

# Assessment of Functional Outcome in the Osteoarthritis Knee Following Vitamin D3 Supplementation using KOOS PS Score

Rahul Bhardwaj<sup>1</sup>, Vipin Sharma<sup>1</sup>, Vipin Kumar<sup>1</sup>, Narinder Singh<sup>1\*</sup>,  
Brandon Eric Dkhar<sup>1</sup> and Akshay Sharma<sup>1</sup>

<sup>1</sup>Department of Orthopaedics, Dr RPGKMC Kangra at Tanda (Himachal Pradesh), India.

## Authors' contributions

*This work was carried out in collaboration among all authors. Authors RB, VS designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors VK and NS managed the analyses of the study. Authors BED, AS managed the literature searches. All authors read and approved the final manuscript.*

## Article Information

### Editor(s):

(1) Dr. Parth Trivedi, Chanchalben Mafatlal Patel College of Physiotherapy, India.

### Reviewers:

(1) Jumaa Salman Chiad, Alnahrain University, Iraq.

(2) Jessica Immonen, University of Nevada Las Vegas, USA.

Complete Peer review History: <http://www.sdiarticle4.com/review-history/67036>

Original Research Article

Received 20 February 2021

Accepted 19 April 2021

Published 30 April 2021

## ABSTRACT

**Objective:** OA is the most common articular disease of the developed world and a leading cause of chronic disability. Vitamin D supplementation has been known to improve knee joint pain and function in patients with OA. The aim of this study was to evaluate effectiveness of vitamin D supplements in knee joint improving pain and function in patients with OA.

**Methods:** 104 patients with knee OA who fulfilled inclusion criteria and consented to participate were enrolled in the study. Patients with knee OA were blinded and randomized to receive either Tab Vit D3 or an identical placebo tablet. The vitamin D3 Tab was administered in a dose of 60000U/Week for 3 months in 12 doses while the placebo tablets with identical dosing schedule were administered to the control group. The patients who received Vitamin D3 tablets were allocated to the treatment group (n=54) while those receiving the identical placebo tablets were allocated to the control group (n=50). Four patients from case group were lost to follow up. Functional outcome score (KOOS PS score) was assessed in both groups at 3 months, 6 months and 1 year.

\*Corresponding author: Email: narinder83@yahoo.in;

**Results:** While baseline KOOS PS Score were comparable in the treatment and the control groups [34.0 vs 30.0, P= 0.612], there was a statistically significant improvement in the follow-up scores in the treatment groups at 3 mo, 6mo and 1 year follow up (Provide P value ex.) \*p<0.5)

**Conclusion:** Vitamin D3 supplementation is effective in improving the KOOS PS (The Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form) score in patients with osteoarthritis knee.

*Keywords: Knee; KOOS PS; osteoarthritis; Vitamin D3.*

## 1. INTRODUCTION

Osteoarthritis (OA) (It is a degenerative joint disease of abnormal inflammatory signaling and is one of the most prevalent) is one of the most prevalent conditions resulting in disability, particularly in the elderly population. OA is the most common disease of the articular cartilage in the developed world and a leading cause of chronic disability. The knee and hip joints are the most commonly affected joints leading to this chronic disability [1]. The economic costs of OA are high, including those related to treatment, for those individuals and their families who must adapt their lives and homes to the disease, and those due to lost work productivity [2].

Patients with OA are at a higher risk of death compared with the general population [CITE]. Clinical history of diabetes, cancer, cardiovascular disease and the presence of walking disability are major risk factors. Excess mortality is observed for all diseases with specific causes of death but is particularly pronounced for cardiovascular complications. Knee OA is more important not only for its high prevalence rate compared with other types of OA but also for its presentation at earlier age groups particularly in younger age groups of obese women. The incidence of knee OA increases with age; increased lifespan and average population weight also factor in to increase prevalence of the disease [3]. Pain and other symptoms of OA may have a profound effect on quality of life, affecting physical function and psychological. Patients with knee OA experience increases in their physical limitations, pain and functional restrictions with disease progression [4].

Vitamin D3 and its receptor (VDR) play an important role in bone metabolism; signaling by way of VDR increases in response to an inflammatory response such as in cancer or OA. VDR has an important function in regulating calcium metabolism and cellular function in bones. There is evidence from a number of epidemiological studies that suggest that low dietary intake of vitamin D3 and low serum 25-

OH-D3 levels are associated with increased radiological progression of knee OA [5,6]. It is debated in the current literature whether improvement in functional outcome in knee OA patients is demonstrated with vitamin D3 therapy. The present study aimed to assess functional outcome of knee OA patients following Vitamin D3 supplementation using KOOS PS score.

## 2. METHODOLOGY

### 2.1 Patients and Methods

This prospective, double-blind, randomized controlled study was conducted at an outpatient department (OPD) of a tertiary care institute over a period of one year ( 2018-19 ). The patients with knee OA and vitamin D3 levels <40 ng/ml and following ACR criteria were enrolled in the study while patients receiving daily supplementation of Vitamin D3, Calcium, and drugs interacting with effects of Vitamin D3, use of steroids, patients undergoing surgery during the study, patients having diseases including lymphoma, sarcoidosis, tuberculosis, hyperparathyroidism, malabsorption disorders, GFR<30, history of inflammatory joint disease, and pregnancy, and not willing to participate were excluded. A total of 104 patients were randomized into two groups (Treatment Group n=54, Control Group n=50) to receive either Tab Vit D3 preparation or an identical looking placebo. Vit D3 supplementation was provided to the treatment group in the form of 60000 U weekly X 3 mo in 12 doses and controls were provided with identical looking placebo tablets.

### 2.2 Outcome Assessment

Knee function assessments were conducted using the Knee Injury and Osteoarthritis Outcome Score Physical Function Short Form (KOOS PS) at 3, 6 and 12 months (Fig. 1).

### 2.3 Statistical Analysis

Data was calculated for frequency, percentage, median, and interquartile range (IQR) measures.

Normality of data was assessed using the Shapiro Wilk test. Categorical variables were compared using Chi Square Test. Skewed data were compared using Mann Whitney U test. P value <0.05 was considered significant. Statistical analysis was performed using SPSS v21.

### 3. RESULTS

Among the treatment group participants (n=54) and age/sex matched controls (n=50), grading of knee OA was comparable (P>0.05 Provide P value) (Table 1). 4 cases were lost to follow up from case group. Assessment by KOOS PS score in both groups was ran at baseline, 3 months, 6 months and 1 year. While baseline KOOS PS Scores were comparable in treatment and control groups [34.0 (27.50,56.0)] vs 30.0 (28.0,60.0), P= 0.612], there was significant improvement for the treatment group (received Vit D3 supplementation) compared to the control group (received placebo); at subsequent follow ups (Table 2). At one year follow up the KOOS PS score was significantly better in cases as compared to controls (p<0.0001); [45.0([38.75, 65.5) in cases vs 23.5 (15.0, 47.25) in controls].

### 4. DISCUSSION

Currently, research on the role of vitamin D in improving outcomes in knee OA is inconclusive. There are many studies analyzing effect of Vitamin D3 supplementation on functional outcome in knee OA patients. Some studies have noted improvement in knee function

following Vitamin D3 supplementation by mean -1.36 (95% CI, -1.87 to -0.85) over the placebo group which had a mean 0.69 (95% CI,-0.03 to 1.41; effect size = 0.06). This was accompanied by significant biochemical changes in serum total calcium, 25(OH)D and alkaline phosphatase. The results above suggested there was a small but statistically significant clinical benefit to vitamin D3 treatment in patients with knee OA [7].

On the contrary, another study demonstrated functional outcome in knee OA following Vitamin D3 supplementation was studied in a discrete subset of patients with higher age and BMI  $\geq 30$  kg/m<sup>2</sup> [8]. This study did not show a difference in functional progression of knee OA between older adults with obesity who took vitamin D supplements at baseline and those who did not, which could be due to less bioavailability of Vit D3 and hence requirement of high doses of Vitamin D3 or higher grades of OA Knee in the study. It could be a reason for no improvement in KOOS functional scale in their study [8].

In another study a two year RCT of 2000 IU/day oral cholecalciferol for patients with vitamin D insufficiency was performed [5]. The primary outcomes were MRI assessed cartilage thickness, radiographic JSN and pain. The population studied had similar baseline concentrations of vitamin D but greater baseline JSW (approximately 5mm vs. 3.5mm). The results demonstrated that despite 63% of patients achieving target concentrations of vitamin D, there were no significant improvements in any of the outcomes [5].

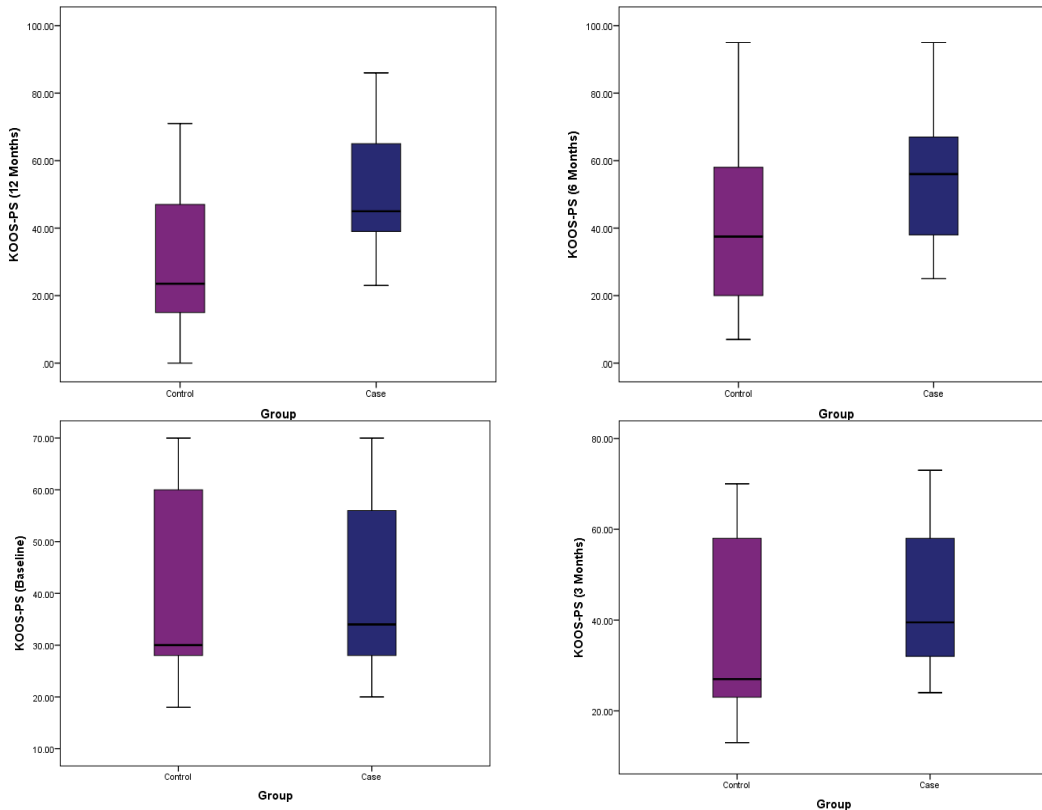
**Table 1. General characteristics (n=104)**

	Cases (n=54)	Controls (n=50)	P value
Age (years)	47.50 [38.75, 55.00]	49.38 [42.0, 57.25]	0.205
Sex (M:F)	13:37	10:40	0.476
<b>Type of knee OA</b>			
Bilateral	24	21	0.971
Left	15	14	
Right	15	15	

**Table 2. Comparison of KOOS PS score between case and controls**

	Cases	Controls	P Value	
<b>KOOS-PS</b>	Baseline	34.0 [27.50, 56.0]	30.0 [28.0, 60.0]	0.612
	3 Months	39.5 [32.0, 58.5]	27.0 [23.0, 58.0]	0.004
	6 Months	56.0 [37.75, 67.75]	37.0 [19.75, 58.25]	0.001
	12 Months	45.0 [38.75, 65.5]	23.5 [15.0, 47.25]	<0.0001

Data expressed as median [IQR]; \*Mann-Whitney U test



**Fig. 1. Box plot showing comparison of KOOS-PS Score between case and controls A) Baseline; B) 3 Months, C) 6 Months and D) 12 Months**

While the present study has shown that vitamin D3 supplementation was effective in improved functional outcome of knee OA patients in terms of KOOS score. While baseline KOOS Scores were comparable in case and control group [38.0 (31.50, 60.0)] vs 34.0 (32.0, 64.0), P= 0.657], there was significant improvement in cases (received Vit D3 supplementation) as compared to controls (who received placebo); at 3 mo, 6mo and 1 year follow up.

## 5. CONCLUSION

Vitamin D3 supplementation in the dose 60000 U weekly for 3 mo in 12 doses is effective in improvement in functional outcome of the patients with OA Knees. KOOS PS score is an effective way to assess functional outcome in Knee OA patients.

## 6. LIMITATIONS

The study has few limitations like small sample size, not considering different Vitamin D3 doses and their effects, and not incorporating any

adverse events reported during study. Multicentric studies with large sample size would be required to arrive at tangible results.

## CONSENT AND ETHICAL APPROVAL

As per international standard or university standard guideline patients consent and ethical approval has been collected and preserved by the authors.

## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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