

A Case Control Study to Establish the Association Between Vitamin D Deficiency with Knee Osteoarthritis

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Abstract

Aim: The study's goal is to compare serum 25-hydroxy vitamin D levels in patients with knee osteoarthritis to age-matched healthy controls, as well as to look into the link between 25-OH vitamin and osteoarthritis.

Materials and Methods: There are 360 patients in the trial, separated into two groups: Group 1 and Group 2. Group 1 consisted of 180 participants with clinical signs of knee osteoarthritis who served as controls, while Group 2 consisted of 180 patients with knee osteoarthritis who functioned as patients. Serum 25-OH vitamin D was measured in all the participants by the ELFA method and concentrations <10ng/ml was considered as deficient.

Results: In Group 1, 81 (45.0%) were males and 99 (55.0%) females, while in Group 2, 74 (41.1%) were males and 106 (58.8%) females. Distribution of vitamin D status according to age, BMI and gender was also made and compared between the groups. Number of patients <60 years were 121 and 113 respectively in Group 1 and Group 2. Serum 25-OH vitamin D deficiency was observed in 104 (57.7%) patients in Group 2 versus 25 (13.8%) of Group 1 ($P = 0.001$). Further analysis of subgroups revealed that the mean serum 25-OH vitamin D level in Group 2 aged <60 years was significantly lower than Group 1. ($P < 0.05$).

Conclusion: The results of this investigation revealed a link between serum 25-OH vitamin D insufficiency and knee osteoarthritis in persons over 60 years old. The measurement of blood 25-OH vitamin D in patients with symptoms suggestive of knee osteoarthritis is advised since it has been linked to the disease.

Keywords: 25 – OH Vitamin D, Osteoarthritis, Body mass index, Age, Knee joint pain.

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Introduction

Osteoarthritis (OA) is one of the major contributing factors for joint pain and impaired mobility, worldwide.[1] Obesity and aging population have raised the number of patients with symptomatic OA.[2]

OA generally progresses with age and is usually seen after 50 years; however recently, it has been increasingly noticed in younger individuals. OA and its associated symptoms such as pain, swelling, and stiffness impair the health-related quality of

life, thereby causing a substantial direct and indirect economic burden. The increasing prevalence of obesity, sedentary lifestyle, sporting activity, and vitamin D deficiency is attributable to this shifting disease trend. [3, 4]

Vitamin D deficiency is a under diagnosed medical condition since a significant proportion of the population in many countries and regions around the world have low serum 25-OH vitamin D levels. [5, 6, 7, 8]

It is known that vitamin D has role in mineralization, demineralization, remodeling, and maintenance of bone. Therefore, its deficiency may be implicated in the pathogenesis of osteoarthritis (OA). [9, 10] The pathogenesis of OA is still unclear. Recent studies on changes in subchondral bone remodeling phases of bone absorption and of bone sclerosis may be responsible for the cartilage damage. The reason behind these changes in the cartilage and bone is that low levels of 25-hydroxyvitamin D. [11, 12, and 13]

Knowledge of the serum status of 25-OH vitamin D may provide additional information to recognize patients at risk for progression of OA knee. The objective of this study is to evaluate the serum 25-OH vitamin D status in patients with knee OA scheduled for joint replacement along with healthy individuals for comparison. And also, to find out association between serum 25-OH vitamin D levels with age and body mass index (BMI) and with the knee osteoarthritis.

Material and Methods:

Study Setting and Design: This is a pilot study conducted in and around the Bettiah city and rural places of Bihar population. Subjects were selected during the medical camps conducted and the study. An informed consent was obtained from all the participants after explaining the purpose of the study. The study consists of 180 ages matched controls (Group 1) and 180

patients with knee osteoarthritis as cases (Group 2). Further study the subjects were divided into two subgroups based on age (<60 years and >60 years) in both group 1 and group 2. Based on body mass index (BMI) there are four subgroups i.e, BMI <20, 20 – 25, 26 – 30 and >30 in each group. Based on vitamin D status there are three subgroups in each group.

Inclusion Criteria:

Patients who presented with knee joint pain to the medical camps conducted by the department of Orthopaedics, Government Medical College, Bettiah, West Champaran, Bihar, were selected for the study. Subjects of the control group were selected over the same period patients without non skeletal symptoms and had no clinical features of knee OA based on history and clinical examination.

Exclusion Criteria:

Patients with history of rheumatic diseases other than osteoarthritis, chronic kidney diseases, gastrointestinal disorders, pulmonary systems, and persons on anticonvulsant drugs were excluded from the study. Patients with physical disabilities were excluded from the study.

Methodology:

Vitamin D status was measured by the serum concentration of 25-OH vitamin D which has a reasonably long half-life in the circulation. Measurement of serum 25-OH vitamin D was made by ELFA using fully automated minividas (Biomerieux, Germany) hormone analyzer. Based on the results obtained vitamin D status was categorized into 3 groups as serum 25-OH vitamin D levels <10 ng/ml, between 10–29 ng/ml, and 30 - 100 ng/ml, indicating vitamin D deficiency, vitamin D insufficiency and vitamin D sufficiency respectively.

Results:

There is total 360 persons, recruited for the study. Study population was divided into two major groups, Group 1 (Controls) and Group 2 (OA Cases). Group 1 includes 180 patients without the clinical symptoms of Knee OA and group 2 consists of 180 knee osteoarthritis (OA). Serum 25-OH vitamin D deficiency was observed in 104(57.7%) patients in Group 2 versus 25(13.8%) of Group 1 (Table 1). Group 1, 81 (45.0%) were males and 99 (55.0%) females, while in Group 2, 74 (41.1%) were males and 106 (58.8%) females (Table 1). Further study subjects were divided into two subgroups based on age in both group 1 and group 2 (<60 years and >60 years). Number of patients <60 years were 121 and 113 respectively in Group 1 and Group 2. Based on body mass index (BMI) there are four subgroups i.e, BMI <20, 20 – 25, 26 – 30 and >30 in each group. Based on vitamin D status there are three subgroups in each group (Table 1).

In table 2 comparisons of age, BMI, and 25-OH vitamin D status in controls and osteoarthritis patients was shown. There is no statistical difference with respect to age of the patients in the both the groups. But statistically significant difference was

observed with respect to BMI and serum 25 – OH vitamin D in both control group (Group 1) and OA group (Group 2) (Table 2).

In the entire study population serum 25-OH vitamin D deficiency was not homogenously distributed across age but was more frequent in subjects aged<60 years compared with >60 years particularly in the patient group. Table 3 shows the distribution of patients according to their vitamin D status and body mass index.

In table 4, Odds ratio, 95% confidence interval (95% CI) by logistic regression analysis showing association of serum 25-hydroxy vitamin D deficiency, age, gender, and BMI with knee osteoarthritis (OA) was shown.

On comparison of data among the same group also, there was a significant difference in 25–OH vitamin D levels of patients <60 and >60 years in Group 2 (Table 4), while it was not significant in control group. There was an association between serum 25-OH vitamin D deficiency and knee OA which was not statistically significant after adjustment for gender (Table 4).

Table 1: Baseline characteristics of study population

		Controls (Group 1) n (%)	Osteoarthritis (Group 2) n (%)
Gender	Male	81 (45.0)	74 (41.1)
	Female	99 (55.0)	106 (58.8)
Age (Years)	< 60 years	Male	54 (30.0)
		Female	67 (37.2)
	> 60 years	Male	40 (22.2)
		Female	53 (29.4)
BMI (Kg/m²)	< 20	7 (3.8)	9 (5.0)
	20 – 25	35 (19.4)	29 (16.1)
	26 – 30	69 (38.3)	117 (61.1)
	> 30	56 (31.1)	45 (25.0)
Vitamin D status	Normal (30 – 100ng/ml)	113 (62.7)	39 (21.6)
	Insufficient (10 – 29ng/ml)	57 (31.0)	60 (33.3)
	Deficient (<10 ng/ml)	25 (13.8)	104 (57.7)

Table 2: Comparison of Age, BMI and 25 – OH vitamin D status in controls and osteoarthritis patients

Parameter	Group 1 All Controls (n=120)	Group 2 All Osteoarthritis (n=120)	P value
Age	75.1 ± 21.4	79.3 ± 18.1	0.31
BMI	37.3 ± 11.9	39.6 ± 10.7	0.006*
25 – OH Vitamin D	68.9 ± 23.5	61.2 ± 15.9	0.02*

*Statistically significant p value

Table 3: Showing the 25 – OH vitamin D status according to body mass index

Vitamin D status	BMI (Body Mass Index)			
	< 20 (n= 03)	20 – 25 (n=16)	26 - 30 (n=70)	> 30 (n=31)
Normal	Nil	44.1 ± 10.2	50.6 ± 2.6	Nil
Insufficient	43.1 ± 20.4	32.0 ± 8.5	42.8 ± 9.5	39.8 ± 5.7
Deficient	Nil	12.8 ± 3.7	16.4 ± 2.1	12.8 ± 3.1

Table 4: Odds ratio, 95% confidence interval (95% CI) by logistic regression analysis showing association of serum 25-hydroxy vitamin D deficiency, age, gender, and BMI with knee osteoarthritis (OA)

Patients	Variables	Odds ratio (95% CI)	P value
Total OA patients	25 – OH vitamin D (< 10 vs >10ng/ml)	1.7 (1.2 – 2.89)	0.03*
	Gender (Female vs Male)	9.8 (2.1 – 11.4)	< 0.001*
	BMI	8.2 (1.4 – 10.6)	< 0.001*
OA patients < 60 year	25 – OH vitamin D (< 10 vs >10ng/ml)	0.89 (0.45–1.36)	0.03*
	Gender (Female vs Male)	6.3 (1.66 – 14.6)	0.011*
	BMI	5.3 (2.6 – 9.1)	0.005*
OA patients >60 year	25 – OH vitamin D (< 10 vs >10ng/ml)	1.72 (0.74 – 8.1)	0.89
	Gender (Female vs Male)	5.0 (2.18–9.70)	0.01
	BMI	7.1 (1.7 – 10.8)	0.003*

Discussion:

Vitamin D deficiency and knee OA occur in elderly people, seen all over the world. [11] The changes in sub-chondral bone play a vital role in the development of cartilage lesions in OA patients. [7, 10, 14, 15]

Low serum 25-OH vitamin D increases osteoblastic activity and bone turnover. [5,13,15,16] Early structural changes in the joints such as defects in cartilage, decrease in volume of cartilage, expansion of sub-chondral bone, and lesions in bone marrow

will appear before the onset of clinical symptoms of OA.[17]

Reports and observations from earlier studies provided a rationale for the measurement of serum 25-OH vitamin D levels with appearance of knee OA in elderly people and encourage supplementation to raise the serum vitamin D concentration to adequate levels. [13,18,19] In another study done by Bergink et al also, reported three times increased risk of knee OA and disease progress was associated with serum 25-OH

vitamin D <20 ng/ml in the Rotterdam Study.[20]

The most important finding of this study is the high prevalence of low serum levels of 25-hydroxyvitamin D in a population with OA, in a region like Bihar of Asian country. This study showed that about 5 patients out of 10 with knee osteoarthritis were vitamin D deficient with serum levels < 10 ng/ml. Several studies have shown a high incidence of vitamin D deficiency in patients with OA of hip or knee. [16, 20]

We also tried to correlate serum levels of vitamin D with related anthropometric predisposing factors such as age, gender, and BMI. A significant association with gender was observed, with female patients having lower serum levels of vitamin D.

The findings of the present study are on par with some previous studies showing a significant positive association between serum 25-OH vitamin D deficiency and OA knee in persons less than 60 years of age and in contrary to some other studies as well. [8, 10, 1

Conclusion:

In the present study it is found that there is overall 57% of vitamin D deficiency in our population. From the present study it can be concluded that there is a significant association between knee osteoarthritis and vitamin D deficiency when compared to control population with respect age, gender and BMI. Low level serum 25-OH vitamin D is expected to give beneficial effects, increase in bone mineral density and even decreases fracture risk in the elderly population

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