

ORIGINAL RESEARCH

Assessment of Vitamin D in Rheumatoid Arthritis and Its Correlation with Disease Activity

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ABSTRACT

Background: To assess vitamin D in rheumatoid arthritis and its correlation with disease activity. **Material and methods:** A prospective, comparative study with one hundred individuals, fifty RA patients and fifty healthy controls, all in the eighteen to seventy-five years of age range, was done. Serum Vitamin D levels had been assessed in patients as well as controls and compared. In order to determine whether there is a link between the two, vitamin D levels in RA patients were also measured at various phases of disease activity. **Results:** The mean serum calcium levels were 7.94 mg/dl in the RA group and 8.66 mg/dl in the control group. This difference was statistically significant. 36 patients (72%) belonging to the RA group had serum Vitamin D levels <30 ng/ml, that is, they were Vitamin D deficient, whereas only 14 participants (28%) belonging to the control group had Vitamin D deficiency. The mean serum Vitamin D levels were 24.12 ng/ml in patients of RA and 36.87 ng/ml in the control group. This difference was also statistically significant. Significant results were obtained while correlating vitamin D levels with disease activity. **Conclusion:** In individuals suffering from RA, vitamin D insufficiency is more prevalent and may contribute to the onset or progression of the illness.

Keywords: Rheumatoid Arthritis, Vitamin D

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INTRODUCTION

Vitamin D is a seco-steroid 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.² Vitamin D has extraskeletal effects as well.^{3,4} The nonclassical actions of vitamin D are currently under discussion. Vitamin D has been found to have immunomodulatory actions.^{5,6} Vitamin D deficiency has been shown to be correlated with the appearance of autoimmune diseases, such as diabetes mellitus type 1 and multiple sclerosis.⁷

Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by inflammatory arthritis and extra-articular involvement. It is a chronic inflammatory disorder caused in many cases by the interaction between genes and environmental factors, including tobacco, that primarily involves synovial joints. It typically starts in small peripheral joints, is usually symmetric, and progresses to involve proximal joints if left untreated. Joint inflammation

over time leads to the destruction of the joint with loss of cartilage and bone erosions. RA with a symptom duration of fewer than six months is defined as early RA, and when the symptoms have been present for more than six months, it is defined as established RA. RA, if untreated, is a progressive disease with morbidity and increased mortality.⁸ Hence, this study was conducted to assess vitamin D in rheumatoid arthritis and its correlation with disease activity.

MATERIAL AND METHODS

In this study, there were one hundred volunteers in all, who were split into two groups. Fifty RA cases made up Group A, and fifty healthy controls made up Group B. Everyone who took part was between the ages of eighteen and seventy five. The American College of Rheumatology-European League Against Rheumatism 2010 criteria were used to diagnose RA in both men and women between the ages of eighteen and seventy five. Those having hyperparathyroidism, hyperthyroidism, diabetes mellitus, malnutrition, hepatic as well as

renal dysfunction, as well as those who had taken vitamin D supplements within the previous six months or who were using drugs that may alter bone and vitamin D metabolism, had been excluded from this study. Statistical analysis was done using SPSS software. In this study, there were one hundred volunteers in all, who were split into two groups. Fifty RA cases made up Group A, and fifty healthy controls made up Group B. Everyone who took part was between the ages of eighteen and seventy-five. The American College of Rheumatology-European League Against

Rheumatism 2010 criteria were used to diagnose RA in both men and women between the ages of eighteen and seventy-five. Those having hyperparathyroidism, hyperthyroidism, diabetes mellitus, malnutrition, hepatic as well as renal dysfunction, as well as those who had taken vitamin D supplements within the previous six months or who were using drugs that may alter bone and vitamin D metabolism, had been excluded from this study. Statistical analysis was done using SPSS software.

RESULTS

Table 1: Gender-wise distribution of subjects

Gender	Number of subjects	Percentage
Males	21	21%
Females	79	79%
Total	100	100%

The mean age of patients in the RA group was 43.5 years, whereas the mean age of participants in the control group was 45.1 years. Among the 50 patients in the RA group, 16 (32%) were male and 34 (68%) were female. Among the 50 participants in the control group, 5 (10%) were male and 45 (90%) were females.

Table 2: Mean serum calcium and vitamin D levels in the study groups

Groups	Mean calcium levels (mg/dL)	Mean vitamin D levels (mg/dL)	p-value
Rheumatoid arthritis	7.94	24.12	0.001 (S)
Control group	8.66	36.87	0.007 (S)

Table 3: Correlation of Vitamin D with Disease Activity

RA patients according to disease activity	Number	Mean Vitamin D levels	p-value
Remission	4	39.5	0.01 (Significant)
Low	11	35.1	
Moderate	16	22.4	
High	19	15.3	

The mean serum calcium levels were 7.94 mg/dl in the RA group and 8.66 mg/dl in the control group. This difference was statistically significant. 36 patients (72%) belonging to the RA group had serum Vitamin D levels <30 ng/ml, that is, they were Vitamin D deficient, whereas only 14 participants (28%) belonging to the control group had Vitamin D deficiency. The mean serum Vitamin D levels were 24.12 ng/ml in patients of RA and 36.87 ng/ml in the control group. This difference was also statistically significant. Significant results were obtained while correlating vitamin D levels with disease activity.

DISCUSSION

Rheumatoid arthritis (RA) is a chronic autoimmune disease that manifests as a chronic inflammatory response, and persistent synovitis leads to progressive deterioration and impairment of joint function.⁹ RA bone fragility is caused by systemic inflammation, circulating auto-antibodies and pro-inflammatory cytokine secretion, which together have harmful effects on bone.¹⁰ Vitamin D (VD) is a fat-soluble hormone that promotes calcium/phosphate metabolism in bones.¹¹ Studies have found that vitamin D has certain effects on other physiological functions and pathological conditions. Specifically,

vitamin D has been widely indicated to have an effect on the immune system.¹² There is evidence that VD may be involved in rheumatoid arthritis (RA). Studies have found that VD can prevent antigen expression and increase and regulate T cell activity.^{13,14} Hence, this study was conducted to assess vitamin D in rheumatoid arthritis and its correlation with disease activity.

In this study, the mean age of patients in the RA group was 43 years, whereas the mean age of participants in the control group was 45 years. Among the 50 patients in the RA group, 16 (32%) were male and 34 (68%) were female. Among the 50 participants in the control group, 5 (10%) were male and 45 (90%) were females. The mean serum calcium levels were 7.94 ± 0.41 mg/dl in the RA group and 8.66 ± 0.35 mg/dl in the control group. This difference was statistically significant. 36 patients (72%) belonging to the RA group had serum Vitamin D levels <30 ng/ml, that is, they were Vitamin D deficient, whereas only 14 participants (28%) belonging to the control group had Vitamin D deficiency. The mean serum Vitamin D levels were 24.12 ± 9.63 ng/ml in patients of RA and 36.87 ± 13.11 ng/ml in the control group. This difference was also statistically significant.

Sirbu E et al¹⁵ analysed the serum levels of vitamin D in patients with RA in comparison to healthy controls and investigated possible correlation with disease activity. This was a retrospective, comparative study conducted on 37 subjects suffering from RA and a group of 21 healthy matched controls. The following were determined in all studied subjects: erythrocyte sedimentation rate (ESR), white blood cells (WBC), hemoglobin (Hb), platelets (PLT), serum calcium (Ca), serum phosphorus (Phos), and serum 25 hydroxy-vitamin D. Moreover, in the RA group the IgM-Rheumatoid Factor (RF) and anti-citrullinated protein antibodies (ACPA) (immune-enzymatic method) were assessed. The Disease Activity Score of 28 joints (DAS28) was calculated for the RA patients. They observed that vitamin D deficiency is more common in RA patients than in healthy controls. No significant correlation between 25OHvitD and DAS28-ESR was found in the study cohort. It was concluded that there was no significant association of serum 25(OH)D with disease severity in a Western Romanian cohort with RA.

Kostoglou A.I. et al¹⁶ evaluated vitamin D status in patients with RA and to assess the relationship between vitamin D levels and disease activity. 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 (Student's t test, $p < 0.001$). 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. It appeared that vitamin D deficiency was highly prevalent in patients with RA, and that vitamin D deficiency may be linked to disease severity in RA. As vitamin D deficiency has been linked to diffuse musculoskeletal pain, these results had therapeutic implications. Vitamin D supplementation may be needed both for the prevention of osteoporosis as well as for pain relief in patients with RA.

CONCLUSION

Patients with RA are more likely to have vitamin D deficiencies, which could be one of the factors contributing to the onset or progression of RA.

REFERENCES

- Holick M. (2011) Vitamin D: evolutionary, physiological and health perspectives. *Curr Drug Targets* 12: 4–18.
- Mason R., Sequeira V., Gordon-Thomson C. (2011) Vitamin D: the light side of sunshine. *Eur J Clin Nutr* 65: 986–993.
- Fernandes de Abreu D., Eyles D., Féron F. (2009) Vitamin D, a neuro-immunomodulator: implications for neurodegenerative and autoimmune diseases. *Psychoneuroendocrinology* 34(Suppl. 1): S265–S277.
- Hewison M. (2012) Vitamin D and immune function: autocrine, paracrine or endocrine? *Scand J Clin Lab Invest Suppl* 243: 92–102.
- Bartley J. (2010) Vitamin D: emerging roles in infection and immunity. *Expert Rev Anti Infect Ther* 8: 1359–1369.
- Bikle D. (2011) Vitamin D regulation of immune function. *Vitam Horm* 86: 1–21.
- Jankosky C., Deussing E., Gibson R., Haverkos H. (2012) Viruses and vitamin D in the etiology of type 1 diabetes mellitus and multiple sclerosis. *Virus Res* 163: 424–430.
- Chauhan K, Jandu JS, Brent LH, Al-Dhahir MA. Rheumatoid Arthritis. 2023 May 25. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan.
- Smolen JS, Aletaha D, McInnes IB. Rheumatoid arthritis. *Lancet*. (2016) 388:2023–38.
- McInnes IB, Schett G. Mechanisms of disease the pathogenesis of rheumatoid arthritis. *N Engl J Med*. (2011) 365:2205–19.
- Bivona G, Agnello L, Ciaccio M. The immunological implication of the new vitamin D metabolism. *Central Euro J Immunol*. (2018) 43:331–4.
- Medrano M, Carrillo-Cruz E, Montero I, Perez-Simon JA. Vitamin D: effect on haematopoiesis and immune system and clinical applications. *Int J Mol Sci*. (2018) 19:2663.
- Székely JI, Pataki Á. Effects of vitamin D on immune disorders with special regard to asthma, COPD and autoimmune diseases: a short review. *Expert Rev Respir Med*. (2012) 6:683–704.
- Luo J, Wen H, Guo H, Cai Q, Li S, Li X. 1,25-dihydroxyvitamin D3 inhibits the RANKL pathway and impacts on the production of pathway-associated cytokines in early rheumatoid arthritis. *Biomed Res Int*. (2013) 2013:101805.
- Sirbu, E., Buleu, F., Tudor, A., & Dragan, S. (2020). Vitamin D and disease activity in rheumatoid arthritis patients: a retrospective study in a Romanian cohort. *Acta biochimica Polonica*, 67(2), 267–272.
- Kostoglou-Athanassiou I, Athanassiou P, Lyraki A, Raftakis I, Antoniadis C. Vitamin D and rheumatoid arthritis. *Ther Adv Endocrinol Metab*. 2012 Dec;3(6):181-7.