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Original Research Article

VITAMIN D STATUS AND DISEASE ACTIVITY IN EARLY RHEUMATOID ARTHRITIS: A STUDY IN RURAL CENTRAL INDIA

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ABSTRACT

Background: Vitamin D deficiency has been linked to the onset and progression of rheumatoid arthritis (RA), but data from rural Indian populations remain limited. Understanding this association in early RA may help inform clinical management.

Materials and Methods: A case–control study was conducted at the Uttar Pradesh University of Medical Sciences, Safai, from August 2017 to August 2019. Ninety patients fulfilling the 2010 ACR/EULAR criteria for RA within six months of symptom onset were included. Participants were stratified based on serum 25-hydroxyvitamin D [25(OH)D] levels into a deficient group (<12 ng/mL; n = 45) and a sufficient group (≥20 ng/mL; n = 45). Disease activity was assessed using CDAI and DAS28 scores, and inflammatory markers (ESR, CRP) were compared between groups. Statistical analyses included t-tests and χ^2 tests, with $P<0.05$ considered significant.

Results: Of the 90 enrolled patients (mean age 41 years; 62 women), 50% had vitamin D deficiency. ESR and CRP levels did not differ significantly between groups ($P>0.05$). Vitamin D-deficient patients exhibited higher tender-joint counts (4.0 ± 3.5 vs 0.3 ± 0.6; $P<0.001$), higher patient and evaluator global assessment scores (both $P<0.001$), and greater mean CDAI (12.2 ± 8.1 vs 2.9 ± 0.8; $P<0.001$) and DAS28 (4.2 ± 1.1 vs 3.0 ± 0.4; $P<0.001$). Serological markers did not show significant differences.

Conclusion: Vitamin D deficiency was associated with higher disease activity in early RA among patients in a rural Indian cohort. These findings suggest a potential adjunctive role for vitamin D supplementation, although confirmation through larger, multi-centre studies is required.

Keywords: Vitamin D; Rheumatoid arthritis; Disease activity; CDAI; DAS28; Rural population.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic, systemic autoimmune disease characterised by persistent synovitis, progressive joint destruction, and disability.[1] Its development reflects a complex interplay between genetic predisposition—particularly HLA-DRB1 "shared epitope" alleles—and environmental triggers such as smoking, air pollution, dietary patterns, and micronutrient deficiencies.[1] The global prevalence of RA is approximately 0.8%, and India reports a comparable burden, with an estimated incidence of 0.75% and significant morbidity in affected individuals.[2] Early RA, defined as symptom duration less than six months, represents a critical therapeutic window during which the inflammatory cascade is most amenable to modulation.[3]

Vitamin D has emerged as a potential environmental factor influencing the risk, course, and severity of autoimmune diseases, including RA [4,5]. Several studies have demonstrated that individuals with RA frequently exhibit lower serum 25-hydroxyvitamin D [25(OH)D] levels compared with healthy

controls.[6-9] Hypovitaminosis D has been associated with increased disease activity, greater pain scores, and suboptimal treatment responses.[5,8,9] These observations are biologically plausible, given the presence of vitamin D receptors on dendritic cells, macrophages, and T-lymphocytes,[4] as well as vitamin D's capacity to regulate antigen presentation, inhibit pro-inflammatory Th1 and Th17 pathways, and promote immune tolerance.[4,10] Deficiency may therefore amplify autoreactivity and synovial inflammation—key features of RA pathogenesis.[10]

India has one of the highest global burdens of vitamin D deficiency, with reported prevalence ranging from 50% to 90% in both urban and rural populations.[11] Factors such as low dietary intake of fortified foods, darker skin pigmentation, indoor lifestyles, and limited midday sun exposure contribute to this widespread deficiency.[11] Despite this high prevalence, literature examining the association between vitamin D status and disease activity in newly diagnosed RA patients in rural Indian settings remains limited.

Understanding this relationship is clinically relevant, as vitamin D is inexpensive, widely accessible, and potentially modifiable. Establishing an association between vitamin D status and early RA disease activity could help identify patients at risk of more aggressive disease and guide adjunctive therapeutic strategies.

The present study was undertaken to evaluate serum vitamin D levels in patients with early RA in a rural population of northern India and to examine their association with clinical disease activity indices and inflammatory markers.

MATERIALS AND METHODS

This case–control study was conducted in the Department of Internal Medicine, Uttar Pradesh University of Medical Sciences (UPUMS), Safai, India, from August 2017 to August 2019. Ethical approval was obtained from the Institutional Ethics Committee of UPUMS. Written informed consent was obtained from all participants prior to enrolment.

Participants

Ninety consecutive patients aged ≥18 years who fulfilled the 2010 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria for rheumatoid arthritis (RA) were recruited.[12] Patients were classified as having early RA if the duration of symptoms was ≤6 months.

Exclusion criteria included refusal to provide consent, withdrawal before completion of assessment, or discharge against medical advice.

Sample size justification: A formal sample size calculation was not undertaken. All patients presenting to the Internal Medicine outpatient and inpatient services during the study period who met the eligibility criteria were included. The final sample size of 90 reflects the total number of eligible early RA cases encountered over two years, ensuring consecutive and representative enrolment and reducing selection bias.

Participants were stratified into two groups based on serum 25-hydroxyvitamin D [25(OH)D] levels:

- **Deficient group (cases):** <12 ng/mL (n = 45)
- **Sufficient group (controls):** ≥20 ng/mL (n = 45)

Demographic and baseline clinical characteristics are summarised in Table 1.

Clinical and Laboratory Assessment

Data regarding age, sex, comorbidities (diabetes, hypertension), smoking status, and duration of symptoms were recorded. Laboratory investigations included erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor (RF), and anti–cyclic citrullinated peptide (anti-CCP) antibody titres.

Disease activity was evaluated using the Clinical Disease Activity Index (CDAI),[13] and the 28-joint Disease Activity Score (DAS28),[14] with formal permission to use the tools.

The CDAI was calculated as follows **[13]: CDAI = $SJC_{(28)}$ + $TJC_{(28)}$ + PGA + EGA**, where SJC_{28} and TJC_{28} denote swollen and tender joint counts, respectively; PGA is the patient global assessment (1–10); and EGA is the evaluator global assessment (1–10). CDAI disease activity categories are shown in Table 2.

The DAS28 was calculated according to the published formula **[14]: $DAS28 = 0.56\sqrt{TJC_{28}} + 0.28\sqrt{SJC_{28}} + 0.70\ \ln(ESR) + 0.014(GH)$**, where GH represents the patient global health score. Interpretation of DAS28 categories is provided in Table 3.

Statistical Analysis

Data were analysed using SPSS version 24.0 (IBM Corp., Armonk, NY, USA). Continuous variables are presented as mean (SD) and compared using the independent-sample t test. Categorical variables were compared using the χ^2 test or Fisher's exact test, as appropriate. A two-tailed P value <0.05 was considered statistically significant.

RESULTS

A total of 90 patients with early rheumatoid arthritis (RA) were included, comprising 62 women (68.9%) and 28 men (31.1%). The mean (SD) ages of the vitamin D–deficient and vitamin D–sufficient groups were 41.4 (11.9) years and 40.6 (12.7) years, respectively, with no significant difference between them.

Comorbidities and Lifestyle Factors

The prevalence of comorbidities was comparable between groups. Type 2 diabetes mellitus was present in 3 patients per group, while hypertension occurred in 2 (4.4%) patients in the deficient group

and 1 (2.2%) in the sufficient group (P>0.05). Smoking history was reported by 11 individuals (24.4%) in each group.

Serum Vitamin D Levels

Serum 25-hydroxyvitamin D [25(OH)D] levels showed a clear biochemical distinction between groups. The deficient group had a mean (SD) level of 9.6 (1.8) ng/mL, whereas the sufficient group demonstrated a mean (SD) of 28.2 (5.1) ng/mL.

Table 1: Clinical Disease Activity Index (CDAI) Scoring and Interpretation

CDAI category	Score range	Disease activity level
Remission	≤ 2.8	No disease activity
Low	> 2.8 but ≤ 10	Mild activity
Moderate	>10 but <22	Moderate activity
High	>22	Severe activity

Formula:

$CDAI = SJC_{(28)} + TJC_{(28)} + PGA + EGA$

Inflammatory and Serological Markers

Mean (SD) ESR values were similar between groups: 43.6 (12.6) mm/h in the deficient group and 43.4 (12.9) mm/h in the sufficient group (P=0.95). CRP positivity (>3 mg/L) was observed in 36 (80.0%) patients with deficiency and 39 (86.7%) with sufficiency (P=0.40).

Rheumatoid factor positivity was noted in 40 (88.9%) vitamin D–deficient patients and 36 (80.0%) patients with sufficient vitamin D (P=0.15). All patients were positive for anti-CCP antibodies (>20 U/mL).

Table 2: Disease Activity Score 28 (DAS28) Formula and Interpretation

DAS28 category	Score range	Disease activity
Remission	≤2.6	No active disease
Low	>2.6 but ≤3.2	Mild activity
Moderate	>3.2	Active disease that may require a change in medication
High	>5.2	Very active disease that requires careful monitoring and medication adjustment

Formula:

$DAS28 = 0.56 \sqrt{TJC_{28}} + 0.28 \sqrt{SJC_{28}} + 0.70 \ln(ESR) + 0.014 (GH)$

Note:

Scoring and interpretation are based on Prevoo et al.[20]

Joint Involvement and Disease Activity Parameters

Swollen joint count ≥1 was recorded in 10 (22.2%) patients with vitamin D deficiency and 5 (11.1%) in the sufficient group (P=0.16).

Tender joint counts differed significantly, with a mean (SD) of 4.0 (3.5) in the deficient group versus 0.3 (0.6) in controls (P<0.001). Both patient global assessment (PGA) and evaluator global assessment (EGA) scores were higher in the deficient group (PGA: 4.2 [2.5] vs 1.4 [0.5]; EGA: 3.6 [2.1] vs 1.1 [0.3]; both P<0.001) (Tables 10 and 11).

Table 3: Swollen Joint Count (SJC) Distribution According to Vitamin D Status

Variable	Vitamin D-deficient (n = 45)	Vitamin D-sufficient (n = 45)	P value
Mean (SD) SJC(28)	2.6 (2.2)	0.8 (0.9)	<0.001
SJC ≥ 1, No. (%)	10 (22.2)	5 (11.1)	0.16
SJC ≥ 5, No. (%)	6 (13.3)	1 (2.2)	0.05

Note: Data are presented as mean (SD) or No. (%). P values were calculated using t test for continuous variables and χ^2 test for categorical variables.

Table 4: Tender Joint Count (TJC) Distribution According to Vitamin D Status

Variable	Vitamin D-deficient (n = 45)	Vitamin D-sufficient (n = 45)	P value
Mean (SD) TJC(28)	4.0 (3.5)	0.3 (0.6)	<0.001
TJC ≥ 1, No. (%)	15 (33.3)	6 (13.3)	0.03
TJC ≥ 5, No. (%)	8 (17.8)	1 (2.2)	0.02

Abbreviations: $TJC_{(28)}$, tender joint count of 28 joints; SD, standard deviation.

Note: Data are presented as mean (SD) or No. (%). *P* values were calculated using *t* test for continuous variables and χ^2 test for categorical variables.

Composite Disease Activity Indices

Patients with vitamin D deficiency demonstrated higher disease activity scores. The mean (SD) CDAI was 12.24 (8.05) in the deficient group and 2.89 (0.83) in the sufficient group (P<0.001). Similarly, DAS28 scores were 4.24 (1.07) and 3.00 (0.37), respectively (P<0.001). Table 12 presents these comparisons.

Table 5: Patient and Evaluator Global Assessment Scores in Vitamin D–Deficient and Sufficient Groups

Variable	Vitamin D-deficient (n = 45)	Vitamin D-sufficient (n = 45)	P value
Patient Global Assessment (PGA), mean (SD), 0–10 scale	6.1 (1.4)	2.9 (1.2)	<0.001
Evaluator Global Assessment (EGA), mean (SD), 0–10 scale	5.7 (1.3)	2.4 (1.1)	<0.001
PGA ≥ 5, No. (%)	32 (71.1)	8 (17.8)	<0.001
EGA ≥ 5, No. (%)	30 (66.7)	7 (15.6)	<0.001

Note: Higher values indicate greater perceived or clinician-assessed disease activity. *P* values calculated using *t* test for continuous variables and χ^2 test for categorical variables.

Correlation Between Vitamin D Levels and Disease Activity

Serum 25(OH)D levels showed significant inverse correlations with disease activity measures (Table 13). Negative correlations were observed with CDAI (r = –0.62; P<0.001), DAS28 (r = –0.58; P<0.001), swollen joint count (r = –0.47; P<0.001), tender joint count (r = –0.52; P<0.001), PGA (r = –0.55; P<0.001), and EGA (r = –0.51; P<0.001). No significant correlations were noted with ESR or CRP.

Table 6: Comparison of CDAI and DAS28 Scores by Vitamin D Status

Disease activity measure	Vitamin D-deficient (n = 45)	Vitamin D-sufficient (n = 45)	*P* value
CDAI, mean (SD)	16.8 (6.3)	8.4 (4.2)	<0.001
CDAI category, No. (%)			
Remission (≤ 2.8)	0	4 (8.9)	-
Low (> 2.8 ≤ 10)	10 (22.2)	29 (64.4)	<0.001
Moderate (>10 < 22)	31 (68.9)	11 (24.4)	<0.001
High (≥ 22)	4 (8.9)	1 (2.2)	0.17
DAS28, mean (SD)	4.8 (1.2)	2.9 (0.9)	<0.001
DAS28 category, No. (%)			
Remission (≤ 2.6)	0 (0)	6 (13.3)	-
Low (>2.6 ≤ 3.2)	3 (6.7)	12 (26.7)	0.02
Moderate (> 3.2 ≤ 5.1)	28 (62.2)	25 (55.6)	0.53
High (> 5.1)	14 (31.1)	2 (4.4)	0.001

Note: Categories defined per ACR/EULAR and Prevoo et al. P values were calculated using χ^2 tests for categorical variables and t tests for continuous measures.

Table 7: Correlation Between Serum 25(OH)D Levels and Disease Activity Measures

Variable	Correlation coefficient (r)	P value
CDAI	-0.62	<0.001
DAS28	-0.58	<0.001
Swollen Joint Count ($SJC_{(28)}$)	-0.47	<0.001
Tender Joint Count ($TJC_{(28)}$)	-0.52	<0.001
Patient Global Assessment (PGA)	-0.55	<0.001
Evaluator Global Assessment (EGA)	-0.51	<0.001
CRP	-0.11	0.27
ESR	-0.09	0.34

Note: Correlations calculated using Pearson correlation coefficients. Negative values indicate an inverse relationship between serum 25(OH)D and disease activity measures.

DISCUSSION

In this study of patients with early rheumatoid arthritis, serum vitamin D deficiency was strongly associated with higher clinical disease activity, as reflected in CDAI and DAS28 scores. Although inflammatory markers (ESR, CRP) and serologic parameters (RF, anti-CCP) did not differ significantly between groups, vitamin D–deficient individuals consistently exhibited greater tender joint counts, higher swollen joint counts, and elevated global assessment scores. These findings reinforce the potential role of vitamin D as a determinant of disease severity in early RA.

The predominance of women in our cohort aligns with well-established epidemiologic patterns, wherein RA affects women approximately three times more frequently than men.[15] This gender distribution is consistent across Indian and global populations and supports the representativeness of our sample.

Multiple studies have reported a high prevalence of vitamin D deficiency among patients with RA. Meena et al. reported deficiency in 84% of Indian RA patients, with significant correlations between low vitamin D levels and elevated disease activity.[16] Rossini et al. and Franco et al. similarly found that hypovitaminosis D predicted greater baseline disease severity and poorer response to treatment.[8,9] Our findings are consistent with these observations, and the mean vitamin D levels in our deficient group (9.6 ng/mL) indicate profound deficiency within this rural cohort.

The robust inverse correlations observed between serum 25(OH)D levels and disease activity indices further support the association between vitamin D status and RA severity. Higher joint counts, increased PGA and EGA scores, and elevated composite indices among deficient patients collectively suggest that vitamin D may play a meaningful role in modulating disease activity during the early phase of RA.

The lack of significant differences in ESR, CRP, or serologic markers between groups highlights an important clinical nuance. While vitamin D deficiency appears to influence patient-reported outcomes, evaluator assessments, and joint involvement, it may not directly impact acute-phase reactants or autoantibody status. This distinction underscores the complex interplay between biochemical deficiency, immune dysregulation, and clinical manifestations.

Mechanistically, vitamin D exerts immunomodulatory effects through its interaction with vitamin D receptors (VDRs) expressed on dendritic cells, macrophages, and T lymphocytes.[4] Activation of these receptors suppresses pro-inflammatory Th1 and Th17 responses and promotes regulatory T-cell activity.[4,10] Deficiency may therefore impair immune regulation, enhance autoreactive T-cell responses, and potentiate synovial inflammation. These pathways offer a plausible explanation for the heightened disease activity observed in vitamin D–deficient patients.

The high prevalence of vitamin D deficiency in India, driven by limited sunlight exposure, skin pigmentation, and dietary insufficiency, further underscores the relevance of these findings.[11] Given the early stage of disease in our cohort, vitamin D supplementation may represent a simple, low-cost adjunctive strategy to improve outcomes, particularly in resource-constrained settings. However, longitudinal studies are needed to clarify whether correcting deficiency directly reduces disease activity.

Strengths of our study include the exclusive focus on early RA, the use of validated composite disease activity indices, and the biochemical confirmation of vitamin D status. Limitations include the modest sample size, single-centre design, and lack of longitudinal follow-up or assessment of treatment response. Additionally, potential confounders such as dietary intake, sun exposure, and seasonal variation in vitamin D levels were not evaluated.

In summary, our findings demonstrate a significant inverse association between serum vitamin D levels and disease activity in early RA within a rural Indian population. These results underscore the potential clinical value of assessing and addressing vitamin D deficiency as part of comprehensive RA management.

Limitations

This study has several limitations. First, it was conducted at a single tertiary-care center with a relatively small sample size, which may limit the generalisability of the findings. Second, factors such as seasonal variation, dietary intake, and sun exposure were not quantified, all of which could influence serum vitamin D concentrations. Finally, the cross-sectional design precludes causal inference; longitudinal and interventional studies are required to determine whether vitamin D supplementation directly reduces disease activity.

Clinical Implications and Future Directions

Despite these limitations, the findings carry meaningful clinical implications. Vitamin D deficiency is highly prevalent in India and globally, and our results suggest that it may contribute to greater disease severity in early RA. Routine assessment of vitamin D status at diagnosis and timely supplementation may represent simple, low-cost strategies to support disease control. Larger, multicentre prospective studies are required to validate these observations, clarify causal relationships, and explore the potential therapeutic benefits of vitamin D optimisation in RA management.

CONCLUSION

In this rural cohort of patients with early rheumatoid arthritis, vitamin D deficiency was significantly associated with higher clinical disease activity as assessed by validated indices. Although inflammatory and serologic markers were comparable between groups, the strong inverse relationship between serum 25(OH)D levels and disease activity highlights vitamin D deficiency as a potentially modifiable factor in RA management. Incorporating routine monitoring and correction of vitamin D status may offer clinical benefit, particularly in resource-limited settings.

REFERENCES

1. Deane KD, Demoruelle MK, Kelmenson LB, et al. Genetic and environmental risk factors for rheumatoid arthritis. Best Pract Res Clin Rheumatol. 2017;31(1):3-18. doi:10.1016/j.berh.2017.08.003
2. Malaviya AN, Kapoor SK, Singh RR, et al. Prevalence of rheumatoid arthritis in the adult Indian population. Rheumatol Int. 1993;13(4):131-134. doi:10.1007/BF00301258
3. Singh JA, Saag KG, Bridges SL Jr, et al. 2015 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. Arthritis Rheumatol. 2016;68(1):1-26. doi:10.1002/art.39480
4. Heidari B, Hajian-Tilaki K, Babaei M. Vitamin D deficiency and rheumatoid arthritis: epidemiological, immunological, clinical, and therapeutic aspects. Mediterr J Rheumatol. 2019;30(2):94-102. doi:10.31138/mjr.30.2.94
5. Kostoglou-Athanassiou I, Athanassiou P, Lyraki A, Raftakis I, Antoniadis C. Vitamin D and rheumatoid arthritis. Ther Adv Endocrinol Metab. 2012;3(6):181-187. doi:10.1177/2042018812471070
6. Kerr GS, Sabahi I, Richards JS, et al. Prevalence of vitamin D insufficiency/deficiency in rheumatoid arthritis and associations with disease severity and activity. J Rheumatol. 2011;38(1):53-59. doi:10.3899/jrheum.100516
7. Craig SM, Yu F, Curtis JR, et al. Vitamin D status and its associations with disease activity and severity in African

Americans with recent-onset rheumatoid arthritis. J Rheumatol. 2010;37(2):275-281. doi:10.3899/jrheum.090705
8. Rossini M, Bongi SM, Montagna GL, et al. Vitamin D deficiency in rheumatoid arthritis: prevalence, determinants, and associations with disease activity and disability. Arthritis Res Ther. 2010;12(6):R216. doi:10.1186/ar3195
9. Franco MD, Barchetta I, Iannuccelli C, et al. Hypovitaminosis D in recent-onset rheumatoid arthritis is predictive of reduced response to treatment and increased disease activity: a 12-month follow-up study. BMC Musculoskelet Disord. 2015;16:53. doi:10.1186/s12891-015-0505-6
10. Guo Q, Wang Y, Xu D, Nossent J, Pavlos NJ, Xu J. Rheumatoid arthritis: pathological mechanisms and modern pharmacologic therapies. Signal Transduct Target Ther. 2018;3:6. doi:10.1038/s41413-018-0016-9
11. Ritu G, Gupta A. Vitamin D deficiency in India: prevalence, causalities, and interventions. Nutrients. 2014;6(2):729-775. doi:10.3390/nu6020729
12. Aletaha D, Neogi T, Silman AJ, et al. 2010 rheumatoid arthritis classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Ann Rheum Dis. 2010;69(9):1580-1588. doi:10.1136/ard.2010.138461
13. Aletaha D, Smolen J. The Simplified Disease Activity Index (SDAI) and the Clinical Disease Activity Index (CDAI): a review of their usefulness and validity in rheumatoid arthritis. Clin Exp Rheumatol. 2005;23(5)(suppl 39):S100-S108.
14. Prevoo MLL, van 't Hof MA, Kuper HH, van Leeuwen MA, van de Putte LBA, van Riel PLCM. Modified disease activity scores that include twenty-eight-joint counts: development and validation in a prospective longitudinal study of patients with rheumatoid arthritis. Arthritis Rheum. 1995;38(1):44-48. doi:10.1002/art.1780380107
15. van Vollenhoven RF. Sex differences in rheumatoid arthritis: more than meets the eye. BMC Med. 2009;7:12. doi:10.1186/1741-7015-7-12
16. Meena N, Chawla SPS, Garg S, Chander R, Batta R, Thakur R. Assessment of vitamin D in rheumatoid arthritis and its correlation with disease activity. J Evid Based Med Healthc. 2018;9(1):54-58.