

## A Study of Vitamin D Estimation in Rheumatoid Arthritis Patients

Himanshu Patel<sup>1</sup>, Ashish Patel<sup>2</sup>, Harshal N Damor<sup>3</sup>, Dharmesh Gamit<sup>4</sup>, Punit Patel<sup>5</sup>

<sup>1</sup>Associate Professor, Department of Biochemistry, Banas Medical College and Research Institute, Palanpur, Gujarat, India

<sup>2</sup>Associate Professor, Department of Biochemistry, Banas Medical College and Research Institute, Palanpur, Gujarat, India

<sup>3</sup>Assistant Professor, Department of Orthopaedics, Smt. NHL Medical College, Ahmedabad, Gujarat, India

<sup>4</sup>Associate Professor, Department of Biochemistry, NAMO Medical Education and Research Institute, Silvassa, Dadra and Nagar Haveli, India

<sup>5</sup>Assistant Professor, Department of Community Medicine, Banas Medical College and Research Institute, Palanpur, Gujarat, India.

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Corresponding author: Dr. Dharmesh Gamit

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### Abstract

**Background:** Vitamin D interacts with the immune system. Vitamin D deficiency is related with increase susceptibility and severity of autoimmune diseases like type 1 diabetes mellitus, multiple sclerosis, inflammatory bowel disease, systemic lupus erythematosus (SLE) and rheumatoid arthritis.

**Objectives:** 1) To study the role of vitamin D deficiency in rheumatoid arthritis patient 2) To study the demographic profile in in rheumatoid arthritis patients

**Material & Method:** In the present case control study, vitamin D was estimated in 70 patients of Rheumatoid arthritis and 70 healthy controls.

**Result:** Mean Serum Vitamin D level was 21.78 ng/ml in rheumatoid arthritis patient's case group, while 25.54 ng/ml in control group. Although Vitamin D deficiency or insufficiency was common in RA group of patients, the difference was not statistically significant ( $p > 0.05$ ) Prevalence of RA is higher among females as compared to males. Mean age in case group was  $43.86 \pm 12.017$  years, while  $40.57 \pm 13.53$  years in control group and maximum disease prevalence is between third and fourth decades.

**Conclusion:** In this study we found that in RA patients, vitamin D deficiency is quite common, but not more common than in age and sex matched controls representative of the general population. Given the evidence regarding the role of vitamin D in overall health, clinicians should consider screening of RA patients to identify and address suboptimal vitamin D levels.

**Keywords:** Vitamin D, Rheumatoid Arthritis.

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## Introduction

Vitamin D is one of the important vitamins which are fat soluble. Vitamin D is mainly produced de novo by exposure of skin to UV rays. Approximately 1 billion persons in the world are having deficient vitamin D State.[1,2] In India also, vitamin D deficiency is very common (50-90%) in all ages and both sexes.[3-5] Though vitamin D is can be acquired from diet, it supplies 20% of recommended dairy requirements of vitamin D. Main source of vitamin D from diet are cod liver oil, salmon & sword fish, canned tuna, cooked beef, yogurt, orange juice, eggs, mushrooms, milk and milk products.[6]

The active form of vitamin D i.e. calcitriol (1,25-dihydroxy Cholecalciferol) is produced from 7-dehydrocholesterol, present in epidermis layer of skin.[7] Now we will review the importance of Vitamin D in immunopathogenesis of various autoimmune disorders. It is well established that Vitamin D interacts with immune system and helps in regulation and differentiation of the various cells of the immune system either directly or indirectly. Various studies have concluded that Severity and increased susceptibility of autoimmune disorders is related to Vitamin D deficiency. [1,8,9]

Vitamin D receptors can be detected on various cells of immune system e.g. dendritic cells, circulating monocytes; activated T cells.[10] Calcitriol inhibits the differentiation of monocytes into dendritic cells.[11-14] Vitamin D stimulates the differentiation of monocytes to macrophages and modulates its responses, and prevents release of inflammatory cytokines and chemokines.[15-18] Many of the autoimmune disorders like rheumatoid arthritis, inflammatory bowel disease, multiple sclerosis, type 1 diabetes mellitus, systemic lupus erythematosus (SLE) are associated with vitamin D deficiency.[1,3]

Rheumatoid arthritis (RA) is a chronic multisystem disorder of unknown cause.

Hallmark features of rheumatoid arthritis is inflammatory synovitis, involving mostly peripheral joints.[19] Prevalence of RA is 0.5-1% worldwide and it increases to 5% in women above the age of 70 years. Women are affected 3 times more than men[19]. During 4<sup>th</sup> and 5<sup>th</sup> decade of life, onset of rheumatoid arthritis (RA) is most common. The prevalence of Rheumatoid arthritis in India is around 0.7%.[20] Patients of RA often present with early morning joint stiffness lasting more than 1 hour and easing with physical activity. The earliest involved joints are typically the small joints of the hands and feet.[19]

T & B lymphocytes, Antigen presenting cells, macrophages and inflammatory cytokines are involved in pathogenesis of the rheumatoid arthritis. The role of the T & B lymphocytes in the pathogenesis of RA has been further established by the therapeutic effectiveness of methods affecting T & B lymphocytes.[21]

Vitamin D suppresses Th1 cells (type 1 T helper cells), which are part of acquired immunity.[22] In patients of Early RA, disease activity, severity and functional disability is inversely related to serum vitamin D. [23] Due to possible role of vitamin D in development of RA and its severity, we conducted this study to find out Vitamin D levels in patients of RA in comparison to normal subjects.

## Material and Method

In this observational case control study, attempt was made to determine role of vitamin D in the development of rheumatoid arthritis. In this study, 70 patients of rheumatoid arthritis diagnosed according to revised criteria of the American college of Rheumatology (ACR) and 70 healthy controls matched in age and sex were included. Vitamin D level was measured by immunochemistry method.

**Inclusion criteria (cases):** 70 patients of Rheumatoid Arthritis diagnosed according

to 2010 revised criteria of the American college of rheumatology[19] were included in the study.

#### Exclusion criteria (cases):

- Patients not consenting to enroll in the study
- Those who do not meet the diagnostic and modified classification standard according to ACR 2010
- Patients less than 18 years of age.
- Patients of RA having chronic renal failure, coronary artery disease, systemic lupus erythematosus, Sjogren syndrome or any other connective diseases.
- Patients on enzyme inducer drug or patients who already received Vitamin D supplements and anti-convulsive therapy during a 6-month period prior to the study.
- Participants with Body mass index (BMI)  $\geq 30\text{kg/m}^2$ . (Regarding the hypothesis which states that 25(OH)D is fat soluble and lower 25(OH)D in overweight individuals may simply be representative of a larger volume of distribution of this vitamin)

#### Inclusion criteria (controls):

70 healthy controls were age and sex matched included in the study.

#### Exclusion criteria (controls):

- Those not consenting to enroll in the study.
- Those who have any type of co-morbidity.

#### Statistical Analysis:

Statistical analysis was performed using the SPSS Statistical Software Package. All values were expressed as percentage, mean  $\pm$  standard deviation (SD). The values were evaluated using Student t-test and Chi Square test was used for pair wise comparison and distribution significance.

#### Results

Table 1 shows the age and sex wise distribution of study participants which include both cases of RA and controls. Maximum number of participants were in age group between 30-39 years. Females outnumbered in each age group. CHI-SQUARE Test (2.476 with 4 degrees of freedom) used, and results shows that there was comparable distribution of male and females in different age group in all study participants.

**Table 1: Age and sex wise distribution of study participants (cases and controls)**

Age group (years)		Sex		Total
		Female	Male	
20-29	No.	15	8	23
	%	14.60%	21.60%	16.40%
30-39	No.	33	10	43
	%	32.00%	27.00%	30.70%
40-49	No.	17	8	25
	%	16.50%	21.60%	17.90%
50-59	No.	29	7	36
	%	28.20%	18.90%	25.70%
More than 59	No.	9	4	13
	%	8.70%	10.80%	9.30%
Total	No.	103	37	140
	%	100.00%	100.00%	100.00%
Chi, df, p value		2.476	4	0.649

Table No.2 shows that 84.28% of the cases were either Vitamin D deficient or

insufficient in their serum Vitamin D levels against the 68.57% of the control

subjects. This difference was not found to be statistically significant when Chi square

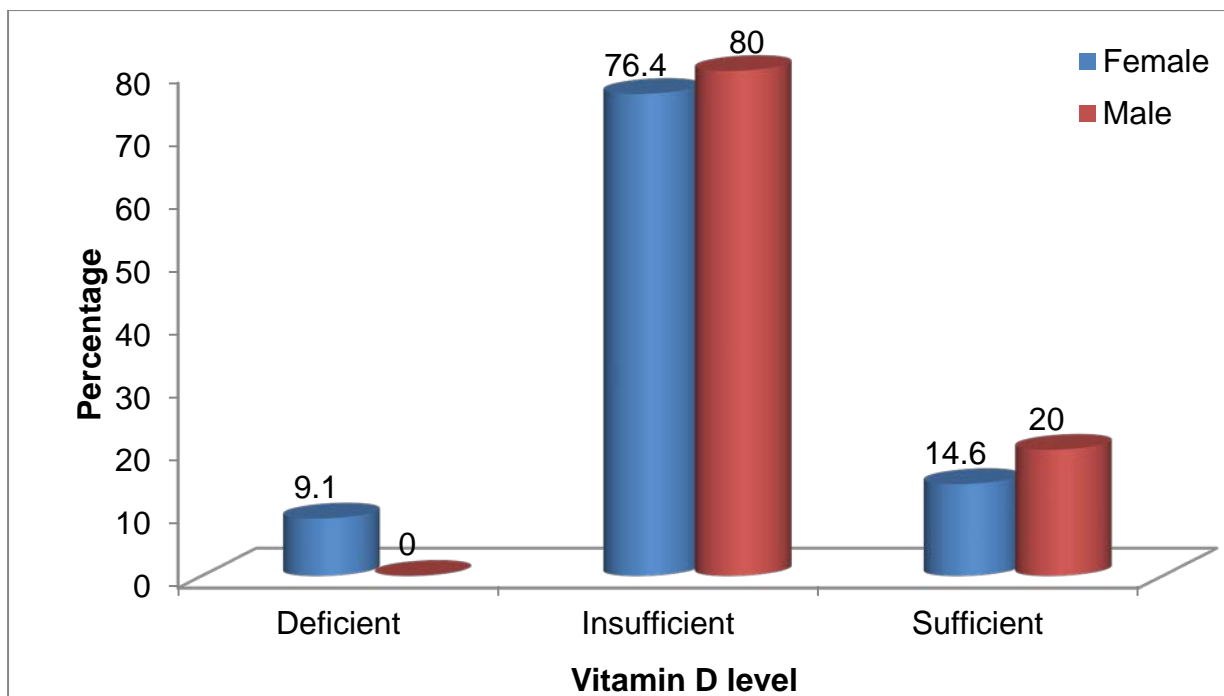
test was used (p value >0.05)

**Table 2: Distribution of Vitamin D among cases and controls**

Vitamin D	Group				Total	
	Case		Control			
	No.	%	No.	%	No.	%
<b>1-Deficient</b>	5	7.14%	5	7.14%	10	7.14%
<b>2-Insufficient</b>	54	77.14%	43	61.43%	97	69.29%
<b>3-Sufficient</b>	11	15.71%	22	31.43%	33	23.57%
<b>Total</b>	70	100.00%	70	100.00%	140	100.00%
	CHI	4.94	df	2	p	0.086

Figure 1 shows that 91% female and 100% male were either Vitamin D deficient or insufficient in their serum. This difference

was not found to be statistically significant when Chi square test was used (p value >0.05).



**Figure 1: Distribution of Vitamin D level among Male and Female (cases)**

**Discussion**

In our study, mean age of the patients of Rheumatoid arthritis (RA) was 43.86 years. Maximum 31.4% of cases were in 30–39-year age group. Mean age in controls was 40.57 years. Maximum 30% of controls were in 30–39-year age group. Student unpaired t test was used which showed p value 0.546 which is statistically not significant which means cases and control were age matched. Similar results

were observed in the studies done by Turhanoglu et al [24], Sharma R et al.[25] and Sahebari et al.[26]

In our study, among RA group of patients, 78.57% cases were females and only 21.43% cases were males. Among control subjects, 31.43% were males and 68.57% were females. Chi square test (1.8 with 1 degree of freedom) was used, and results showed that cases and controls were sex matched (p>0.05). Our results were similar

with the studies done by Silman et al.[27] and Rossini et al.[28]

In our study, mean serum Vitamin D level in cases of RA was 21.78 ng/ml while mean serum Vitamin D level in controls was 25.54 ng/ml. This difference was not found to be statistically significant when Chi square test was used ( $p > 0.05$ ). Even though combined Vitamin D deficiency and insufficiency was present in higher percentage of rheumatoid arthritis patients in our study, yet it was statistically not significant when compared to controls. Baykal et al.[29] and Aisha Yassin et al.[30] showed that there was a statistically significant difference of vitamin D deficiency in patients of rheumatoid arthritis as compared to healthy controls. Similarly Sharma R et al.[25] reported vitamin D deficiency was 90% in patients of rheumatoid arthritis as against 70% in control subjects and this difference was found to be statistically significant. Whereas Sahebari M et al.[26], Attar SM et al.[31] and Rossini et al.[28] observed no statistically difference of Vitamin D deficiency in patients of rheumatoid arthritis as compared to healthy control subjects.

In our study, there was no statistically significant correlation was found between 25(OH) vitamin D level among male and female in RA group of patients ( $p > 0.05$ ). Similar results were also reported by Sharma R et al.[25], Sahebari et al.[26] and Yassin et al.[30]

### Conclusion

In this study we found that in RA patients, vitamin D deficiency is quite common, but not more common than in age and sex matched controls representative of the general population. Given the evidence regarding the role of vitamin D in overall health, clinicians should consider screening of RA patients to identify and address suboptimal vitamin D levels. Further, appropriate training should be given to the patients to ensure the intake of

the recommended amount of vitamin D per day through diet or supplement. Further studies should be performed on the efficacy of treatment of rheumatoid arthritis patients with vitamin D alone or with other anti-rheumatic drugs

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