

## Original Research Article

# A study on correlation between deficiency of vitamin D and knee osteoarthritis among patients attending a tertiary care hospital in Andhra Pradesh

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### ABSTRACT

**Background:** The prevalence of vitamin D deficiency is the burning topic worldwide. 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-hydroxy (OH) vitamin D levels. The aim of this study was to investigate the association between serum vitamin D deficiency and knee osteoarthritis (OA).

**Methods:** The study population consists of 200 patients divided into two groups, group 1 and group 2. Group 1 with 100 subjects with no clinical features of knee osteoarthritis served as controls and group 2 consists of 100 patients of patients diagnosed with knee osteoarthritis. Serum 25-OH vitamin D was measured in all the participants by the enzyme-linked fluorescence assay (ELFA) method and concentrations <20 ng/ml was considered as deficient.

**Results:** In group 1, 47% were male and 53% were female whereas in group 2, 41% were male and 59% were female. In group 1, only 8% are vitamin D deficiency whereas in group 2, 61% have vitamin D deficiency. There was a significant association between serum vitamin D and staging of knee OA.

**Conclusions:** The present study findings showed a significant association between serum 25-OH vitamin D deficiency and in patients with knee OA.

**Keywords:** Osteoarthritis, Knee joint pain, 25-OH vitamin D, Andhra Pradesh

### INTRODUCTION

Vitamin D deficiency is common, with several epidemiologic studies having demonstrated that low levels of vitamin D are associated with higher levels of knee pain, increased prevalence of osteoarthritis (OA), as well as development and progression of knee OA.<sup>1-4</sup> The main function of vitamin D is to absorb calcium and phosphate: vitamin D deficiency in children leads to rickets, and, in adults, to osteomalacia.<sup>5-8</sup> In men with vitamin D deficiency, the prevalence of OA has been reported to be significantly higher compared to those with sufficient levels.<sup>9</sup> Other studies showed that vitamin D deficiency is age-dependent and could be high in elderly patients; these

patients are at higher risk of OA in their life.<sup>10,11</sup> Mild to moderate vitamin D deficiency could be asymptomatic, whereas long-term vitamin D deficiency can cause hypocalcaemia with secondary hyper-parathyroidism and bone mineralization disorder.<sup>12-14</sup> OA is the most common form of arthritis. Although OA can affect both spine and peripheral joints, it most commonly occurs in the joints of the hands, neck, waist, knees and pelvis. Existing treatments for OA could reduce disease progression and pain in patients, and improve their joint functions.<sup>13-16</sup> Many factors such as age, gender, bone deformities or abnormalities, weight, profession and also many underlying diseases such as diabetes, hypothyroidism, gout or Paget's bone disease could increase the risk of OA.<sup>17-19</sup> The pathogenesis of OA is still unclear. Recent

studies on changes in sub-chondral bone remodeling phases of bone absorption and of bone sclerosis may be responsible for the cartilage damage.<sup>20,21</sup> The reason behind these changes in the cartilage and bone is that low levels of 25-hydroxy (OH) vitamin D.

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 OA.

## METHODS

### *Study setting and design*

This is a case-control study conducted at the Department of Orthopedics, Great Eastern Medical School and Hospital, Srikakulam, Andhra Pradesh during November 2018 to November 2019. The study was approved by the institutional ethics committee. An informed consent was obtained from all the participants after explaining the purpose of the study.

The study consists of 100 ages matched controls (group 1) and 100 patients with knee osteoarthritis as cases (group 2). Further study the subjects were divided into two sub groups based on age (<60 years and >60 years) in both group 1 and group 2. Based on 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. American College of Rheumatology classification was considered as standard for the diagnosis of knee osteoarthritis.

### *Inclusion criteria*

Patients who are presented with knee joint pain with clinical and radiological findings. 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*

Stage 4 Kelegren-Lawrence stage, severe radiographic knee OA, and those with knee joint instabilities. Patients with physical disabilities, 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.

### *Sampling and data collection*

Demographic information such as age, gender, height, weight, place of residence, history of smoking, education

level, and history of arthritis were collected from the participants. Radiographs were done in two posterior anterior and lateral views of the knees with radiographic apparatus (Shimadzu Diagnostic Radiography RAD speed series D digital).

The Kellgren-Lawrence grading system is a radiological classification of knee OA. It ranges from grade 0 to grade 4, and is based on X-ray findings. Radiographs were reviewed and divided into the following stages- grade 1: doubtful narrowing of joint space and possible osteophytic lipping, grade 2: definite osteophytes, definite narrowing of joint space, grade 3: moderate multiple osteophytes, definite narrowing of joints 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 contour.

Venous blood samples were obtained from both groups and serum 25-OH vitamin D levels were also measured in the laboratory by radioimmunoassay. Serum 25-OH vitamin D level 30 ng/ml and above was defined as normal, 20-29 ng/ml was considered scant, and 20 ng/ml and lower indicated deficiency.

### *Statistical analysis*

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of Statistical Package for the Social Sciences version 20 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics included computation of percentages, means and standard deviations.

## RESULTS

A total of 200 patients recruited for the study. Study population was divided into two groups: group 1 (controls) and group 2 (OA cases). Group 1 includes 100 patients without the clinical symptoms of knee OA and group 2 consists of 100 knee OA. In group 1, 47% were male and 53% were female whereas in group 2, 41% were male and 59% were female.

In both group 1 and group 2, more than 50% were above 60 years. More than 50% of them are with BMI of 26-30 and above. Most of our study population are daily wage workers (Table 1).

In group 1, only 8% are vitamin D deficiency whereas in group 2, 61% have vitamin D deficiency (Table 2).

In Table 3, comparisons of age, BMI, and 25-OH vitamin D status in controls and OA patients are shown. There is no statistical difference with respect to age of the patients in the both the groups. But, statistical 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 3).

**Table 1: Characteristics of study population.**

Variables			Group 1 (controls)	Group 2 (cases)
			N (%)	N (%)
Sex	Male		47 (47)	41 (41)
	Female		53 (53)	59 (59)
Age (years)	<60	Male	21 (21)	24 (24)
		Female	28 (28)	25 (25)
	>60	Male	29 (29)	25 (25)
		Female	32 (32)	31 (31)
BMI (kg/m <sup>2</sup> )	<20		1 (1)	3 (3)
	20-25		22 (22)	18 (18)
	26-30		49 (49)	52 (52)
	>30		28 (28)	26 (26)
Profession	Salaried employee		15 (15)	12 (12)
	Daily wage worker		68 (68)	72 (72)
	Not working		17 (17)	16 (16)

**Table 2: 25-OH vitamin D status in controls and OA patients.**

Vitamin D status	Group 1 (controls)	Group 2 (OA cases)
	N (%)	N (%)
Normal (>30 ng/ml)	68 (68)	16 (16)
Insufficient (20-29 ng/ml)	24 (24)	23 (23)
Deficient (<20 ng/ml)	8 (8)	61 (61)

**Table 3: Comparison of age, BMI and 25-OH vitamin D status in controls and OA patients.**

Variables	Group 1 (controls)	Group 2 (OA cases)
Age (in years)	56.8±9.2	58.4±9.6
BMI	25.2±8.1	28.6±7.2
25-OH vitamin D	40.2±14.8	35.2±10.8

**Table 4: Association between 25-OH vitamin D level and stage of the disease.**

Vitamin D level (ng/ml)	Stage of the disease		
	Grade 1	Grade 2	Grade 3
	N (%)	N (%)	N (%)
<20	3 (3)	26 (26)	32 (32)
20-29	5 (5)	10 (10)	8 (8)
>30	6 (6)	8 (8)	2 (2)

In patients with knee OA according to Kellgren-Lawrence criteria, 14 (14%) patients were in grade 1, 44 (44%) in grade 2, 42 (42%) in grade 3 (Table 4). There was a significant association between serum vitamin D and staging of knee OA.

**DISCUSSION**

Early structural changes in the joints such as defects in cartilage, decrease in volume of cartilage, expansion of

subchondral bone, and lesions in bone marrow will appear before the onset of clinical symptoms of OA. 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.<sup>21,23-26</sup> Epidemiological studies showed an association between dietary intake and serum levels of 25-OH vitamin D and the progression of hip and knee OA.<sup>20,21,23</sup> In a recent study, decreased serum level of 25-OH vitamin D was reported in a significant proportion of patients with OA of hip and knee joints.<sup>21,23-26</sup> All these epidemiological suggests that by achieving normal serum vitamin D level may prevent or delay loss of cartilage loss and reduce the pain and other symptoms of OA.<sup>23-25</sup> Observation from studies on knee osteoarthritis evaluated by Cao et al suggested that serum 25-OH vitamin D level play an important role in structural changes of knee OA.<sup>25</sup>

The most important finding of this study is the high prevalence (61% deficiency and 23% insufficiency; around 84%) of low serum levels of 25-OH vitamin D in a population with OA, in a sunny region like south India of Asian country.

The main finding of this study is the association between the grade of knee OA and vitamin D levels. Our observations concur with those of Bergink et al who showed that low vitamin D intake increases the risk of radiographic progression of knee OA, especially when the patient’s bone mineral density (BMD) is low. Therefore, improving vitamin D levels in patients may have a protective role against the development of OA, especially in those patients with low BMD.<sup>4</sup> Similarly, Mc Alindon et al demonstrated significant relationship between serum vitamin D level and progression of OA, so that those with more advanced OA had lower vitamin D levels.<sup>3</sup> In a study by Muraki et al no significant relationship was found between vitamin D levels and radiographic OA of the

knee, but low levels of 25-OH vitamin D were more associated with knee pain.<sup>22</sup>

Keeping the limitations of earlier studies in view, present study was planned and executed effective to obtain results which are not affected by seasonal variation, diet, and exposure to sunlight or less physical activity due to pain and other confounders because patients and control population recruited for this study were selected from the same geographic territory who had unique racial and cultural backgrounds, with similar diet and sunlight exposure.

## CONCLUSION

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. Results showed that there was a significant association between knee OA grade based on Kellgren-Lawrence criteria and serum vitamin D levels. Therefore, identification of high risk subjects and correction of risk factors such as 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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