Osteoporosis in Postmenopausal Females with Primary Knee Osteoarthritis in a Vitamin D Deficient Population

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**Abstract**

**Aim and Objective:** To find prevalence of osteoporosis (OP) in postmenopausal females with primary knee osteoarthritis (OA) in India, where there is widespread Vitamin D deficiency (VDD).

**Material and Methods:** 75 postmenopausal women (PMW) fulfilling ACR criteria for Knee OA between 40 - 60 years of age, having OA grade 2 or more as per Kellgren Lawrence grade on anterior-posterior radiograph of the right knee were enrolled. 34 PMW of the same age with normal right knee radiograph were taken as controls. Bone mineral density (BMD) of lumber spine (L1-L4), total hip and left forearm was performed using Dxa in all patients and controls. The results were expressed in absolute values (g/cm²) and as per WHO criteria – Osteoporosis: T score < -2.5, Osteopenia: T score between -1 and -2.5. Vitamin D Level was done by ELISA.

**Results:** Body mass index (BMI) of patients was significantly higher than controls (p = 0.006). There was no difference in BMD between patients and controls at any site. Forty percent patients and 53% controls had osteopenia (p = ns), while 34.6% patients and 41.1% controls had osteoporosis at any site (p = ns). When this comparison was made at each site there was no difference between patients and controls.

**Conclusion:** Prevalence of osteoporosis in PMW with primary knee OA is similar to that in general population.

**Editorial Viewpoint**

- Western studies have shown inverse relationship between osteoarthritis and osteoporosis.
- However, in this study osteoporosis in patients with osteoarthritis of knees was as prevalent as in general population.

**Background**

Due to increase in longevity and changing lifestyle of Indian women, menopausal and postmenopausal health has now become an important concern. It was expected that by the year 2015, India would have about 150 million females who will live beyond menopause.\(^1\) Morbidities associated with long term changes in ovarian hormonal levels include osteoporosis (OP) and osteoarthritis (OA). The prevalence and severity of OA and OP increase in postmenopausal women (PMW).\(^2\) A study from western India which assessed 500 PMW, reported that 51.6% females had OA while 62% females had OP. Vitamin D deficiency (VDD) which is rampant in India in all age groups, increases in severity in PMW. This may be due to a number of factors – dietary deficiency, undetected fat malabsorption, reduced cutaneous synthesis. VDD is also related to both osteoarthritis and osteoporosis.\(^3,4\)

Literature coming from the west has found an inverse relationship between OA and OP.\(^5-8\) Local factors such as osteophyte formation and subchondral sclerosis can increase measured values from the bone density assessments of the spine and hip done by DEXA (Dual Energy X ray Absorptiometry). However the study of osteoporotic fractures provided data on women with severe OA. According to that study, BMD (bone mineral density) increased at remote sites such as proximal and distal sites of the radius and calcaneous relatively more in patients with OA compared to individuals without OA.\(^6\) Some data from the west suggest that the prevalence of OP in OA is same as in general population.\(^9\) There is paucity of Indian data in...
Significant value (ng/ml) Vitamin D (IU/L) S. Alkpo4 (mg/dl) BMI (Kg/m2) 29.1 ± 4.6 26.4 ± 4.8 0.006* 66.5 ± 10.6 62.1 ± 13.2 0.06 Weight (kg) Height (cm) 151 ± 5.7 152.7 ± 6. 0.15 Present study only included PMW, confirm their finding. Besides the study by Ghosh et al., it serves to this regard. There has been only one study by Ghosh et al which stated that the prevalence of OP is similar in OA and in general population and VDD correlated with both OA and OP. Though this study was done parallel to the study by Ghosh et al., it serves to confirm their finding. Besides the present study only included PMW, unlike the study by Ghosh et al., which did not exclude males and premenopausal females.10 Thus the main aim of this study was to find the prevalence of OP in PMW with OA in a country like India, where there is widespread VDD.

Material and Methods

The study was a cross-sectional; hospital based observational study conducted in the outpatient Department of Rheumatology. The Research protocol and informed consent was approved by the Institutional Ethical committee.

Seventy-five (75) postmenopausal female patients of age between 40 – 60 years, attending the Rheumatology OPD, identified to have primary knee osteoarthritis on the basis of clinico-radiological ACR criteria of 1987, were studied.11 Thirty-four (34) postmenopausal females of similar age were taken as controls. All the patients and controls provided written informed consent. None of the patients and controls had inflammatory joint disease, medical renal disease, metabolic bone disease, hyperparathyroidism or were on any drugs like steroid which affect the bone health. The control population was representative of the general population. A complete history was taken and examination was done for each subject. Demographic variables were noted for all subjects.

Radiographs of the right knee were taken and evidence of knee OA was studied as per the Kellgren and Lawrence (KL) grade 1- 4.13 Osteoarthritis was classified as present, if KL grade of 2 or more was present while controls had normal x-rays. Bone mineral density (BMD) of lumbar spine (L1- L4), total hip and left forearm was performed using by dual x-ray energy absorptiometry (DXA) using Lunar prodigy Densitometer 12165 (GE medical systems) in all patients and controls. All BMD results were expressed in absolute values (g/cm2) and T-Score i.e. number of standard deviation above or below the mean results of young female adults. [Reference population - USA (Combined NHANES (Ages 20-30)/ Lunar (ages 20-40)]. Osteoporosis was defined as per the WHO guidelines T score < -2.5 and osteopenia between -1 and -2.5.13

Blood samples were collected from all patients and controls. Serum calcium was done by the OCPC method (LYPHOZYME-BEACON diagnostics); Serum alkaline phosphate was done by DGKC-SCE method (Agappe diagnostics). Vitamin D analysis was done by Enzyme immunoassay (Immuno diagnostic systems). The following cut - off values, as mentioned with the kit, were used: deficient: <20 ng/ml, Suboptimal – between 20 -30 ng/ml and optimal- >30 ng/ml.

Statistical Analysis

For the comparison of baseline characteristics between the groups independent sample t-test was used. The BMD among the groups, adjusted for the significantly different baseline characteristics, were compared using Analysis of Covariance (ANCOVA). The analysis was performed using SPSS software version 20.0.

Results

75 patients and 34 controls were enrolled in the study. The demographic variables and disease variables are as shown in Table 1. Among the demographic variables, there was a significant difference in the body mass Index (BMI) between patients and controls (p = 0.006). Among the other variables, there was no difference between patients and controls. Out of the 75 patients, 43 (57%) had grade-2 OA, 26 (35%) had grade 3- OA, while 6 (8%) had grade-4 OA. The mean BMD at the three sites is shown in Table 2. There was no significant difference in between patients and controls at any site. There was no relationship between BMD and severity of OA. There was no difference between BMD of patients and controls at any site even after adjusting it for BMI (Table 2). As per BMD T-score, 26 (34.6%) patients and 14 (41.1%) controls had osteoporosis at any site, while 30 (40%) patients and 18 (53%) controls had osteopenia at any site (p ns). When this comparison was made at individual sites, no difference was found between patients and controls (Figure 1).
Vitamin D Deficiency

70 (93.4%) patients and 32 (94%) controls had suboptimal vitamin D levels (p ns). Amongst the patients, 44 (59%) had vitamin D deficiency, while 26 (34.6%) had vitamin D insufficiency. Among the controls 20 (59%) had vitamin D deficiency, while 12 (35%) had vitamin D insufficiency. Out of the 26 patients with suboptimal vitamin D, 9 (34.6%) had osteoporosis and 16 (50%) had osteopenia at any site. Out of the 9 controls with suboptimal vitamin D, 7 (77.8%) had osteoporosis while 3 (25%) had osteopenia at any site. Out of the 44 patients with vitamin D deficiency, 15 (34%) had osteoporosis and 16 (36.3%) had osteopenia at each site. When the comparison was made at each site, controls with suboptimal vitamin D were significantly more osteoporotic at forearm compared to the patients (Table 3). When the absolute BMD values were compared in patients and controls, the difference was not found to be significant (Table 4).

Discussion

The results of the study show that there is no relation of OA and OP in VDD post menopausal women. There was a significant difference between patients and controls with suboptimal vitamin D at forearm. But as the sample size of the study is too small, it is very difficult to interpret whether this difference proves any relation between OA and OP. The result is similar to the study by Ghosh et al. The study had 98 cases and 108 age-matched controls. VDD was present in 55% patients and 34% controls. In the present study almost all the subjects had low vitamin D. The reason for this difference may be because Ghosh et al. had also included males and pre-menopausal females, while the present study only had post-menopausal females. Even though varying degree of VDD is rampant in India among all age groups, according to various studies published earlier, VDD gets aggravated after menopause because of traditional clothing pattern and these females often remain indoor. In multiple studies from various parts of India the prevalence of VDD in postmenopausal females ranges from 50 – 80%,17,18. In the study by Ghosh et al., almost 80% patients and controls had low BMD. The result of the present study is similar.10 Another study from north India which looked for prevalence of primary
osteoarthritis in postmenopausal females, reported prevalence of OP to be 37.8% with maximum at spine and minimum at femur.20 In the present study maximum OP was at forearm and minimum at hip. Ghosh et al found VDD to be associated with both OA and OP, but did not find any relation between the two conditions.10 In the present study also there was no relation between OA and OP, where almost all subjects had low vitamin D. This means that OA does not provide protection for development of OP. Osteopenia and osteoporosis does occur in patients with knee OA. There are some clinical implications of this. Some patients with knee OA may require a knee replacement in future. So early detection and treatment of OP in patients of knee OA might improve the outcome of joint replacement surgery.

This sample size of this study is too small to know the exact relation between the two. So this may be considered a pilot study and a multi-centric study with a large sample size must be planned on this to know the exact relation between OA and OP in India.

References