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A comparative study of serum vitamin d levels in patients with knee osteoarthritis and age matched healthy population

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Abstract

Objective: Measurement of Serum Vitamin D levels in patients with knee osteoarthritis and compare with age matched healthy population in order to assess their association.

Design: Prospective clinical control study.

Methods: Clinically proven two hundred patients of osteoarthritis knee (OA) and two hundred control included in study according to inclusion and exclusion criteria on OPD basis after getting written and informed consent, Serum 25-OHD was measured by the ELISA method and concentrations <20 ng/ml were considered as deficient levels.

Results: Four hundred subjects participated in study. The mean ages of patients and controls were 59.2 ± 12.9 and 58.9 ± 10.2 years respectively. The mean 25OHD in OA patients aged <60 years was significantly lower than controls (19.8 ± 18.8 vs. 36.7 ± 27.5 ng/ml, $p < 0.01$). In this age group knee OA was significantly associated with serum 25-OHD deficiency. The association between OA and serum 25-OHD deficiency in patients aged ≥ 60 years did not reach a significant level.

Conclusions: These findings indicate a significant association between serum 25-OHD deficiency and knee OA in patients aged <60 years and suggest serum 25-OHD measurement in any patient with symptoms suggestive of knee OA particularly at the initial stage of disease.

Keywords: Knee Osteoarthritis, Vitamin D

Introduction

Osteoarthritis (OA) is the most common disease of joints in adults around the world [1]. Worldwide, it is estimated to be the fourth leading cause of disability [2]. Nearly one-third of all adults have radiological signs of osteoarthritis [3]. Clinically too, significant osteoarthritis of the knee, hand, or hip is reported to affect around 8.94% of the adult population [4]. Its prevalence increases gradually in individuals older than 40 years. Studies suggests that prevalence of OA knee is >60% in subjects older than 70 years [5, 6]. Community survey data in rural and urban areas of India shows the prevalence of osteoarthritis to be in the range of 17 to 60.6% [7, 8, 9]. The disease usually evolves with increasing levels of pain, mobility restriction and physical disability [5, 10]. About 80% of persons affected by OA already report having some movement limitation and 20% report not being able to perform major activities of daily living; with an 11% of the total affected population reporting the need of personal care [11].

Both vitamin D deficiency and OA knee are age dependent and worldwide problem [12]. Vitamin D status influences the incidence and progression of knee OA [13]. Sunlight exposure and serum 25-OHD levels are both associated with decreased knee cartilage loss [14]. Previous studies also suggest that in serum 25-OHD deficient men the prevalence of OA was two times greater than those with sufficient levels [15]. In OA, changes in subchondral bone play an essential role in the onset and progression of cartilage lesions. In this condition bone resorption markers are higher and bone formation markers are lower compared with a control group. In progressive OA, bone metabolism and bone turnover are increased similar to that observed in patients with osteoporosis. Low serum 25-OHD increases osteoclastic activity and bone turnover [16]. Raising serum 25-OHD to sufficient levels with supplemental vitamin D will decrease the rate of bone turnover, suppress the PTH level, increase BMD and even decrease fracture risk in the elderly population [17].

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So, knowledge of the serum status of 25-OHD may provide additional information to recognize patients at risk for progression of OA knee. Till date very few studies have been done on this topic so data on this subject are lacking.

The present study was conducted to evaluate the association between serum Vitamin D level and osteoarthritis of knee.

Materials and methods

After approval from institutional ethical committee (IEC), clinically diagnosed two hundred adult patients of both sexes of knee pain with symptomatic osteoarthritis knee (OA Knee) and two hundred control included in study and patients with any history of systemic illness or major general medical conditions which can interfere with assessment of results, known or suspected joint infection, history of endocrinal abnormality, history of intake of Vitamin D or calcium supplement in past 3 months, Patient having significant cardiovascular disease, renal or hepatic disease, pregnancy, malignancy, diabetes, excluded from study. All the patients were explained about the study and an informed consent was obtained. Only those providing consent to participate in the study were enrolled in. Subjects of the control group were selected among patients who presented to the same hospital over the same period for nonskeletal symptoms like respiratory etc. The control group had no clinical features of knee OA based on history and clinical examination. Serum 25-OHD was measured by ELISA method in the laboratory of same hospital. Serum 25-OHD levels less than 20 ng/ml were considered as deficient.

Statistical analysis

The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 15.0 statistical Analysis Software. The values were represented in Number (%) and Mean \pm SD.

Results

400 persons were included in this study with 200 in both OA group (Group A) and control group (Group B).

In Group A, 93(46.5%) were males and 107 (53.5%) females of, while in Group B, 91(45.5%) were males and 109 (54.5%) females. In Group A, age range was 36-71 years age group with a mean age of 59.2 years and in Group B, range was 35-68 years with a mean age of 58.9 years. (Table-1). Number of patients <60 years were 104 and 106 respectively in Group A and Group B.

Serum 25-OHD deficiency was observed in 90(45%) of patients in Group A versus 56(28%) of Group B ($P=0.005$).

On subgroup analysis, it was found that the mean serum 25-OHD level in Group A aged <60 years was significantly lower than Group B (19.8 ± 18.8 vs. 36.7 ± 27.5 ng/ml, $P < 0.01$). In this age group, knee OA was significantly associated with serum 25-OHD deficiency. The association between OA and mean serum 25OHD levels in patients aged ≥ 60 years did not reach a significant level among both groups (43.9 ± 39.3 vs. 42.7 ± 38.9 $P=0.83$) (Table-2).

Percentage of number of patients with deficiency was significantly higher in Group A than Group B (61.5 vs 28.3, $p<0.01$) for age <60 while for age ≥ 60 , percentage of number of patients with VitD deficiency was not significant (28.1 vs 27.6, $p=0.96$). (Table 3).

Thus, additional analysis in respect to mean serum 25-OHD and proportion of serum 25-OHD deficiency demonstrated a

significant difference in age of less than 60 years in Group A vs Group B, but was not significant when compared with 60 years and older.

On comparison of data among the same group also, there was a significant difference in VitD levels of patients <60 and ≥ 60 years in Group A ($p<0.01$), while it was not significant in control group ($p=0.21$)

Discussion

Both vitamin D deficiency and OA knee are age dependent and worldwide problem [12]. Early joint structural changes such as cartilage defects, loss of cartilage volume, subchondral bone expansion and bone marrow lesions are present before the appearance of clinical symptoms [18]. These defects tend to progress in symptomatic knee OA. Several mechanisms which are related to serum vitamin D levels such as alterations in mechanical properties of bones, increasing bone resorption by raising PTH level, increasing bone turn over, or direct effect of vitamin D metabolites on articular chondrocytes were postulated to explain the contribution of vitamin D deficiency in the progression of OA [19]. These observations made in earlier studies provided a rationale for the measurement of correlation and association of serum 25OHD levels with appearance of knee OA in aging population and encourage supplementation to raise the serum concentration to adequate levels.

Cao *et al* evaluated findings from studies on knee osteoarthritis and suggested that serum 25OHD appears to play a role in structural changes of knee osteoarthritis [20]. According to analysis done by McAlindon *et al*, there was a 3-fold increased risk of progression among individuals with serum 25OHD < 30 mg/L [21]. Bergink *et al* also reported a 3-fold increased risk of knee osteoarthritis progression associated with serum 25OHD < 20 ng/mL in the Rotterdam Study, although the association became statistically nonsignificant after adjustment of multiple confounders [22]. The Institute of Medicine, after reviewing >1000 studies, proposed a threshold of low vitamin D status as 20 ng/mL to identify individuals at increased risk of adverse bone health [23]. The findings of our study are consistent with other studies showing a significant positive association between serum 25OHD deficiency and OA knee in persons less than 60 years of age.

Hence, serum 25OHD measurement and its supplementation if deficiency is found should be considered in any patients with symptoms suggestive of knee OA even before the appearance of radiographic changes, because by the time radiographic OA is detected 10% of knee joint cartilage is already lost [24].

Our study shows a significant positive association between serum 25OHD deficiency and OA knee in persons less than 60 years of age. As the knee articular cartilage damage generally starts in 5th decade of life this association is most consistent with initiation of early OA symptoms. Identification of high risk subjects and modification of risk factors such as correction of serum 25OHD deficiency at this stage is expected to exert beneficial effects.

Table 1: Demography

	OA Group (n=200)	Control Group (n=200)
Sex	M- 93(46.5%), F-107(53.5%)	M-91(45.5%), F-109(54.5%)
Age	36-71 yrs(59.2 \pm 12.9)	35-68yrs(58.9 \pm 10.2)

Table 2: Mean serum 25 hydroxyvitamin D (25OHD) in patients with knee osteoarthritis (OA) compared with controls.

Age	<60 years		≥60 years	
Group and No of Patients	OA (n = 104)	controls (n = 106)	OA (n = 96)	controls (n = 94)
Mean serum 25OHD (ng/ml)	19.8 ± 18.8 p=0.01	36.7 ± 27.5	43.9 ± 39.3 p=0.83	42.7 ± 38.9

p=0.01 (Significant, Unpaired t-test)

Table 3: Proportion of serum 25OHD deficiency in patients with knee osteoarthritis (OA) compared with controls.

Age	<60 years		≥60 years	
Group and No of Patients	OA (n = 104)	controls (n = 106)	OA (n = 96)	controls (n = 94)
Serum 25OHD Deficiency*, n (%)	63 (61.5) p<0.01	30 (28.3)	27 (28.1) p=0.94	26 (27.6)

p=0.01 (Significant, Chi square test)

*Serum 25OHD deficiency <20 ng/ml

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