



**Research Article**

**TO STUDY VITAMIN D LEVEL IN RHEUMATOID ARTHRITIS PATIENTS AND ITS CORRELATION WITH DISEASE ACTIVITY**

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**ABSTRACT**

**Objective:** To study Vitamin D level in Rheumatoid Arthritis Patients and its correlation with disease activity.

**Material and Methods:** Our study was observational study which was performed on patients attending as outpatients and admitted as inpatients in General Medicine and allied departments of Sri Aurobindo Medical College and Post Graduate Institute, Indore, Madhya Pradesh. A total of 100 pre-diagnosed or newly diagnosed cases of Rheumatoid Arthritis (based on ACR/EULAR 2010 criteria) were included in the study from December 2018 to May 2020. Vitamin D level of patients were measured and DAS 28 was calculated.

**Results:** Mean Vitamin D level in our study was  $19.07 \pm 6.75$  ng/ml. 95% patients had Vitamin D deficiency out of which 6% patients had severe vitamin D deficiency, 54% were vitamin D deficient, 35% were vitamin D insufficient and 5% had normal vitamin D level. Mean Vitamin D was  $15.31 \pm 4.65$  ng/ml,  $20.27 \pm 6.19$  ng/ml,  $28.28 \pm 3.50$  ng/ml and  $29.97 \pm 1.42$  ng/ml in high disease activity, moderate disease activity, low disease activity and remission group respectively.

**Conclusion:** We observed that, Vitamin D deficiency was seen in RA patients and Vitamin D level is significantly low in patients of RA. The lower the Vitamin D, the higher the disease activity score. There was significant negative correlation between Vitamin D and disease activity score

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**INTRODUCTION**

Vitamin D is an essential nutrient acquired from the diet and through solar ultraviolet B (UVB) radiation-catalysed synthesis in the skin. Vitamin D regulates calcium balance and bone mineralization, and also does numerous other functions such as modulating immune function, and regulating cellular proliferation, differentiation, and apoptosis. Rheumatoid arthritis (RA) is an autoimmune systemic disease which is chronic in nature and characterized predominantly by synovial inflammation, leading to joint destruction. The percentage of people having RA all over the globe is 0.3-1% according to WHO (1) and the disease leads to reduced life expectancy.

The synovium forms inflammatory tissue, known as pannus. Pannus is formed by the proliferation of fibroblast-like synovial cells and synoviocytes, angiogenesis, infiltration of macrophages and lymphocytes and migration of polymorphonuclear cells to the synovial tissue (2). The immune modulatory characteristics of Vitamin D may have therapeutic implications in RA patients (3). The Vitamin D receptor (VDR) was found on antigen-presenting cells, dendritic cells and lymphocyte.

Also, found at sites of cartilage erosion in RA patients [4,5]. Calcitriol (1,25-dihydroxyvitamin D) is an active metabolite of Vitamin D which maintains balance between Th1, Th17 and Th2 cells [6] by inhibiting the synthesis of interleukins 1, 6, 12 and TNF- $\alpha$  by the macrophages, suppresses the interleukin 2 secretion by Th1 lymphocytes and decreases antigen-presenting activity of macrophages. Calcitriol also inhibits plasma-cell differentiation and B-cell proliferation (7).

**AIM AND OBJECTIVE**

To study Vitamin D level in Rheumatoid Arthritis Patients and its correlation with disease activity

**MATERIAL AND METHODS**

The study was performed on 100 patients attending as outpatients and admitted as inpatients in General Medicine and allied departments of Sri Aurobindo Medical College and Post Graduate Institute, Indore, Madhya Pradesh. It was an observational study.

**Inclusion criteria:** Patients of both sex of age 18 to 90 years fulfilling the American College of Rheumatology (ACR) and European League Against Rheumatism (EULAR) Criteria 2010 for diagnosis of Rheumatoid Arthritis i.e. score >6 fulfilling the requirement of definite RA.

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**Exclusion criteria:** Patients not willing for the study, Patient with malnutrition, hepatic dysfunction renal dysfunction, hyperthyroidism diabetes mellitus, Patients on Vitamin D supplementation in the past 6 months or Patients on drugs that can affect bone and Vitamin D metabolism. Venous blood samples were obtained for Random Blood Sugar, CBC, SGPT, Creatinine, ESR, Rheumatoid factor and Vitamin D. Activity of disease measured by DAS-28 (disease activity score) .The DAS28 (Disease Activity Score 28) is a system developed and validated by the EULAR (European League Against Rheumatism) to measure the progress and improvement of Rheumatoid arthritis.

**Table 1** DAS 28 activity scoring

≤ 2.6	Remission
>2.6 but ≤ 3.2	Low disease activity
> 3.2 to 5.1	Moderate disease activity
≥ 5.1	Severe disease activity

**Table 2** Vitamin D Level

<10ng/ml	Severe Vitamin D deficiency
<20ng/ml	Vitamin D deficiency
20-<30ng/ml	Vitamin D insufficiency
30-100ng/ml	Vitamin D sufficiency

**RESULTS**

An observational study to study Vitamin D level in Rheumatoid Arthritis Patients and its correlation with disease activity.

**Table 3** Important clinical and blood parameters of the study population

	N	Mean	Std. Deviation
Age(years)	100	47.67	11.446
TJC	100	14.52	6.093
SJC	100	5.15	4.384
DAS28	100	4.7004	0.91238
ESR(mm/hr)	100	20.36	8.809
VITAMIN D(ng/ml)	100	19.0708	6.751

The study population included total of 100 patients in which mean age of patient was 47.67±11.44years. Mean total joint count 14.52±6.09 and mean swollen joint count was 5.15±4.38. Mean DAS28 was 4.70±0.91. Mean ESR was 20.36±8.80mm/hr. Mean Vitamin D level was 19.07±6.75ng/ml.

**Table 4** Gender distribution in study population

	Frequency	Percent
Male	17	17.0
Sex Female	83	83.0
Total	100	100.0

In our study population 83(83%) patients were females and 17 (17%) were males. There was female preponderance.

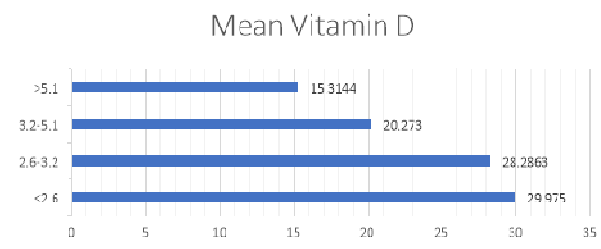
**Table 5** Distribution of DAS 28 in study population

	Frequency	Percent
<2.6(Remission)	4	4.0
2.6-3.2(Low)	8	8.0
DS28 3.2-5.1(Moderate)	43	43.0
>5.1(High)	45	45.0
Total	100	100.0

In the study population, there were maximum number of patients 45% in high disease activity group ,43%in moderate disease activity group,8% patients in low disease activity group and only 4% patients were in remission group.

**Table 6** Correlation of DAS 28 with vitamin d level in RA patients

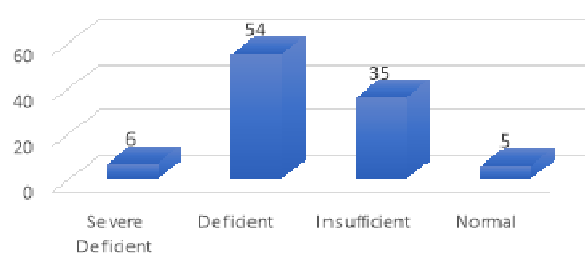
DAS28	N	Mean Vitamin D (ng/ml)	Std. Deviation	P value
<2.6(Remission)	4	29.9750	1.42393	<0.001
2.6-3.2(Low)	8	28.2863	3.50597	
3.2-5.1(Moderate)	43	20.2730	6.19686	
>5.1(High)	45	15.3144	4.65932	
Total	100	19.0708	6.75120	



**Graph 1** Bar Diagram showing correlation of DAS28 with Vitamin D in RA patients

Mean Vitamin D was 15.31± 4.65ng/ml,20.27± 6.19ng/ml, 28.28± 3.50ng/ml,29.97± 1.42ng/ml in high disease activity, moderate disease activity, low disease activity and remission group respectively. There was statistically significant correlation between Vitamin D and DAS28 in RA patients. ANOVA test was applied. p value was <0.001.

**Distribution of patients according to Vitamin D level**



**Graph 2** Bar Diagram showing Distribution of RA patients according to Vitamin D level

**Table 7** Distribution of RA patients according to vitamin d level

Vitamin D group (ng/ml)	Frequency	Percent
Severe Deficient (<10ng/ml)	6	6.0
Deficient (<20ng/ml)	54	54.0
Insufficient (20-<30ng/ml)	35	35.0
Normal (30-100ng/ml)	5	5.0
Total	100	100.0

Out of 100 RA patients in our study,95% patients had Vitamin D deficiency out of which 6% patients had severe Vitamin D deficiency ,54% were Vitamin D deficient ,35% were vitamin D insufficient and 5% had normal vitamin D level.

**Table 8** Correlation between vitamin d and various variables of RA patients

Vitamin D	Correlation coefficient	P value
Age	-0.273**	0.006
TJC	-0.583**	<0.001
SJC	-0.449**	<0.001
DAS SCORE	-0.632**	<0.001
ESR	-0.248*	0.013

Correlation is significant at the 0.05 level. Karl Pearson correlation coefficient Calculated. There was statistically significant correlation between Vitamin D levels and age ( $p=0.006$ ), tender joint count ( $p<0.001$ ), swollen joint count ( $p<0.001$ ), DAS Score ( $p<0.001$ ) and ESR ( $p=0.013$ ).

## DISCUSSION

In our study, we included a total of 100 pre-diagnosed and new cases of Rheumatoid Arthritis attending as outpatients or admitted as inpatients in the department of general medicine and allied at Sri Aurobindo Medical College and Post Graduate Institute, Indore, Madhya Pradesh during the period of study from December 2018 to May 2020. The purpose of our study was to study Vitamin D level in Rheumatoid Arthritis patients and its correlation with disease activity.

In our study, the mean age observed was  $47.67 \pm 11.44$  years. The mean age in our study was similar to the study done by, Meena N *et al* 2018(8), where mean age of the study group was  $44.92 \pm 13.06$  years. The age was also similar to the study done by, Rai T *et al* 2017(9), in which mean age in years of rheumatoid arthritis patients was  $44.35 \pm 10.05$  years. There were 83 females (83%) and 17 males (17%) in our study, which coincides with the study done by, Meena N *et al* 2018(8) and Rai T *et al* 2017(9). Meena N *et al* 2018(8) in their study, reported 43(86%) females and 7(14%) males; out of 50 RA patients taken. Rai T *et al* 2017(9) in their study, reported 34(85%) females and 6(15%) males; out of 40 RA patients taken.

In the study population, there were maximum number of patients 45% in high disease activity group, 43% in moderate disease activity group, 8% patients in low disease activity group and only 4% patients were in remission group. Mean DAS28 in our study group was  $4.700.9 \pm 1$ .

The distribution of DAS28 in our study groups were partly similar to study done by Meena N *et al* 2018(8). In their study they reported, out of 50 RA patients maximum number of patients 44% in high disease activity group, 38% in moderate disease activity group, 6% patients in low disease activity group and 12% patients were in remission group. In our study, Mean Vitamin D level was  $19.07 \pm 6.75$  ng/ml. The mean Vitamin D in our study was similar to the study done by, Meena N *et al* 2018(8), where mean Vitamin D of the study group was  $21.05 \pm 10.02$  ng/ml. In the study done by, Rai T *et al* 2017(9), Mean Vitamin D level of 40 RA patients was  $14.14 \pm 10.26$  ng/ml.

It was also comparable to study done by, Sharma R *et al* 2014(10), Vojinovic J *et al* 2017(11), Kostoglou *et al* 2012(12), Niharika Agrawal *et al* 2020(13), where mean vitamin D level of RA patients were  $17.20 \pm 10.74$  ng/ml,  $17.62 \pm 9.76$  ng/ml,  $15.26 \pm 1.07$  ng/ml,  $18.93$  ng/ml  $\pm 6.64$  ng/ml respectively.

In our study, RA patients were divided into four groups according to Disease Activity Score.

Mean Vitamin D was  $15.31 \pm 4.65$  ng/ml,  $20.27 \pm 6.19$  ng/ml,  $28.28 \pm 3.50$  ng/ml, was  $29.97 \pm 1.42$  ng/ml in high disease activity, moderate disease activity, low disease activity and remission group respectively. There was statistically significant correlation between Vitamin D and DAS28 in RA patients. P value was  $<0.001$ . Similar findings were seen in the study done by Meena N *et al* 2018(8) in which Mean Vitamin

D was  $14.21 \pm 6.97$  ng/ml,  $22.47 \pm 6.18$  ng/ml,  $33.80 \pm 4.1$  ng/ml,  $35.28 \pm 9.0$  ng/ml in high disease activity, moderate disease activity, low disease activity and remission group respectively.

The partly similar findings were seen in study done by Sharma R *et al* 2014(66), in which Mean Vitamin D was  $8.79 \pm 5.17$  ng/ml,  $21.35 \pm 10.01$  ng/ml,  $24.70 \pm 9.68$  ng/ml in high disease activity, moderate disease activity and low disease activity group respectively.

ANNOVA test was applied and it was found that there was statistically significant negative correlation of Vitamin D level and severity of disease as assessed by DAS28.

Patients with high disease activity had significantly lower vitamin D levels in comparison to patients with low or moderate disease activity. p value was  $<0.001$ .

In our study, patients were divided into four groups according to Vitamin D levels. Out of 100 RA patients in our study, 95% patients had Vitamin D deficiency out of which 6% patients had severe vitamin D deficiency, 54% were vitamin D deficient, 35% were vitamin D insufficient and 5% had normal vitamin D level.

In the study done by, Vojinovic J *et al* 2017(11), 25% patients had severe Vitamin D deficiency, 66% were Vitamin D deficient, 27% were Vitamin D insufficient and 6% had normal Vitamin D level. Gorkhan Akdag *et al* (14) 2020, in their study, reported out of 91 patients of RA 89% had Vitamin D deficiency. 33(33%) patients with RA had Vitamin D deficiency, 56% (51) had insufficiency, and 11% (10) had optimal level. In the study done by, Niharika Agrawal *et al* 2020(13), 30 RA patients were taken. All 30 patients had hypo vitaminosis D, out of which 50% were deficient and 50% were insufficient.

## CONCLUSION

We observed that, Vitamin D deficiency was seen in RA patients and Vitamin D level is significantly low in patients of RA. The lower the Vitamin D, the higher the disease activity score. The correlation was significant between Vitamin D and DAS28. Similar results were seen in other studies also, reflecting that, Vitamin D is an important factor to control disease activity and has a negative correlation with DAS28. Hence, Vitamin D level should be checked in all patients of RA and there should be prescription of Vitamin D along with DMARDs. Follow up study may be required to study therapeutic implication of Vitamin D in Disease activity of RA patients.

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