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Assessment of vitamin D status in rheumatoid arthritis patients

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Abstract---Background: Vitamin D is a secosteroid hormone involved in bone and calcium metabolism. It is involved in the regulation of calcium homeostasis, as it regulates calcium absorption from the gastrointestinal system. The present study was conducted to assess vitamin D status in RA patients. Materials & Methods: 112 Rheumatoid arthritis patients of both genders were put in group I. Healthy subjects were also enrolled and put in group II. Disease activity score of RA patients was calculated. Disease severity was assessed according to the value of DAS28 score as follows- Remission: DAS28 $\leq$ 2.6 Low disease activity: 2.6 5.1. 25 (OH)-Vitamin D Xpress ELISA Kit was used for the quantitative measurement of Vitamin D3 {25 (OH)-D3} in serum. Results: Group I had 62 males and 50 females and group II had 70 males and 42 females. Disease activity was remission, low, moderate and high with mean serum calcium level (mg/dl) as 8.92, 8.34, 8.22 and 8.01 and vitamin D (mg/dl) as 35.6, 31.4, 22.3 and 14.8 respectively. The difference was significant ($P < 0.05$). The mean serum vitamin D level found to be 21.5 ng/ml in group I and 34.8 ng/ml in group II. The difference was significant ($P < 0.05$). Conclusion: There was low vitamin D level in Rheumatoid arthritis patients as compared to healthy subject.

Keywords---Calcium, Rheumatoid arthritis, Vitamin D

Introduction

Vitamin D is a secosteroid hormone involved in bone and calcium metabolism. It is involved in the regulation of calcium homeostasis, as it regulates calcium absorption from the gastrointestinal system.¹ The hormone is synthesized in the skin by the action of ultraviolet irradiation. Vitamin D promotes absorption of calcium in the gut and maintains adequate serum calcium and phosphate concentrations to enable normal mineralization of bone and to prevent hypocalcemic tetany.² It is also needed for bone growth and bone remodeling by osteoblasts and osteoclasts. In addition, Vitamin D has other roles in the body, including modulation of cell growth, neuromuscular and immune function, and reduction of inflammation. Many genes encoding proteins that regulate cell proliferation, differentiation, and apoptosis are modulated in part by Vitamin D.³

Rheumatoid arthritis (RA) is an autoimmune disease of unknown aetiology. Both T and B lymphocytes are involved in the pathogenesis of the disease.⁴ The role of T lymphocytes as well as that of B lymphocytes in the pathogenesis of RA has been further proved by the therapeutic efficacy of methods affecting both T and B lymphocytes, namely the biological agents. The immunomodulatory activities of Vitamin D might be particularly efficient in RA patients and support a therapeutic role of Vitamin D in these patients. The VDRs have been demonstrated in macrophages, chondrocytes, and synoviocytes in rheumatoid synovium and at sites of cartilage erosion in RA patients.⁵ The present study was conducted to assess vitamin D status in RA patients.

Materials & Methods

The present study comprised of 112 Rheumatoid arthritis patients of both genders. The consent was obtained from all patients.

Data such as name, age, gender etc. was recorded. RA patients were put in group I. Healthy subjects were also enrolled and put in group II. Disease activity score of RA patients was calculated as per the guidelines of American College of Rheumatology, which indicated the disease severity, that is, low-, moderate-, and high-disease activity. Calculation of DAS28 score was done by following measures 1. Counting the number of swollen joints (out of 28) 2. Counting the number of tender joints (out of 28) 3. Taking blood to measure the erythrocyte sedimentation rate (ESR). Asking the patient to make a "global assessment of health". These results were incorporated into a mathematical formula to produce the overall disease activity score: $DAS28 = 0.56\sqrt{(28TJC)} + 0.28\sqrt{(28SJC)} + 0.70 \ln(ESR) + 0.014VAS$. (Here TJC = Tender joint count, SJC = Swollen joint count, Ln = log, VAS = Visual analog scale) Disease severity was assessed according to the value of DAS28 score as follows- Remission: $DAS28 \leq 2.6$ Low disease activity: 2.6 5.1. 25 (OH)-Vitamin D Xpress ELISA Kit was used for the quantitative measurement of Vitamin D3 {25 (OH)-D3} in serum. The estimation process was done in Biotek ELX-800 autoanalyzer. The assay utilized a competitive ELISA technique. Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

Results

Table I Distribution of patients

Groups	Group I	Group II
Status	RA patients	Healthy
M:F	62:50	70:42

Table I shows that group I had 62 males and 50 females and group II had 70 males and 42 females.

Table II Mean serum calcium and vitamin D levels in rheumatoid arthritis patients according to their disease activity

Disease activity	Number	Serum calcium	Serum vit D	P value
Remission	20	8.92	35.6	0.02
Low	19	8.34	31.4	
Moderate	30	8.22	22.3	
High	43	8.01	14.8	

Table II, graph I shows that disease activity was remission, low, moderate and high with mean serum calcium level (mg/dl) as 8.92, 8.34, 8.22 and 8.01 and vitamin D (mg/dl) as 35.6, 31.4, 22.3 and 14.8 respectively. The difference was significant ($P < 0.05$).

Graph I Mean serum calcium and vitamin D levels in rheumatoid arthritis patients according to their disease activity

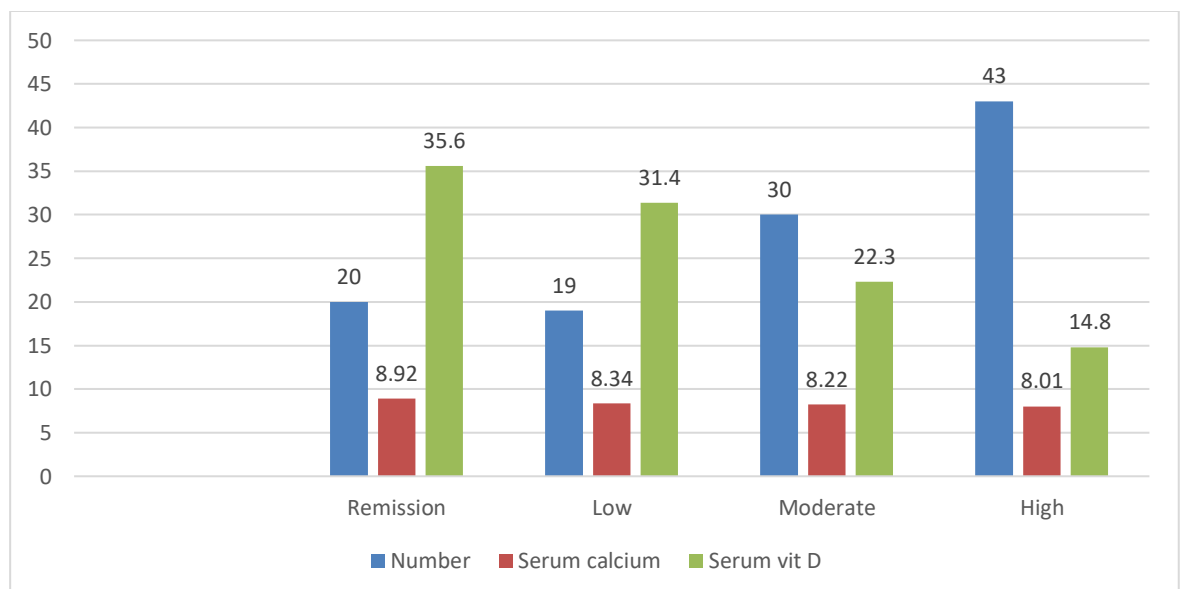
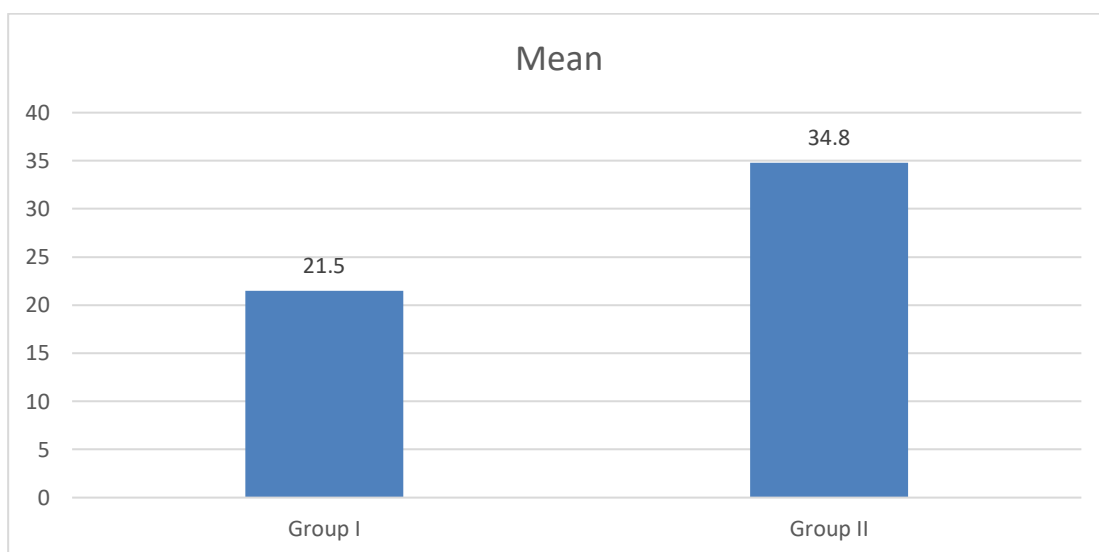


Table III Serum Vitamin D levels in both groups

Groups	Mean	P value
Group I	21.5	0.01
Group II	34.8	

Table III, graph II shows that mean serum vitamin D level found to be 21.5 ng/ml in group I and 34.8 ng/ml in group II. The difference was significant ($P < 0.05$).

Graph II Serum Vitamin D levels in both groups

Discussion

Vitamin D has been found to have immunomodulatory actions. Vitamin D deficiency has been shown to be correlated with the appearance of autoimmune diseases, such as diabetes mellitus type 1 and multiple sclerosis.⁶ Vitamin D, as a prohormone, is considered to be able to play potential immune-suppressive roles and to exert an endocrine action on the immune system cells, generating anti-inflammatory and immunoregulatory effects.⁷ The rationale behind relating vitamin D and RA is based on two facts. The first one is that there is evidence indicating that patients with RA have low levels of vitamin D. The second one is that the presence of vitamin D and VDR in macrophages, chondrocytes, and synovial cells in the joints of those patients has also been demonstrated.⁸

In fact, RA is an autoimmune disorder with a very complex physiopathology. The first triggering event could be the activation of antigen-dependent T cells leading to an essentially Th1 type immune response.⁹ The subsequent effects are multiple, including the activation and the proliferation of endothelial and synovial cells, recruitment and activation of proinflammatory cells, secretion of cytokines and proteases by macrophages and fibroblast-like synovial cells, and production of autoantibodies.^{10,11} The present study was conducted to assess vitamin D status in RA patients.

In present study, group I had 62 males and 50 females and group II had 70 males and 42 females. Meena et al¹² determined the relationship between the severity of RA and serum levels of Vitamin D. This prospective, comparative study was conducted on 100 participants, 50 cases of RA and 50 healthy controls, all in the age group of 18–75 years. Serum Vitamin D levels were measured and compared in cases and controls. Vitamin D levels in RA patients were also assessed in different stages of disease activity to assess the correlation between the two. Eighty-four percent patients of RA were Vitamin D deficient versus only 34% of controls. The serum Vitamin D levels were also significantly lower in the RA patients (mean value of 21.05 ± 10.02 ng/ml), as compared to the controls (mean value of 32.87 ± 14.16 ng/ml). There was a significant inverse correlation between serum Vitamin D levels and RA disease activity. The mean serum Vitamin D levels were 35.28 ± 9.0 ng/ml, 33.80 ± 4.1 ng/ml, 22.47 ± 6.18 ng/ml, and 14.21 ± 6.97 ng/ml in the remission, low disease activity, moderate disease activity, and high disease activity groups, respectively.

We found that disease activity was remission, low, moderate and high with mean serum calcium level (mg/dl) as 8.92, 8.34, 8.22 and 8.01 and vitamin D (mg/dl) as 35.6, 31.4, 22.3 and 14.8 respectively. Kostoglou-Athanassiou et al¹³ evaluated vitamin D status in patients with RA and to assess the relationship between vitamin D levels and disease activity. Methods: In a cohort of 44 patients with RA, 25-hydroxyvitamin D3 [25(OH)D3] levels, parathyroid hormone levels, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were measured. Disease activity was evaluated by calculating the 28-joint Disease Activity Score (DAS28). A control group (n = 44), matched for age and sex, was evaluated as well. In the cohort of 44 patients with RA 25(OH)D3 levels were found to be low compared with the control group, 25(OH)D3 being 15.26 ± 1.07 ng/ml [mean $\pm$ standard error of the mean (SEM)] and 25.8 ± 1.6 ng/ml in the patient and control group respectively. Parathyroid hormone levels were 71.08 ± 7.02 pg/ml (mean $\pm$ SEM) (normal values 10.0–65.0 pg/ml), CRP 7.6 ± 1.57 mg/litre (mean $\pm$ SEM) (normal values < 3 mg/litre) and ESR was 38.0 ± 4.6 mm/h (mean $\pm$ SEM) in the group of patients with RA. Levels of 25(OH)D3 were found to be negatively correlated to the DAS28, the correlation coefficient being -0.084 . Levels of 25(OH)D3 were also found to be negatively correlated to CRP and ESR, the correlation coefficient being -0.115 and -0.18 , respectively.

We found that mean serum vitamin D level found to be 21.5 ng/ml in group I and 34.8 ng/ml in group II. Hajjaj Hassssouni et al¹⁴ evaluated vitamin D status in 1413 RA patients of COMORA study from 15 countries and to analyze relationship between patients' RA characteristics and low levels of vitamin D. All demographic, clinical, and biological data and RA comorbidities were completed. The results showed that the average of vitamin D serum dosage was $27.3 \text{ ng/mL} \pm 15.1$ 0.1–151. Status of vitamin D was insufficient in 54.6% and deficient in 8.5% of patients. 43% of RA patients were supplemented with vitamin D and absence of supplementation on vitamin D was related to higher prevalence of vitamin D deficiency. Absence of supplementation on vitamin D was related to higher prevalence of vitamin D deficiency. Low levels of vitamin D were associated with patients characteristics (age, BMI, and educational level), RA (disease activity and corticosteroid dosage), and comorbidities (lung disease and osteoporosis therapy).

Conclusion

Authors found that there was low vitamin D level in Rheumatoid arthritis patients as compared to healthy subject.

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