

Association of Vitamin D Deficiency with Early Onset of Osteoarthritis

Nusrat Rasheed, Asadullah Makhdoom, Muhammad Shafiq Khan,
Naseem Rasheed, Muhammad Hassan Khan

ABSTRACT

OBJECTIVE: To evaluate the association of serum vitamin D deficiency and early onset of osteoarthritis (OA) knee joints.

METHODOLOGY: This single-blinded comparative OPD based study, conducted at Dow University Hospital, Karachi. Patients ≤ 40 years of age having knee pain for the last six months were included. Osteoarthritis was classified according to the Kellgren Lawrence (KL) scale. Randomization was done, dividing the patients in two groups. One with normal vitamin D level whereas the other group had low levels of vitamin D. Both groups were compared based on X-ray findings to evaluate the association of OA with vitamin D deficiency.

RESULTS: In our study, out of 152 patients, 106 were diagnosed with Osteoarthritis. The mean age was 36.84 years. Serum calcium level normal in 100 (65.8%) patients. Based on radiological findings, 75 (49.3%) were KL grade 1 while 31 (20.4%) were grade 2, 75 (49.3%) had right-sided knee involvement. In the group with low levels of serum vitamin D, 32 (40%) had right knee affected, 25 (31.3%) had left, 20 (25%) had bilateral knee involvement, whereas three had normal knee joints. The Chi-square test showed a positive relationship between low levels of vitamin D and osteoarthritis.

CONCLUSION: The above study shows statistically significant association between vitamin D deficiency and early onset of osteoarthritis. Cartilage loss and radiographic progression of the disease are important factors to understand the disease pathogenesis. Therapeutic or preventive role of vitamin D in osteoarthritis may be established but for that long term studies are needed.

KEYWORDS: Osteoarthritis, Vitamin D, Kellgren Lawrence scale, BMI.

This article may be cited as: Rasheed N, Makhdoom A, Khan MS, Rasheed N, Khan MH. Association of Vitamin D Deficiency with Early Onset of Osteoarthritis. J Liaquat Uni Med Health Sci. 2020;19(04):267-70. doi: 10.22442/jlumhs.201940703

INTRODUCTION

Osteoarthritis (OA) is a disease affecting the joints, cartilage, bone, and muscles. Human articular chondrocytes have Vitamin D receptors and 1, 25 dihydroxy vitamin D₃¹. They regulate the expression of matrix metalloproteinase and prostaglandin E₂. It is believed that

Vitamin D enhances the metabolism of musculoskeletal system through its effects on bone and cartilage. It strengthens the muscles and improve muscles function and strengthening by cellular growth and protein synthesis. This is how vitamin D affects the disease progression and overall controls the metabolism^{2,3}.

Vitamin D is an important fat-soluble vitamin which mainly regulates calcium metabolism. Certain factors influence serum levels of vitamin D like sunlight exposure, dietary intake, and certain systemic disorders^{5,6}. The risk of many chronic illnesses is decreased when there is a sufficient level of Vitamin D. On the other hand, its inadequacy causes many pathological conditions including Osteomalacia and osteoarthritis^{7,8}. Vitamin D deficiency causes cartilage loss in knee joints. The prevalence of osteoarthritis is

two times higher in those who are vitamin D deficient than those who have sufficient vitamin D.

During the onset and progression of cartilage destruction, massive changes also take place simultaneously in subchondral bone, which is evident by the fact that markers of bone turnover are high and those of bone formation are low⁹. As the disease progresses, bone turnover and metabolism increase accordingly which can be decreased by raising serum vitamin D levels in the form of supplemental vitamin D^{8,10,11}. Decreased levels of vitamin D in patients of OA indicate that the rate of disease progression is higher. Therefore, it is the need of the hour that this risk factor should be identified and treated timely so that disease progression could be stopped^{12,13}.

Very few studies have been done up until now regarding this emerging issue. So, this study may fill the gaps in the literature and will highlight the association of vitamin D with the early onset of OA.

METHODOLOGY

This single-blinded comparative outpatient department based study, conducted at Dow University Hospital, Karachi from December 2019 to March 2020, after ethical approval from the Institutional review board. By

using open EPI Software for sample size calculation, taking the mean of increase in medial tibial plateau bone area as 1.6%±2.8%, the sample size came out to be 152, taking confidence interval as 95% and power of test as 80%.

To be considered having OA, a patient had to meet the American College of Rheumatology criteria for knee osteoarthritis i.e. knee pain and osteophyte on radiographs and one of the following (a) crepitus on knee range of motion (b) Morning stiffness of short duration of 30 minutes. Patients up to 40 years of age having knee pain for six months were registered. OA was classified according to the Kellgren Lawrence scale, tenderness on medial joint line with crepitus, and decreased range of motion. All patients had BMI <22.

Patients were randomized into two groups, all were worked up for vitamin D level. One group was with normal vitamin D level (<20 mg/dl) whereas the other group had low levels of vitamin D (<20 mg/dl). X-ray knee joint Anteroposterior and lateral, weight bearing view from Dow Radiology centre with standard distance and radiations, view done in both groups. The group with normal vitamin D was compared with another group with a low vitamin D group in accordance with X-ray findings to find the incidence of vitamin D level in both groups. Exclusion criteria were age more than 40 years, secondary osteoarthritis due to any other cause, patients having a chronic disease like asthma, chronic obstructive pulmonary disease, chronic renal failure, and malignancy.

Patients were selected by pre-defined criteria. After taking informed consent from the participants, a questionnaire comprising of 15 questions, was filled by the research team members. Serum Vitamin D levels of the patients fulfilling inclusion criteria were sent. Based on history and clinical examination, X-rays were done. The results were entered into the proforma for all variables. After completion of data

entry, results were compiled using SPSS version 16.

RESULTS

In our study, the mean age of the participants was 36.84 years, 43(28.3%) were males and 109(71.7%) were females. There were no significant differences in physical activity scores, smoking, alcohol consumption, vitamin D intake, race, or ethnicity. Serum calcium level was found normal in 100(65.8%) and low in 52(34.2%). Radiological classification according to Kellgren Lawrence classification is given in Table I. Out of 152 patients, 106 were having

TABLE I: RADIOLOGICAL CLASSIFICATION ACCORDING TO THE KELLGREN LAWRENCE SCALE

	Fre- quency	Per- centage	Valid Percent	Cumulative Percent
Valid	Grade 1	75	49.3	70.8
	Grade 2	31	20.4	29.2
	Total	106	69.7	100.0
Missing System	46	30.3		
Total	152	100.0		

TABLE II: BASAL METABOLIC INDEX

	Fre- quency	Per- centage	Valid Percent	Cumulative Percent
Valid	<18	50	32.9	32.9
	18-23	67	44.1	77.0
	23-30	24	15.8	92.8
	>30	10	6.6	99.3
	12.00	1	.7	100.0
Total	152	100.0	100.0	

TABLE III: ASSOCIATION OF THE SIDE OF THE KNEE AFFECTED WITH VITAMIN D LEVELS

		Serum vitamin D LEVEL		Total	P-Value
		<20	>20		
Affected knee	Right	Count	32	19	51
		% within Serum vit D LEVEL	40.0%	26.4%	33.6%
	Left	Count	25	8	33
		% within Serum vit D LEVEL	31.3%	11.1%	21.7%
	Both	Count	20	2	22
		% within Serum vit D LEVEL	25.0%	2.8%	14.5%
None	Count	3	43	46	
	% within Serum vit D LEVEL	3.8%	59.7%	30.3%	
Total	Count	80	72	152	
	% within Serum vit D LEVEL	100.0%	100.0%	100.0%	

osteoarthritis diagnosed on a radiological basis. Out of the 75(49.3%) had Right-sided knee involvement, 31(20.4%) had Left side affected, 22 (14.5%) had bilateral involvement, 50(32.9%) had BMI <18, 67(44.1%) had BMI between range of 18-23 and 10(6.6%) had BMI >30 (Table II).

As shown in Table III, in the group of patients having low levels of serum vitamin D, 32(40%) had Right knee affected, 25(31.3%) had Left knee affected, 20 (25%) had bilateral knee involvement whereas 3 had normal knee joints. On the other hand, those with adequate serum vitamin D levels, 19(26.4%) had Right Knee affected, 8(11.1%) had Left-sided involvement, 2(2.8%) had both knees involved. 47 (59.7%) had no knee involvement.

The Chi-square test showed a positive relationship between low levels of vitamin D and osteoarthritis.

DISCUSSION

Our study shows greater frequency of osteoarthritis in those patients who were vitamin D deficient. OA not only affects the health of individuals but also has a strong impact on working ability¹⁴. A recent analysis done in Canada shows 44.4% of non-employment was due to disability caused by OA¹⁵. Literature shows a positive relationship between the deficiency of vitamin D and the development of OA¹⁶.

A study conducted by Sanghi D et al¹⁷ shows an association between serum 25-OH D and knee OA. It shows a significant decrease in knee pain evident on mean Visual Analogue Score that was 0.26% and 0.55% on the WOMAC index (Western Ontario and McMaster Universities Arthritis Index) in participants who were given Vitamin D as compared to those given Placebo respectively.

A study done by Zhang FF 2002¹⁸ shows the participants with low vitamin D levels had a risk of progression to knee OA 2 folds more than those who had greater vitamin D level. A systematic review and meta-analysis, done in 2017, which included a sample size of 1136 showed a significant reduction in WOMAC pain and function after vitamin D supplementation, although no change was observed in WOMAC¹⁹. A study conducted by Bergink AP et al²⁰ shows that individuals having a low serum vitamin D had three folds increased risk of knee OA.

Contrary to our study, the Framingham Offspring cohort shows no association between vitamin D and OA progress²¹.

Our study had certain limitations, with no consideration of the confounding factors like sunlight exposure, dietary habits, and dermal vitamin D production which already have an individual association with vitamin D.

CONCLUSION

The study shows statistically significant association between vitamin D deficiency and early onset of

osteoarthritis. Cartilage loss and radiographic progression of the disease are important factors to understand the disease pathogenesis. Therapeutic or preventive role of vitamin D in osteoarthritis may be established but for that long term studies are needed.

Ethical permission: Dow University of Health Sciences, Karachi Letter No. IRB-1369/ DUHS/ Approval/2019, Dated 19-12-2019.

Conflict of interest: There is no conflict of interest in authors.

Funding: There was no funding from any agency.

AUTHOR CONTRIBUTIONS

Rasheed N: Literature search, Data analysis, citation

Makhdoom A: Literature review

Khan MS: Data entry

Rasheed N: Literature review

Khan MH: Reference search

REFERENCES

1. Tetlow LC, Woolley DE. Expression of vitamin D receptors and matrix metalloproteinases in osteoarthritic cartilage and human articular chondrocytes in vitro. *Osteoarthritis Cartilage*. 2001; 9: 423-431. doi:10.1053/joca.2000.0408
2. McAlindon TE. Nutraceuticals: do they work and when should we use them?. *Best Pract Res Clin Rheumatol*. 2006; 20: 99-115. doi:10.1016/j.berh.2005.09.002
3. Holick MF. High prevalence of vitamin D inadequacy and implications for health. *Mayo Clin Proc*. 2006; 81: 353-373. doi:10.4065/81.3.353
4. Bischoff-ferrari HA, Giovannucci E, Willett WC, Dietrich T, Dawson-Hughes B. Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes. *Am J Clin Nutr*. 2006; 84: 18-28. doi:10.1093/ajcn/84.1.18
5. Lee P, Eisman JA, Center JR. Vitamin D deficiency in critically ill patients. *N Engl J Med*. 2009; 360: 1912-4.
6. Mäkinen TJ, Alm JJ, Laine H, Svedström E, Aro HT, Svedström E. The incidence of osteopenia and osteoporosis in women with hip osteoarthritis scheduled for cementless total joint replacement. *Bone*. 2007; 40: 1041-7.
7. Heidari B, Shirvani JS, Firouzjahi A, Heidari P, Hajian-Tilaki K. Association between nonspecific skeletal pain and vitamin D deficiency. *Int J Rheumatol*. 2010; 13: 340-6.
8. Pérez-López FR. Vitamin D and its implications for musculoskeletal health in women: an update. *Maturitas*. 2007; 58: 117-137.
9. Chaganti RK, Parimi N, Cawthon P, Dam TL, Nevitt MC, Lane NE. Association of 25-hydroxyvitamin D with prevalent osteoarthritis of

- the hip in elderly men: the osteoporotic fractures in men study. *Arthritis Rheum.* 2010; 62: 511-4.
10. Bettica P, Cline G, Hart DJ, Meyer J, Spector TD. Evidence for increased bone resorption in patients with progressive knee osteoarthritis: longitudinal results from the Chingford study. *Arthritis Rheum.* 2002; 46: 3178-3184.
 11. Von Hurst PR, Stonehouse W, Kruger MC, Coad J. Vitamin D supplementation suppresses age-induced bone turnover in older women who are vitamin D deficient. *J Steroid Biochem Mol Biol.* 2010; 121: 293-296.
 12. Adams JS, Hewison M. Update in vitamin D. *J Clin Endocrinol Metab.* 2010; 95: 471-476.
 13. Bischoff-Ferrari HA, Zhang Y, Kiel DP, Felson DT. Positive association between serum 25-hydroxyvitamin D level and bone density in osteoarthritis. *Arthritis Rheum.* 2005; 53: 821-6.
 14. Cross M, Smith E, Hoy D. The global burden of hip and knee osteoarthritis: estimates from the Global Burden of Disease 2010 study. *Ann Rheum Dis.* 2014; 73: 1323-1330.
 15. Hubertsson J, Turkiewicz A, Petersson IF, Englund M. Understanding occupation, sick leave, and disability pension due to knee and hip osteoarthritis from a sex perspective. *Arthritis Care Res (Hoboken).* 2017; 69: 226-233.
 16. Bortoluzzi A, Furini F, Scire CA. Osteoarthritis and its management-Epidemiology, nutritional aspects and environmental factors. *Autoimmunity reviews.* 2018; 17: 1097-1104.
 17. Sanghi D, Mishra A, Sharma AC, Singh A, Nandu S M, Agarwal S. Does vitamin D improve knee: A randomized controlled pilot trial. *Clin Orthop.* 2013; 471: 3356-3562.
 18. Zhang FF, Driban JB, Lo GH. Vitamin D deficiency is associated with progression of knee osteoarthritis. *J Nutr.* 2014; 144(12): 2002-8. doi:10.3945:2002-2008.
 19. Diao N, Yang B, Yu F. Effect of vitamin D supplementation on knee osteoarthritis: a systematic review and meta-analysis of randomized clinical trials. *Clin Biochem.* 2017; 50: 1312-6.
 20. Bergink AP, Uitterlinden AG, Van Leeuwen JP, Buurman CJ, Hofman A, Verhaar JA, et al. Vitamin D status, bone mineral density, and the development of radiographic osteoarthritis of the knee: the Rotterdam Study. *J Clin Rheumatol.* 2009; 15: 230-7.
 21. Felson DT, Niu J, Clancy M. Low levels of vitamin D and worsening of knee osteoarthritis: results of two longitudinal studies. *Arthritis Rheum.* 2007; 56: 129-136.



AUTHOR AFFILIATION:

Dr. Nusrat Rasheed (*Corresponding Author*)

Associate Professor, Department of Orthopedic Surgery
Dow International Medical College, Dow University of
Health Sciences
Karachi, Sindh-Pakistan.
Email: dr.nusrat_amir@hotmail.com

Dr. Asadullah Makhdoom

Associate Professor, Department of Orthopedic Surgery
Liaquat University of Medical & Health Sciences
Jamshoro, Sindh-Pakistan.

Dr. Muhammad Shafiq Khan

Assistant Professor, Department of Orthopedic
DHQ Teaching Hospital D.I.Khan, Pakistan.
E-mail: drshafiqorthosurg@gmail.com

Dr. Naseem Rasheed

Associate Professor
Department of Obs and Gynae
Baqai Medical University, Karachi, Sindh-Pakistan.

Dr. Muhammad Hassan Khan

Resident, Department of Orthopedic
Dow University Hospital, Karachi, Sindh-Pakistan.