Section: General Medicine

Original Research Article

SERUM VITAMIN 25(OH) D LEVELS AS A PREDICTOR OF DISEASE ACTIVITY IN RHEUMATOID ARTHRITIS: EVIDENCE FROM SOUTH INDIA

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ABSTRACT

Background: Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disorder characterized by joint destruction and systemic complications. Vitamin D, known for its immunomodulatory properties, has been implicated in the pathogenesis of autoimmune diseases. This study aimed to investigate the association between serum vitamin D status and disease activity in patients with RA.

Materials and Methods: A cross-sectional observational study was conducted at Bhaskar Medical College and Bhaskar General Hospital from March 2024 to February 2025, including 120 adult RA patients fulfilling the 2010 ACR/EULAR criteria. Disease activity was assessed using the Disease Activity Score-28 (DAS28), and serum 25-hydroxyvitamin D [25(OH)D] levels were measured by chemiluminescence immunoassay. Patients were categorized into deficient (<20 ng/mL), insufficient (20–30 ng/mL), and sufficient (>30 ng/mL) groups. Statistical analyses included ANOVA, Pearson correlation, and multivariate linear regression.

Results: Vitamin D deficiency was prevalent in 60% of patients. Mean DAS28 scores were significantly higher in vitamin D-deficient individuals (5.8 ± 0.6) compared to those with insufficient (4.3 ± 0.7) and sufficient levels (2.9 ± 0.8) ($p < 0.001$). Multivariate regression revealed vitamin D level as an independent predictor of DAS28 ($\beta = –0.41$, 95% CI: –0.56 to –0.26, $p < 0.001$). Despite high DMARD usage, the majority remained in moderate to high disease activity categories.

Conclusion: Serum vitamin D levels show a significant inverse correlation with RA disease activity. Routine screening and correction of vitamin D deficiency may serve as an effective adjunct in RA management.

Keywords: Rheumatoid arthritis, Vitamin D, DAS28, Disease activity, Autoimmunity, Inflammatory arthritis.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic autoimmune disorder primarily affecting the synovial joints, characterized by persistent inflammation, progressive joint destruction, and significant functional disability. It affects approximately 0.5–1% of the global population and remains a major contributor to morbidity and healthcare burden, particularly among middle-aged women.[1] The pathogenesis of RA involves a complex interplay of genetic predisposition, immune dysregulation, and environmental triggers, leading to sustained synovitis and systemic inflammation.[2]

In recent years, there has been growing interest in the role of micronutrients in modulating autoimmune responses, with particular focus on vitamin D. Traditionally recognized for its role in calcium homeostasis and bone metabolism, vitamin D has now emerged as a key immunomodulatory hormone. It exerts its effects through the vitamin D receptor (VDR), which is expressed on various immune cells including T lymphocytes, B cells, macrophages, and dendritic cells.[3] Active vitamin D (1,25-

dihydroxyvitamin D) is known to suppress pro-inflammatory cytokines such as IL-6, TNF-α, and IL-17, while promoting regulatory T-cell responses and immune tolerance.[4]

Several studies have suggested a potential link between low serum vitamin D levels and increased disease activity in RA patients. Deficiency of vitamin D has been implicated in heightened inflammatory activity, increased disease severity, and reduced response to treatment.[5] However, existing literature remains inconclusive, with some studies failing to establish a clear relationship, likely due to heterogeneity in population demographics, assay methods, and disease characteristics.[6] Furthermore, vitamin D deficiency is highly prevalent in the general Indian population, raising concerns about its underrecognized contribution to disease modulation in chronic inflammatory disorders such as RA.[7]

Given this context, the assessment of vitamin D status in RA patients assumes clinical importance not only as a potential disease marker but also as a possible adjunctive therapeutic target. In India, despite abundant sunlight, hypovitaminosis D is prevalent due to lifestyle factors, clothing practices, and skin pigmentation.[8] This further complicates disease outcomes in autoimmune conditions and warrants rigorous investigation.

The present study was designed to explore the association between serum vitamin D levels and rheumatoid arthritis disease activity in patients attending a tertiary care center in South India. By employing a standardized disease activity score (DAS28) and stratifying patients based on their vitamin D levels, this study aimed to examine the extent to which vitamin D deficiency correlates with inflammatory burden in RA. The findings may provide further insight into whether serum vitamin D could serve as a reliable biomarker for disease activity and whether it should be routinely evaluated in the management of RA patients.[9]

This study seeks to bridge the existing gaps by correlating biochemical vitamin D status with clinical disease activity parameters.

MATERIALS AND METHODS

This cross-sectional observational study was conducted in the Department of Medicine, Bhaskar Medical College and Bhaskar General Hospital, Telangana, India, over a 12-month period from March 2024 to February 2025. The objective was to assess the relationship between serum vitamin D levels and rheumatoid arthritis (RA) disease activity using standardized clinical and laboratory criteria.

Study Population and Inclusion Criteria

Patients aged 18 years and above, previously diagnosed with RA based on the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria, were consecutively recruited from the outpatient and inpatient departments. Individuals on vitamin D supplementation in the past three months, those with comorbid conditions affecting bone metabolism (e.g., chronic kidney disease, hyperparathyroidism), pregnancy, malignancies, or other autoimmune diseases were excluded.

Sample Size and Sampling Technique

A total of 120 patients were included based on consecutive sampling. The sample size was calculated considering a prevalence of vitamin D deficiency in RA patients at 60%, with 95% confidence level and 10% margin of error, leading to a minimum required sample of 92 patients; however, to increase power and accommodate exclusions, 120 patients were enrolled.

Data Collection Procedure

After obtaining written informed consent, a structured case-record form was used to document demographic details (age, sex), clinical features (duration of disease, comorbidities), and anthropometric measures (height, weight, BMI).

Disease activity was assessed using the Disease Activity Score-28 joints (DAS28), which includes the tender joint count (TJC), swollen joint count (SJC), erythrocyte sedimentation rate (ESR), and the patient's global health assessment (GH, on a 100-mm visual analog scale). DAS28 scores were categorized as: remission (<2.6), low (2.6–3.2), moderate (3.2–5.1), and high (>5.1) activity.

Serum 25-hydroxyvitamin D [25(OH)D] levels were measured using a standardized chemiluminescence immunoassay (CLIA). Vitamin D status was classified as follows:

- Deficient: <20 ng/mL
- Insufficient: 20–30 ng/mL
- Sufficient: >30 ng/mL

Blood samples were collected under aseptic precautions in fasting state and processed in the hospital's central laboratory. Routine laboratory parameters including ESR were also measured.

Statistical Analysis: Data were entered into Microsoft Excel and analyzed using SPSS version 26.0. Continuous variables were expressed as mean ± standard deviation (SD) or median with interquartile range (IQR), while categorical variables were expressed as frequencies and percentages. The association between vitamin D levels and disease activity was assessed using one-way ANOVA or Kruskal–Wallis test as appropriate. Pearson correlation was used for continuous variables. Multivariate linear regression was performed to identify independent predictors of DAS28 scores. A two tailed p-value <0.05 was considered statistically significant.

Ethical Considerations: The study was approved by the Institutional Ethics Committee. All procedures followed the ethical standards of the 1964 Helsinki Declaration and its later amendments.

RESULTS

This cross-sectional study of 120 rheumatoid arthritis (RA) patients revealed a compelling association between serum vitamin D levels and disease activity as measured by the DAS28 scoring system. The majority of participants were female (71.7%) with a mean age of 49.2 ± 11.6 years and a median disease duration of 6 years, reflective of the known epidemiological patterns of RA. Despite being in a region with adequate sunlight, 60% of the study population exhibited vitamin D deficiency (<20 ng/mL), while only 12.5% had sufficient levels (>30 ng/mL), underscoring the endemic nature of hypovitaminosis D in Indian RA patients.

A clear inverse trend was observed between vitamin D status and disease severity. Among vitamin D deficient individuals, 38.3% had high disease activity (DAS28 > 5.1) with a mean DAS28 score of 5.8 ± 0.6. In contrast, patients with sufficient vitamin D levels had significantly lower disease activity, with a mean DAS28 of 2.9 ± 0.8 and only 8.3% achieving remission. The p-values for these differences were highly significant ($p < 0.001$ for deficient vs sufficient, $p < 0.01$ for insufficient), suggesting a robust and clinically meaningful relationship.

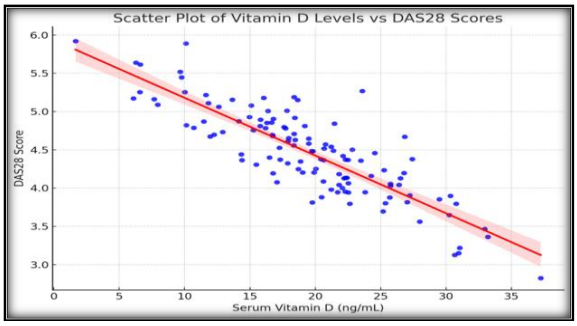

Figure 1: Scatter plot of Vitamin D levels vs DAS28 scores

Multivariate regression further reinforced this finding, identifying serum vitamin D as an independent predictor of RA activity. A beta coefficient of –0.41 (95% CI: –0.56 to –0.26, $p < 0.001$) indicated that each unit increase in vitamin D was associated with a substantial reduction in DAS28 scores. Other factors such as age, BMI, and disease duration showed no statistically significant contribution to disease activity, emphasizing the dominant influence of vitamin D.

Notably, despite a high proportion of patients receiving standard DMARD therapy—methotrexate (79.2%), hydroxychloroquine (68.3%), and corticosteroids (50%)—over 78% of the cohort remained in moderate to high disease activity states. This suggests that inadequate vitamin D levels may act as a limiting factor in achieving therapeutic remission, possibly by perpetuating immune dysregulation and inflammation despite pharmacologic intervention.

The accompanying scatter plot visually substantiates these observations, displaying a pronounced downward trendline indicating an inverse linear correlation between vitamin D concentrations and DAS28 scores. The dispersion pattern reflects consistency across the cohort, lending further support to the statistical significance observed.

Overall, these findings highlight the potential of serum vitamin D not only as a biomarker of disease activity but also as a modifiable factor with therapeutic implications. Vitamin D repletion, if validated through prospective interventional trials, could become a simple, cost-effective adjunct in the comprehensive management of RA.

Table 1: Demographic Characteristics

Variable	Value
Age (mean ± SD)	49.2 ± 11.6
Female (%)	86 (71.7%)
Male (%)	34 (28.3%)
BMI (mean ± SD)	24.7 ± 3.9
Disease Duration (years, median [IQR])	6 [3–10]

Table 2: Medication Usage Among RA Patients

Medication	Number of Patients (%)
Methotrexate	95 (79.2%)
Hydroxychloroquine	82 (68.3%)
Sulfasalazine	40 (33.3%)
Prednisolone	60 (50%)
Biologics (e.g., TNF-α inhibitors)	12 (10%)

Table 3: Vitamin D Status in Study Participants

Vitamin D Status	Number of Patients (%)
Deficient (<20 ng/mL)	72 (60%)
Insufficient (20–30 ng/mL)	33 (27.5%)
Sufficient (>30 ng/mL)	15 (12.5%)

Table 4: DAS28 Distribution

DAS28 Category	Patients (%)
Remission (<2.6)	10 (8.3%)
Low (2.6–3.2)	16 (13.3%)
Moderate (3.2–5.1)	48 (40%)
High (>5.1)	46 (38.3%)

Table 5: Correlation Between Vitamin D and DAS28

Vitamin D Status	Mean DAS28 Score (±SD)	p-value
Deficient	5.8 ± 0.6	<0.01
Insufficient	4.3 ± 0.7	<0.01
Sufficient	2.9 ± 0.8	Reference

Table 6: Multivariate Regression Analysis

Variable	Beta Coefficient	95% CI	p-value
Vitamin D (ng/mL)	–0.41	–0.56 to –0.26	<0.001
Age (years)	0.02	–0.01 to 0.05	0.18
BMI	0.03	–0.01 to 0.07	0.11
Female Gender	0.11	–0.08 to 0.30	0.25
Disease Duration	0.07	–0.01 to 0.14	0.07

DISCUSSION

Rheumatoid arthritis (RA) is a progressive inflammatory disease with a well-established autoimmune basis, and its clinical course is marked by variable degrees of synovial inflammation and joint destruction. In recent years, vitamin D has gained attention for its immunomodulatory roles, particularly in autoimmune conditions such as RA. The present study assessed the relationship between serum vitamin D levels and disease activity in RA patients and found a strong inverse correlation, thereby reinforcing the growing body of literature on the topic.

The high prevalence of vitamin D deficiency in this cohort (60%) is consistent with reports by Song et al,[10] who found that over 50% of RA patients had suboptimal vitamin D levels. Similarly, Craig et al,[11] observed that vitamin D deficiency was common among RA patients even in sun-rich regions, suggesting factors beyond sun exposure such as lifestyle, reduced mobility, and chronic inflammation.

Our findings demonstrated that patients with deficient vitamin D levels had significantly higher disease activity scores (mean DAS28: 5.8 ± 0.6) compared to those with sufficient levels (2.9 ± 0.8). These results are in accordance with Patel et al,[12] who found a significant negative correlation between 25(OH)D levels and DAS28 in RA patients ($r = –0.45$; $p < 0.001$). Similarly, Kostoglou-Athanassiou et al,[13] reported that vitamin D deficiency was associated with increased joint swelling and pain severity.

Importantly, in multivariate regression, vitamin D level emerged as an independent predictor of disease activity ($\beta = –0.41$; 95% CI: –0.56 to –0.26; $p < 0.001$). This echoes the findings of Ghosh et al,[14] who noted that after adjusting for confounders like age, gender, and disease duration, serum 25(OH)D levels continued to significantly predict RA activity indices. Our study also observed that neither BMI nor gender had a statistically significant effect on disease activity, consistent with the conclusions drawn by Cutolo et al.[15]

Despite the widespread use of disease-modifying antirheumatic drugs (DMARDs), including methotrexate (79.2%) and hydroxychloroquine (68.3%), a significant proportion of patients continued to exhibit moderate to high disease activity, which may reflect underlying vitamin D deficiency may impair optimal immunoregulation. This aligns with the observation by Amital et al,[16] who suggested that low vitamin D may dampen the efficacy of conventional RA therapy.

From a clinical perspective, the findings underscore the importance of evaluating vitamin D levels in all RA patients as part of routine care. Given its affordability, safety profile, and potential to improve disease control, vitamin D supplementation could serve as a valuable adjunct to immunosuppressive therapies, especially in resource-limited settings.

However, this study has certain limitations. The cross-sectional design precludes establishing causality, and potential confounding variables such as dietary intake and seasonal variability were not evaluated. Longitudinal and interventional studies are warranted to further elucidate the therapeutic role of vitamin D in RA management.

CONCLUSION

This cross-sectional study demonstrated a significant inverse association between serum vitamin D levels and rheumatoid arthritis disease activity. Vitamin D deficiency was highly prevalent among RA patients and correlated strongly with elevated DAS28 scores, even after adjusting for potential confounders. These findings suggest that serum vitamin D may serve not only as a biomarker of disease activity but also as a modifiable risk factor in RA pathogenesis.

Given the widespread availability and low cost of vitamin D supplementation, routine screening and correction of hypovitaminosis D in RA patients could

be considered as a pragmatic adjunct to standard therapeutic strategies. Although this study provides compelling evidence for the association, interventional trials are needed to establish the therapeutic benefit of vitamin D in modulating disease outcomes.

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