoarthritis (OA) is a degenerative disease frequently manifested in the elderly. Advancing age constitutes a primary risk factor for OA development, in addition to other factors such as obesity, gender, genetics, and joint injuries.[1] OA profoundly impacts an individual's quality of life by causing chronic pain, physical limitations, and psychological conditions such as depression, ultimately hindering participation in social, occupational, and community activities.[2] As the most prevalent form of arthritis among the elderly, OA most commonly affects the knee joints, followed by the hips and hands.[3] According to the Global Burden of Disease Study 2019, approximately 528 million people worldwide suffer from OA, representing a 113% increase in cases from 1990 to 2019. Notably, 73% of

individuals with OA are over 55 years old, with 60% being female.[4] In Indonesia, the prevalence of OA rises with age, reaching 5% of individuals under 40 years, 30% of those aged 40–60 year, and 65% of individuals over 60 years. Specifically, the prevalence of knee OA in Indonesia is reported at 15.5% in males and 12.7% in females.[5]

The major circulating form of vitamin D in the body is 25-hydroxyvitamin D 25(OH) D. Vitamin D, as a dietary nutrient and endogenously synthesized hormone, plays a crucial role in maintaining bone health by regulating calcium and phosphorus concentrations within physiologically normal limits, supporting bone mineralization, and maintaining essential cellular functions.[6] Furthermore, vitamin D exerts an inhibitory effect on bone turnover and cartilage degradation, suggesting a potential role in averting the initiation and advancement of osteoarthritis.[7] Several studies have shown that individuals with vitamin D deficiency may experience faster progression of knee OA compared to those with sufficient vitamin D levels.[7,8] A previous study found an association between low average serum 25(OH)D levels in OA patients and the severity of knee OA based on Kellgren-Lawrence radiological criteria, categorizing patients with low 25-hydroxyvitamin D serum levels as grade III–IV.[9] However, another study suggested no correlation between vitamin D levels and joint symptoms such as pain, stiffness, and functional impairment in knee OA patients.[10] Elderly individuals are particularly susceptible to vitamin D deficiency due to reduced skin synthesis, dietary factors, and chronic health issues. This deficiency may exacerbates the risks associated with OA.

The study examining the association between serum 25-dihydroxyvitamin D levels and the risk of knee osteoarthritis in Indonesia is still limited, specifically among the elderly in nursing home in North Jakarta. While the global burden of osteoarthritis continues to increase, particularly among the elderly, the role of vitamin D in the progression of this degenerative disease remains controversial. Previous studies have produced conflicting results regarding the correlation between vitamin D deficiency and osteoarthritis severity. By concentrating on a specific and vulnerable population, this study aimed to determine the association between serum 25-dihydroxyvitamin D level and the risk of knee osteoarthritis among the elderly in one nursing home in North Jakarta, Indonesia with the hope that the findings of this study could have significant public health implications, potentially leading to targeted vitamin D supplementation strategies to prevent or mitigate osteoarthritis among the elderly as well as providing local data that could address the scarcity of research in Indonesia and contribute to the global understanding of osteoarthritis.

Methods

This cross-sectional study was conducted from August to September 2023 at one of the nursing homes in North Jakarta, Indonesia. A total of 70 elderly residents were included. The inclusion criterias were residents of this nursing home aged 60 years or older and agreed to participate by signing the informed consent. Exclusion criteria were residents who had been diagnosed with knee osteoarthritis, rheumatoid arthritis, gout or cognitive impairment, for example dementia, had a history of knee joint injuries six months prior to this study and had obesity (defined as a body mass index less than 25 kg/m^2).

Data collected were demographic data such as age, gender, history of illness, history of vitamin D supplementation, medications, and physical examination findings based on the American College of Rheumatology clinical diagnostic criteria for knee osteoarthritis (sensitivity 95%, specificity 69%).

Participants were classified as high risk for knee OA if they experienced knee pain accompanied by three or more of the following additional criteria: crepitus during active movement, morning stiffness lasting less than 30 minutes, age over 50 years, bony enlargement, joint margin tenderness, and absence of warmth in the knee joints. Participants were classified as low risk if they did not report knee pain or had pain with fewer than three of the additional criteria.

For measurement of serum 25-hydroxyvitamin D [25(OH)D] levels, 5 mL of blood was collected from each participant. Samples were immediately placed in a cooler box and transported within 15 minutes to the laboratory at the Faculty of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia (a distance of 2.8 km). The blood samples were centrifuged at 5000 rpm for 10 minutes to separate the serum, which was then stored at −20°C for up to three months. Within one week of collection, serum 25(OH) D levels were measured using the 25-HVD3 (25-hydroxyvitamin D3) ELISA Kit from

Table 1 Distribution of Participants' Characteristics (n=48)

Characteristic	n	%
Age (year)		
60–69	9	18.7
70–79	23	47.9
80–89	13	27.1
90–100	3	6.3
Gender		
Male	17	35.4
Female	31	64.6
Outdoor activity duration in a day		
None	23	47.9
10–29 minutes	10	20.8
30–60 minutes	12	25.0
>60 minutes	3	6.3
25-hydroxyvitamin D status		
Sufficient	25	52.1
Insufficient	11	22.9
Deficient	12	25.0
Risk of knee OA		
Low	18	37.5
High	30	62.5

Note: 25(OH)D=25-hydroxyvitamin D; KOA=Knee osteoarthritis

Elabscience. Vitamin D status was classified as follows: sufficient (>75 nmol/L or >30 ng/mL), insufficient (50–75 nmol/L), or deficient (<50 nmol/L or <20 ng/mL).

The collected data was analyzed using univariate and bivariate analyses. The Chi-square test was used for bivariate analysis. Ethical approval for this study was obtained from the Ethics Committee of the School of Medicine and Health Sciences, Atma Jaya Catholic University of Indonesia (Approval No. 04/07/KEP-FKIKUAJ/2023).

Results

Out of 70 elderly participants initially enrolled, 22 were excluded due to one or more exclusion criteria, including speech or hearing impairments, a history of knee joint injury, or being classified as obese (BMI ≥25 kg/m^2). Among the 48 remaining participants, the predominant age group was 70 to 79 years. The majority of the participants were female, comprising 31 participants (64.6%). Out of the entire cohort, 25 individuals (52.1%) were

Table 2 Association Between Sun Exposure and 25-hydroxyvitamin D Status

Sun exposure	25(OH)D Status		P*
	Sufficient n(%)	Insufficient and deficient n(%)	
Not exposed	8 (34.8)	15(65.2)	0.021
Exposed	17(68.0)	8(32.0)	

Note: 25(OH)D=25-hydroxyvitamin D, *Chi square test

Table 3 Description of 25-hydroxyvitamin D Serum Status and Risk of Knee Osteoarthritis

25(OH)D Status	Risk of KOA	
	Low n(%)	High n (%)
Sufficient	13 (52.0)	12 (48.0)
Insufficient	4 (36.4)	7 (63.6)
Deficient	1 (8.3)	11 (91.7)

Note: 25(OH)D=25-hydroxyvitamin D; KOA=Knee osteoarthritis

Table 4 25-hydroxyvitamin D Status and the Risk of Knee Osteoarthritis

25(OH)D Status	Risk of KOA		P*	Odds ratio	95%CI	
	Low n(%)	High n (%)			Lower	Upper
Sufficient	13(52.0)	12(48.0)	0.031	3.9	1.102	13.803
Insufficient and deficient	5(21.7)	18(78.3)				

Note: 25(OH)D=25-hydroxyvitamin D; KOA=Knee osteoarthritis; *Chi square test

actively engaged in outdoor activities, with most of them (52%) engaging in 30 to 60 minutes of sunlight exposure per day.

Regarding vitamin D status, 11 participants (22.9%) were classified as having 25(OH)D insufficiency, and 12 (25%) were classified as deficient. Additionally, 30 participants (62.5%) were identified as being at high risk for knee osteoarthritis (KOA) based on clinical criteria (Table 1).

Individuals who engaged in outdoor activities and receivedsunlight exposed, the majority (68%) had sufficient 25(OH) D levels, meanwhile among those who did not engage in outdoor activities, the majority (65.2%) were classified as either insufficient or deficient 25(OH)D. A statistically significant association was observed between sunlight exposure and 25(OH)D status (p=0.021) (Table 2).

Out of 48 elderly, a higher proportion of women were identified to be at a greater risk of knee osteoarthritis (KOA) compared to men. However, statistical analysis revealed that there was no significant difference in KOA risk between men and women (OR=0.364, 95% CI 0.106–1.242). Furthermore, no significant association was found between gender and the risk of KOA in this study.

In terms of vitamin D status and KOA risk, the majority (52%) of participants with sufficient 25(OH)D levels were at low risk for KOA. In contrast, 63.6% of those with insufficiency and 91.9% of those with deficiency were at high risk of developing KOA (Table 3). Statistical analysis results indicated a significant association between 25(OH) D status and the risk of knee osteoarthritis (p=0.031). Participants with insufficient or deficient 25(OH)D levels had a 3.9-fold increased risk of KOA compared to those with sufficient levels (OR=3.9, 95% CI 1.102–13.803) (Table 4).

Discussion

Almost half of the participants in this study were found to be in the 25(OH)D deficiency category. This finding is consistent with a study reporting that among 2,493 elderly people in China, 35.7% were classified as vitamin D deficient and 41.3% as vitamin D insufficiency.[11] Similarly, in a study involving 298 elderly people in India, 56.3% were classified as vitamin D deficient and insufficiency.[12]

Serum 25(OH)D levels can be influenced by various factors, including sunlight exposure, sunscreen use, concealing clothing, dietary intake, age, skin pigmentation, digestive disorders, especially those causing fat malabsorption, and the use of certain medications.[13,14] In this study, most elderly people did not engage in outdoor activities exposed to sunlight every day, such as walking and sunbathing. Among the elderly who engaged in outdoor activities, the majority were active for 30–60 minutes every day and were classified as having sufficient 25(OH) D. Conversely, among those who did not engage in outdoor activities, a large number experienced vitamin D deficiency. These findings support existing study indicating that sunlight exposure is the primary source of vitamin D. Moreover, vitamin D synthesized through sun exposure remains in circulation for at least twice as long as vitamin D obtained from dietary sources.[13]

Previous interventional studies support the beneficial effects of outdoor sunlight exposure on improving serum 25(OH)D levels among the elderly. For instance, a study conducted in a Swedish nursing home found a significant increase in 25(OH)D levels (p=0.011) after elderly participants engaged in daily outdoor activities for 20–30 minutes over two months during the summer.[15] Similarly, another study involving elderly individuals with an average age of 76 years demonstrated that sunbathing for 15–30 minutes, five days per week for one month, significantly elevated vitamin D levels compared to a control group.[16] These findings reinforce the importance of sunlight as a natural and effective intervention for maintaining adequate vitamin D status in older adults.

In this study, limited outdoor exposure was

particularly evident among elderly people with mobility impairments, including those with knee pain or requiring assistive devices such as canes or wheelchairs. These functional limitations may reduce opportunities for sunlight exposure, thus contributing to lower 25(OH)D levels. Furthermore, although participants received a standardized diet, differences in individual consumption patterns likely influenced dietary vitamin D intake. These variations emphasize the need for tailored nutritional strategies and mobility support to address vitamin D deficiency in the elderly population.

The high proportion of elderly individuals at risk for KOA was found in this study. This finding align with the global and regional trends indicating a high burden of knee osteoarthritis (KOA) among older adults, including in Asian populations.[14,17]

A systematic review stated that female are at a higher risk of developing knee osteoarthritis than male.[18] In support of this, another systematic review and meta-analysis found that female are 1.84 times more likely to experience knee osteoarthritis than men.[19] However, the findings of this study differ, showing no significant difference in the risk of knee osteoarthritis between male and female. The mechanisms underlying the influence of gender on the risk of knee osteoarthritis remains unclear. In postmenopausal women, decreased estrogen levels are associated with an increased risk of knee osteoarthritis. In men aged ≥50 years, low free testosterone levels are associated with increased cartilage loss and reduced cartilage volume in the knee joint, potentially increasing the risk of osteoarthritis.[20]

Age remains a well-established risk factor for knee osteoarthritis. The prevalence increases significantly in individuals aged 50 years and older, reaching approximately 40% in men and 47% in women.[21] In the current study population, the average age was 78 years for female and 76 years for male. Aging processes is associated with heightened oxidative stress and inflammatory responses, enhancing the activity of cartilage-degrading enzymes such as matrix metalloproteinases (MMPs) and aggrecanase, while reducing collagen type II synthesis, factors that collectively contribute to the progression of osteoarthritis.[22] Given the discrepancy in findings regarding sex-based risk differences, further research is needed to explore the potential association between sex hormones, aging, and the risk of knee osteoarthritis in diverse elderly populations..

In a study, it was demonstrated that elderly individuals classified as vitamin D insufficient and deficient experienced clinical symptoms such as knee pain, mobility difficulties, and decreased knee function in maintaining body balance. all of which significantly elevated the risk of knee osteoarthritis ($p<0.05$).[23] Similarly, another research found that elderly individuals with insufficient or deficient vitamin D levels were 1.2 times more likely to develop knee osteoarthritis compared to those with sufficient levels.[24] Both of these findings are consistent with the present study, which observed a significant association between 25(OH)D status and the risk of knee osteoarthritis ($p = 0.031$). Furthermore, elderly individuals classified as vitamin D deficient in this study exhibited a 3.9-fold higher risk of developing knee osteoarthritis compared to those with sufficient vitamin D levels. This association may be attributed to the fact that vitamin D deficiency can induce changes in several bone mechanisms, such as increased bone resorption by elevating parathyroid hormone (PTH) levels, enhancing bone turnover, or directly affecting metabolites in articular chondrocytes in the joints, eventually leading to osteoarthritis.[25]

Contradictory results have been reported in some studies. There was no correlation between vitamin D levels and the risk of knee osteoarthritis.[26] Additionally, other studies asserted that vitamin D supplementation in individuals already affected by knee osteoarthritis could significantly alleviate knee pain symptoms, but it did not prevent the progression of cartilage loss in the knee joints.[27,28] Therefore, the association between vitamin D deficiency and an increased risk of osteoarthritis remains an area that requires further investigation and cohort study.

This study has several limitations that should be considered. Firstly, the cross-sectional design limits the ability to establish causality between vitamin D levels and the risk of knee osteoarthritis, highlighting the need for longitudinal studies to determine the directionality of this relationship. Secondly, the study was conducted in a single nursing home in North Jakarta with only 48 participants which may limit the generalizability of the findings to other populations or regions. Future studies could be conducted in various geographical locations with different environmental conditions. Thirdly, the reliance on self-reported data for demographic information, history of illness, and vitamin D supplementation introduces the potential for

recall bias and inaccuracies. Lastly, the clinical diagnostic criteria for knee osteoarthritis, with a sensitivity of 95% and specificity of 69%, may lead to misclassification, particularly in borderline cases, affecting the conclusions about the risk of knee osteoarthritis.

In conclusion, this study demonstrates a clear association between vitamin D status and the risk of knee osteoarthritis among the elderly. Elderly individuals with insufficient or deficient 25-hydroxyvitamin D levels are more likely to be at risk for developing knee osteoarthritis, suggesting that vitamin D may play a protective role in maintaining joint health. While the relationship between vitamin D and osteoarthritis remains complex and occasionally controversial, these findings underscore the importance of ensuring adequate vitamin D levels in aging populations, especially in institutionalized settings.

Encouraging outdoor activity and increasing safe sun exposure may be a simple yet effective strategy to maintain adequate vitamin D levels and potentially reduce the risk of osteoarthritis. Prioritizing a balanced and health-conscious lifestyle is crucial for the elderly population, particularly those at higher risk for vitamin D deficiency and associated health conditions.

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