Decoding the Role of Vitamin D Deficiency in Subjects with Osteoarthritis: A Clinico-Observational Study

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ABSTRACT

Background: OA most commonly affects the knee joint, knee osteoarthritis being the most common musculoskeletal disease globally reported in nearly 4% of the total world's population. Previous literature data has established a clear link between vitamin D deficiency and prevalence and increased progression of knee OA. However, few studies deny any such association.

Aims: The present study was conducted to assess the role of Vitamin D deficiency in subjects with Osteoarthritis.

Materials and Methods: The study included 200 subjects of both genders within the age range of 40-65 years with the confirmed clinical and radiographic diagnoses of osteoarthritis. The study subjects were divided into 2 groups of 100 subjects each Group I included 100 subjects newly diagnosed clinically and radiographically for osteoarthritis and Group II had age-matched controls. Under the strict aseptic and sterile conditions, intravenous blood is collected from the antecubital vein for biochemical investigations. The collected blood was allowed to clot and collected clear serum was centrifuged at 3000 rpm for 15 minutes. Vitamin D assay was done using CHEMILUMINESCENT MICROPARTICLE IMMUNOASSAY (CMIA) method. Calibration Range: 0.0 – 160.0 ng/ml (0.0- 400.0nmol/l) and the reference Range: 15.7 -60.3 ng/ml.

Results: OA Grades are found to be strongly and positively correlated with WOMAC Score (r =0.94, p-value = <0.01) which means with an increase in the WOMAC SCORE, there is an increase in the grades, the severity of the disease. However, Vitamin D level is strongly and negatively correlated with grades of osteoarthritis (r = - 0.272, p-value = 0.006). A significant association of dependent ordinal variable OA Grades with continuous variables i.e., age, Vitamin D level, and WOMAC score was seen. The association is evaluated using ordinal regression. Age and WOMAC Score were positively associated with OA Grades (p-value = 0.005* and <0.001* respectively). However, Vitamin D level is negatively associated with OA Grades (p-value = 0.02*).

Conclusion: The present study concludes that a significant association between osteoarthritis and vitamin D deficiency and also there was a significant association between grades of osteoarthritis and serum Vitamin D levels. Vitamin D level is strongly and negatively correlated with grades of osteoarthritis which implies that with the decrease in the Vitamin D level there is an increase in the grades of disease.

Keywords: joint disease, knee osteoarthritis, knee replacement, osteoarthritis, vitamin D deficiency.

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INTRODUCTION

Osteoarthritis (OA) is a degenerative and progressive disease of the joints and most commonly affects the weight-bearing synovial joints of the body, and is characterized by inflammation of the synovium, abnormal growth, and remodeling of subchondral bone, and loss and degradation of articular cartilage. OA most commonly affects the knee joint, knee osteoarthritis being the most common musculoskeletal disease globally reported in nearly 4% of the total world's population.[1] Knee OA has uniform prevalence worldwide. However, high prevalence is seen in developing nations. Also, higher prevalence is seen with increased age and the maximum reported incidence is over 50 years of age. Recently, a change in trend is noticed with the younger population being affected. The most commonly associated symptoms are joint stiffness, swelling, and/or pain posing a high burden on the healthcare sector.[2]

Kellgren-Lawrence grading system is used for assessing osteoarthritis and radiographic joint changes severity for OA symptoms including bone contour loss, osteophyte formation, joint space narrowing, and subchondral bone sclerosis.[3] OA has varying etiologies with vitamin D deficiency being the most commonly associated etiology. Vitamin D has varying functions including calcium homeostasis, bone metabolism, cell survival in immune disorders, and cellular differentiation and proliferation. With increased age, the capacity of the body to synthesize Vitamin D is reduced. Other risk factors of OA are also linked to Vitamin D levels including age, exercise, and BMI (body mass index). The possible role of vitamin D deficiency in OA has been a topic of investigation for a long.[4]

Also, the shift in disease trends towards the younger population can be attributed to VDD (vitamin D deficiency), sports activity, sedentary lifestyle, and obesity. Previous literature data has established a clear link between vitamin D deficiency and prevalence and increased progression of knee OA.[5] However, few studies deny any such association. One such study of 2019 by Vaishya et al has where the association between OA progression and vitamin D deficiency was found to be

moderate with limited evidence of vitamin D supplements causing pain relief and cartilage regeneration.[6]

Until recently, OA was considered a wear and tear disease with no possible management apart from temporary pain relief and limited joint use. Subjects with severe OA were managed with joint replacement surgeries which had satisfactory results for nearly 20 years reducing the surgical age range. Assessing other etiologic factors including Vitamin D deficiency can help manage OA non-surgically and for a longer time with acceptable results and newer methods.[7] The present study was conducted to assess the role of Vitamin D deficiency in subjects with Osteoarthritis.

MATERIALS AND METHODS

The present observational study was conducted to assess the role of Vitamin D deficiency in subjects with Osteoarthritis. The study was conducted at….from….to…after obtaining clearance from the concerned Ethical committee. The study population was comprised of the subjects visiting the Outpatient Department of the Institute. After explaining the detailed study design, informed consent was taken from all the subjects.

The study included 200 subjects of both genders within the age range of 40-65 years with the confirmed clinical and radiographic diagnoses of osteoarthritis. X-ray knee was taken in a semi-flexed and standing position for lateral and AP (anteroposterior) view respectively. Kellgren Lawrence grading scale assessed knee OA grade depending on bony deformities, osteophytes presence, and joint space narrowing, and WOMAC scale[8] (western Ontario & McMaster universities of the index) assessed physical function, stiffness, and pain on a total score of 96.

The study subjects were divided into 2 groups of 100 subjects each were Group I included 100 subjects newly diagnosed clinically and radiographically for osteoarthritis and Group II had age-matched controls with no history, clinical or radiographic symptoms of osteoarthritis ruled out for OA later who reported for checkup test, general population, paramedical staffs, and doctors. The inclusion criteria for the study were symptomatic subjects of age 40-65 years from both genders, diagnosed with knee osteoarthritis, who were symptomatic and were willing to participate in the study. The exclusion criteria were non-cooperative subjects having comorbid conditions including septicemia, other arthritis (lupus arthritis, psoriatic arthritis, or rheumatoid arthritis), any other joint pain cause including menisci or ligament injury in the knee, arthroscopy, or knee trauma, drugs affecting vitamin D metabolism, alcoholics, smokers, malignancy, autoimmune disease like mental disorder, neuropathy, or paresis, history of vitamin D supplementation within 30 days.

After final inclusion, detailed history was taken for all the subjects followed by clinical and radiographic examination. Under the strict aseptic and sterile conditions, intravenous blood is collected from the antecubital vein for biochemical investigations. The collected blood was allowed to clot and collected clear serum was centrifuged at 3000 rpm for 15 minutes. Vitamin D assay was done using CHEMILUMINESCENT MICROPARTICLE IMMUNOASSAY (CMIA) method. Calibration Range: 0.0 – 160.0 ng/ml (0.0- 400.0nmol/l) and the reference Range: 15.7 - 60.3 ng/ml.

Data obtained during the research work were statistically analyzed by using SPSS version 20. All results are expressed in mean ± standard deviation (Mean ± SD). Parameters are calculated using

chi-square and their association was evaluated, P-value < 0.05 was considered statistically significant.

RESULTS

The present observational study was conducted to assess the role of Vitamin D deficiency in subjects with Osteoarthritis. The study subjects were divided into 2 groups of 100 subjects each Group I included 100 subjects newly diagnosed clinically and radiographically for osteoarthritis and Group II had age-matched controls with no history, clinical or radiographic symptoms of osteoarthritis. The demographic characteristics of the study subjects are listed in Table 1. The mean age in controls and cases was 49.33±7.77 and 52.02 ±7.84years respectively (p=0.015). There were 52 males in controls and 64 in cases, whereas, there were 38 females in controls and 36 in cases. The mean serum Vit D (ng/ml) levels were significantly higher in control (20.11±10.69ng/ml) compared to cases (17.51±5.99ng/ml) with p=0.035. Among females and similar results were seen in females with p=0.09 and males with p=0.22 (Table 1).

On assessing the distribution and association of Vitamin D levels with different study parameters, it was seen that significantly higher subjects were in <20ng/ml levels compared to 20-30ng/ml in all the age ranges with p=0.001. More subjects from cases and controls were in <20ng/ml with 65 and 57 subjects compared to 20-30ng/ml with 34 and 29 subjects respectively, and >30ng/ml with 1 and 14 subjects respectively which was statistically significant with p=0.02. Concerning OA grades, in <20ng/ml vitamin D levels, there were 13, 27, 20, and 5 subjects respectively in OA grades 1, 2, 3, and 4, in 20-30 ng/ml vitamin D levels, there were 18, 12, 3, and 1 subject respectively, and in >30ng/ml vitamin D levels only 1 subject was with grade 3 OA. This difference was statistically significant with p=0.03 (Table 2).

Spearman correlation coefficient is used for assessing the correlation between the ordinal variable (OA grades) and continuous variables (WOMAC Score, Vitamin D level, and age). OA Grades are found to be strongly and positively correlated with WOMAC Score (r =0.94, p-value = <0.01) which means with an increase in the WOMAC SCORE, there is an increase in the grades and severity of the disease. However, Vitamin D level is strongly and negatively correlated with grades of osteoarthritis (r = - 0.272, p-value = 0.006) which implies that with the decrease in the Vitamin D level there is an increase in the grades of disease. Lastly, age has been also found to be positively correlated with OA grades which means as the age advances in the cases, severity was seen to be increased (Table 3).

A significant association of dependent ordinal variable OA Grades with continuous variables i.e., age, Vitamin D level, and WOMAC score was seen. The association is evaluated using ordinal regression. Age and WOMAC Score were positively associated with OA Grades (p-value = 0.005* and <0.001* respectively). However, Vitamin D level is negatively associated with OA Grades (p-value = 0.02*). This means that with the increase in the age and WOMAC Score severity of the disease increases and with a decrease in the Vitamin D level, the severity of the disease increases. The Chi-square value is found to be 248.321(p-value = <0.001*) and Cox and Snell R square value is 0.917 (Table 4).

DISCUSSION

This study demonstrates several important observations regarding the association between vitamin D deficiency and osteoarthritis among the age group 40-65 years. In our study we found an association between osteoarthritis patients and healthy populations with deficient serum vitamin D levels and the association is found to be significant [p = 0.02], which that shows the level of vitamin D in Osteoarthritis patients is lower compared to the control group (23.8 ± 18.8 vs. 34.5. ± 29.6 ng/ml, p = 0.01). Similar results were reported by Heidari et al[9] (2011) where authors reported a high vitamin D deficiency prevalence was significantly associated with osteoarthritis knee in < 60 years age subjects. However, radiographic evaluation was not done in the study.

In the present study, low vitamin D association was seen with worsening radiographic knee Osteoarthritis, and most of the osteoarthritis patients of grade 3 and grade 4 were deficient in vitamin D levels. This association was supported by Anari H et al[10] (2019) where mean vitamin D in controls and OA subjects were 28.1±5.3 and 26.8±6.2ng/ml, respectively (p=0.36) and a significant association was seen between knee OA staging and serum vitamin D levels (p=0.001 and Bergink et al[11] (2009) they reported that vitamin D concentration was associated with an increased risk for progression of osteoarthritis (p=0.03). On the contrary, Al-Jarallah et al[12] in 2012 reported no association between radiographic knee OA grades, functional status, and Vitamin D levels and among 99 patients, 92 (92.9%) had vitamin D deficiency.

The present study also depicted that radiographic severity had a strongly positive correlation with clinical severity and WOMAC score. These results showed that in osteoarthritis assessing the clinical parameters has similar importance as radiological findings. These findings were consistent with the results of Minafra et al[13] where clinical and radiographic findings in OA subjects had a significant association, whereas, Bija et al[14] in 2015 found no correlation between clinical and radiographic findings including pain severity in subjects with knee OA in subjects with Knee x-ray showing 35.5% of grades III and IV subjects following Kellgren and Lawrence classification.

The study results showed that Vitamin D deficiency was associated with the severity of Osteoarthritis and subjects with lower vitamin D levels had a significantly high disease severity assessed on WOMAC score in the age group 40-65 years. These results were in agreement with Laslett et al[15] where the mean WOMAC score was 3.2 and moderate vitamin D deficiency was seen in 4.2% of subjects with p=0.002 and moderate vitamin D deficiency was associated with clinical findings of Osteoarthritis in adults of age 50-80 years. Also, Muraki et al[16] in 2009 reported that occupational activities had an inverse association with knee OA grade >or=2 knee. lower vitamin D levels might be associated with increased knee pain rather than radiographic changes.

CONCLUSION

Within its limitations, the present study concludes that a significant association between osteoarthritis and vitamin D deficiency, and also there was a significant association between grades of osteoarthritis and serum Vitamin D levels. Vitamin D level is strongly and negatively correlated with grades of osteoarthritis which implies that with a decrease in the Vitamin D level there is an increase in the grades of disease. Further evaluation with a larger sample size and more assessment tools is required to establish the relationship as the role of vitamin D deficiency in the development and progression of osteoarthritis. Also with advancing age, grades of osteoarthritis and severity of

disease increase. The present study had a few limitations including a small sample size, shorter monitoring period, and geographical area biases. Hence, more longitudinal studies with a larger sample size and longer monitoring period will help reach a definitive conclusion.

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TABLES

Characteristic	Controls	Cases	p-value
Mean age (years)	49.33±7.77	52.02 ±7.84	0.015
Age Range (years) n (%)			
40 – 50	61(61)	49(49)	
51 – 60	28(28)	35(35)	
61 – 65	11(11)	16(16)	
Gender n (%)			
Males	52 (52)	64 (64)	
Females	38 (38)	36 (36)	
Mean serum Vit D (ng/ml)			
Mean	20.11±10.69	17.51±5.99	0.035
Females	20.81±10.86	17.43±6.18	0.09
Males	19.47±10.60	17.56±5.93	0.22

Table 1: Demographic and disease characteristics of the study subjects

Parameters	Vitamin D levels			p-value
	<20ng/ml	20-30ng/ml	>30ng/ml	
Age range (years)				
40 – 50	59	51		**0.001**
51 – 60	48	15		
61- 65	18	9		
Study groups				
Cases	65	34	1	**0.02**
Controls	57	29	14	
OA grades				
1	13	18	0	**0.03**
2	27	12	0	
3	20	3	1	
4	5	1	0	

Table 2: Distribution and association of Vitamin D levels with different study parameters

		OA GRADES	WOMAC SCORE	VIT D LEVEL	AGE
OA GRADES	Correlation Coefficient	1.000	.924**	-.272**	.858**
	Sig. (2-tailed)	.	0.000	0.006	0.000
WOMAC SCORE	Correlation Coefficient		1.000	-.226*	0.766**
	Sig. (2-tailed)		.	0.024	0.000
VIT D LEVEL	Correlation Coefficient			1.000	-0.201*
	Sig. (2-tailed)			.	0.045
AGE	Correlation Coefficient				1.000
	Sig. (2-tailed)				.

**. Correlation is significant at the 0.01 level (2-tailed).

*. Correlation is significant at the 0.05 level (2-tailed).

Table 3: Correlation between ordinal and continuous study variables

	Estimate	Std. Error	Df	Sig.	95% Confidence Interval	
					Lower Bound	Upper Bound
[OAGRADES = 1]	31.81	9.75	1	0.001*	12.68	50.93
[OAGRADES = 2]	46.22	12.76	1	0.0*	21.19	71.23
[OAGRADES = 3]	59.75	15.84	1	0.0*	28.70	90.80
AGE	0.53	0.19	1	0.005*	0.16	0.91
VITDLEVEL	-0.27	0.12	1	0.029*	-0.50	-0.03
WOMAC SCORE	0.48	0.12	1	0.0*	0.23	0.72

Link function: Logit.

Table 4: Association of OA grades with continuous variables