Original Article

Vitamin D Deficiency and Its Association with Musculoskeletal Pain

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Abstract

Background: Vitamin D plays a significant role in the mechanisms of bone metabolism and muscle function and has more recently been connected to chronic musculoskeletal pain associated with deficiency. The relationship between Vitamin D deficiency and musculoskeletal pain warrants further investigation, given conflicting prevalence estimates and variable outcomes with supplementation. **Material and Methods:** This cross-sectional observational study included 200 adults aged 18-65, of whom 120 had musculoskeletal pain and 80 were considered healthy, recruited from a tertiary care center between January 2024 and June 2025. Serum levels of 25-hydroxyvitamin D [25(OH)D] were analyzed using a chemiluminescent immunoassay. Vitamin D status was categorized as deficient (<20 ng/mL), insufficient (20-29 ng/mL), or sufficient (≥30 ng/mL). The Visual Analogue Scale (VAS) was used to rate pain intensity. The statistical analyses included Pearson's correlation and multivariate logistic regression. **Results:** Vitamin D deficiency was significantly more prevalent in patients with musculoskeletal pain (56.7%) than in controls (22.5%; $p < 0.001$). Additionally, mean serum 25(OH)D levels were lower in the pain group (17.8 ± 7.4 ng/mL) than in the control group (28.9 ± 8.2 ng/mL). There was a significant inverse relationship between vitamin D levels and pain severity ($r = -0.61$, $p < 0.001$). Independent predictors of deficiency included gender (OR 2.12; 95% CI 1.11– 4.03) and low UV exposure (OR 3.25; 95% CI 1.68–6.28). **Conclusion:** The prevalence of vitamin D deficiency is high among those with chronic musculoskeletal pain, and it is inversely related to the severity of pain. Regular screening and selective correction of deficiency may be helpful in the management of musculoskeletal pain of unknown origin.

Keywords: Vitamin D deficiency; Musculoskeletal pain; 25-hydroxyvitamin D; Pain severity; Sunlight exposure.

Received: 01 October 2025 **Revised: 25 October 2025** **Accepted: 12 November 2025** **Published: 18 December 2025**

Introduction

Vitamin D is essential for calcium homeostasis, bone mineralisation, and muscle function. Classic vitamin D deficiency is characterized by osteomalacia, bone pain, and proximal muscle weakness. Less overt vitamin D insufficiency has been associated with muscle performance and falls in adults and older adults.[1,2] The biological rationale for vitamin D's potential to modulate pain relates to its receptor expression in muscle and nervous system tissue, regulation of calcium-dependent processes, and immunomodulatory properties, particularly in relation to nociception and inflammatory pain pathways.[3,4]

Clinical and epidemiological studies document the high prevalence of low serum 25-hydroxyvitamin D (25[OH]D) in a variety of chronic musculoskeletal pain populations, including chronic widespread pain, low back pain, and myalgia; however, estimates of prevalence vary by both population and definition of vitamin D deficiency.[5,6] Multiple large cross-sectional studies and case series report an excess of vitamin D deficiency in patients with persistent musculoskeletal pain relative to general population studies, leading to the hypothesis that hypovitaminosis D is a modifiable contributor to pain burden.[7,8]

Still, the strength and consistency of these associations remain controversial. Meta-analyses and systematic reviews have been put forth in a contradictory fashion: some suggest increased odds of vitamin D deficiency among individuals with musculoskeletal pain and modest positive effects of supplementation in certain populations; others, on the other hand, are concluding that heterogeneity across the literature exists with marginal impact of treatment for nonspecific chronic pain.[2,3,8] Heterogeneity is likely present due to differences across studies in study design, baseline vitamin D status, phenotyping of pain (localized vs widespread), supplementation, and outcomes. The result is that it is difficult to draw causal relationships or recommendations.

Randomized trials provide further detail: Several RCTs report little or no overall benefit of vitamin D supplementation for chronic pain, but in some subgroup analyses, there is improvement in chronic pain from correction of deficiency, or with specific chronic pain phenotypes (such as some cohorts with back pain, or patients with severe deficiency).[5] Various contemporary reviews thus recommend targeted testing and replacement for patients with unequivocal deficiency and/or

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DOI:
10.21276/amit.2025.v12.i3.256

How to cite this article: Kumar D, Vijh V. Vitamin D Deficiency and Its Association with Musculoskeletal Pain. Acta Med Int. 2025;12(3):1206-1210.

musculoskeletal symptoms, while suggesting against routine high-dose supplementation for nonspecific chronic pain until better-quality evidence is collected.[5,8]

Given a plausible biological explanation, the high observed prevalence of deficiency among individuals with musculoskeletal pain, and the inconsistent results seen with intervention studies, clearly demonstrate the need for additional well-designed and adequately powered studies that (1) carefully phenotype pain, (2) recruit subjects with confirmed deficiency, (3) use a standardized supplementation regimen and validated pain outcome measures, and (4) evaluate mechanism-related biomarkers. This study is intended to contribute to that evidence base by brief statement of your study objective — e.g., "examining the association between serum 25(OH)D and musculoskeletal pain severity in a clinic-based cohort and examining pain change after a standardized vitamin D repletion".

Materials and Methods

Study Design and Participants: An observational cross-sectional study was conducted in the Department of Medicine at a tertiary care teaching hospital between January 2024 and June 2025. Two hundred adult patients (aged 18-65 years) who presented with musculoskeletal pain for at least 3 months were enrolled. Musculoskeletal pain was defined as pain affecting either muscles, bones, ligaments, or tendons without an identifiable inflammatory, infectious, or malignant cause.

Patients who had chronic kidney disease, chronic liver disease, endocrine disorders causing calcium metabolism dysfunction, current use of vitamin D or calcium supplementation in the last three months, or on medications interfering with vitamin D metabolism (e.g., glucocorticoids, anticonvulsants, or rifampicin) were excluded. Healthy controls with no musculoskeletal symptoms were recruited from hospital staff and attendants for comparison and matched to the cases based on age and sex.

Informed written consent was obtained from all participants before taking part in the study, and the institutional ethics review board approved the study protocol. In accordance with the Declaration of Helsinki, the identities of all participants were maintained in confidence.

Data Collection and Laboratory Analysis

All participants underwent a comprehensive clinical history and physical examination. Each participant's data included demographics (age, sex, BMI, occupation), pain duration and severity, and associated lifestyle factors (sun exposure, dietary habits, and intensity of physical activity). Pain was measured from a 10-point Visual Analogue Scale (VAS). Response codes were organized into mild (1–3), moderate (4–6), and severe (7–10) pain categories. Participants provided venous blood samples in the morning after an overnight fast. Serum concentrations of 25-hydroxyvitamin D [25(OH)D] were measured using chemiluminescent immunoassay (CLIA). Vitamin D status was classified by the Endocrine Society Clinical Practice Guidelines – Deficiency: <20 ng/mL, Insufficiency: 20–29 ng/mL, Sufficiency: >30 ng/mL. Additionally, to exclude secondary causes of bone pain, biochemical parameters were assessed, including serum calcium, phosphate, alkaline phosphatase, and parathyroid hormone (PTH).

Statistical Analysis: All analyses were performed using SPSS 26.0 (IBM Corp., Armonk, NY). Continuous variables are denoted as mean ± standard deviation (SD) and compared using an independent t-test or ANOVA, as appropriate. Categorical variables are presented as frequencies and percentages, and compared using chi-square tests. Pearson's correlation coefficient was used to assess serum 25(OH)D status in relation to pain severity (VAS scores). Logistic regression analyses were used to identify independent predictors of vitamin D deficiency among study subjects with musculoskeletal pain, while controlling for age, sex, BMI, and sunlight exposure. Statistical significance was determined as $p < 0.05$.

Results

Baseline Characteristics: 200 subjects participated in the study, including 120 with musculoskeletal pain (study group) and 80 healthy controls (comparison group). The mean age in the study group was 42.6 ± 11.3 years, with 64% of participants being female. BMI(Body Mass Index), occupational distribution, and mean sunlight exposure were statistically different between the study and comparison groups ($p < 0.05$).

[Graph 1] Average 25(OH)D in the study vs. control group: A bar graph displayed the significantly lower mean serum 25(OH)D levels in the musculoskeletal pain group (17.8 ± 7.4 ng/mL) than controls (28.9 ± 8.2 ng/mL, $p < 0.001$).

2. Vitamin D Status and Severity of Pain: Among musculoskeletal pain participants, 68 (56.7%) were defined as having vitamin D deficiency, 32 (26.7%) had insufficiency, and 20 (16.6%) had sufficient vitamin D status. Mean VAS pain values were significantly higher in the vitamin D deficiency group versus the other groups ($p < 0.001$).

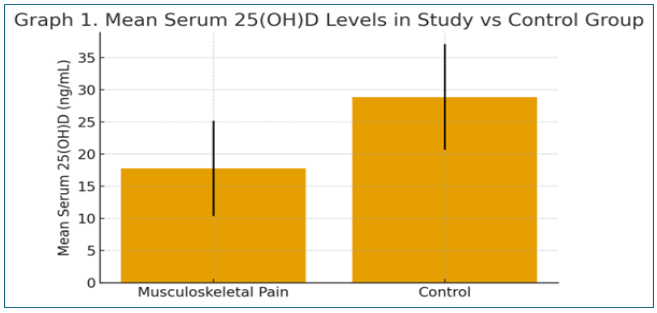


Table 1: Baseline characteristics of study and control groups

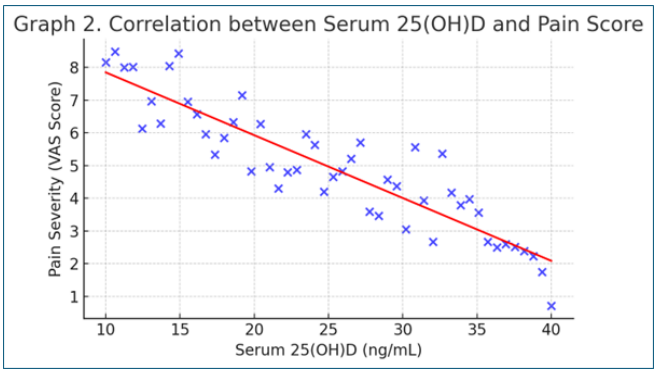
Variable	Musculoskeletal Pain Group (n=120)	Control Group (n=80)	p-value
Age (years, mean ± SD)	42.6 ± 11.3	41.1 ± 10.9	0.42
Female (%)	64 (53.3%)	36 (45%)	0.27
BMI (kg/m²)	26.9 ± 4.8	24.7 ± 4.3	0.01*
Mean sunlight exposure (hours/day)	0.9 ± 0.6	1.6 ± 0.7	<0.001*
Sedentary lifestyle (%)	70 (58.3%)	28 (35%)	0.004*

Table 2: Distribution of vitamin D status and pain intensity in the study group

Vitamin D Status	n (%)	Mean VAS Score ± SD	Pain Severity Category
Deficient (<20 ng/mL)	68 (56.7%)	7.4 ± 1.9	Severe
Insufficient (20–29 ng/mL)	32 (26.7%)	5.6 ± 1.5	Moderate
Sufficient (≥30 ng/mL)	20 (16.6%)	3.1 ± 1.2	Mild
Total	120 (100%)	—	—

Correlation analysis: Serum 25(OH)D levels showed a significant inverse correlation with VAS scores ($r = -0.61$, $p < 0.001$).

[Graph 2] Association between serum 25(OH)D and pain score: A negatively sloped scatter plot showing that greater serum vitamin D concentrations are associated with lower pain intensity (VAS score). Pearson correlation coefficient = −0.61 ($p < 0.001$).

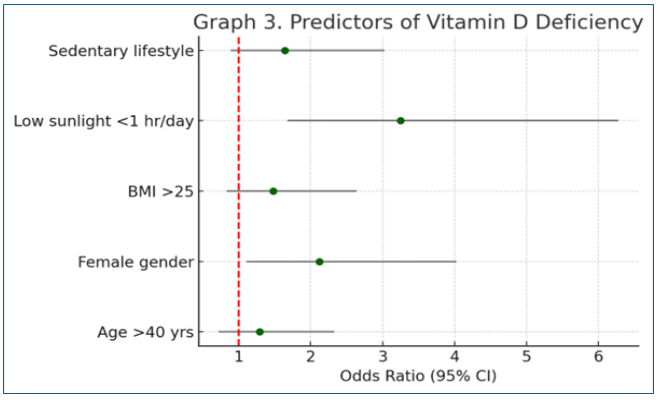


3. Biochemical Parameters and Predictors of Vitamin D Deficiency: Patients in both groups had serum calcium and phosphate levels that were within normal ranges. However, PTH levels were significantly higher in vitamin D–deficient patients. Logistic regression demonstrated low sunlight exposure (<1 hour/day) and female gender as independent predictors of vitamin D deficiency.

Table 3: Logistic regression analysis of predictors of vitamin D deficiency

Variable	Odds Ratio (OR)	95% Confidence Interval (CI)	p-value
Age >40 years	1.29	0.72–2.33	0.39
Female gender	2.12	1.11–4.03	0.02*
BMI >25 kg/m²	1.48	0.83–2.64	0.18
Sunlight exposure <1 hr/day	3.25	1.68–6.28	<0.001*
Sedentary lifestyle	1.64	0.89–3.02	0.10

[Graph 3] Variables that predict vitamin D deficiency (description of forest plot results): A forest plot provides a visual representation of odds ratios (ORs) for characteristics of vitamin D deficiency. The strongest predictors were low sunlight exposure (OR 3.25, 95% confidence interval (CI) 1.68-6.28) and female gender (OR 2.12, 95% CI 1.11-4.03).



Discussion

In this cohort examined in the clinic, we observed a high rate of vitamin D deficiency among patients with chronic musculoskeletal pain (56.7%), an inverse relationship between serum 25(OH)D and pain intensity ($r = -0.61$), and independent associations of deficiency with female sex and low exposure to sunlight. Our results generally support several other observational and intervention studies while also affirming the heterogeneity of the literature.

Several clinical trials and combined-modality studies have suggested an association between correcting vitamin D deficiency and reduced pain or improved function when vitamin D is used in combination with existing treatments. For example, a randomized trial of vitamin D supplementation combined with physiotherapy reported greater pain improvement than physiotherapy alone, suggesting supplementation may be a beneficial strategy to manage symptoms in patients with chronic musculoskeletal pain when deficiency is present.[9] This is consistent with our finding that pain severity was highest among those who were frank vitamin D deficient, and that modifiable exposures (sunlight) predicted deficiency.

Simultaneously, systematic reviews and pooled analyses have shown an inconsistent benefit from vitamin D supplementation in unselected populations with chronic pain. Multiple meta-analyses and narrative reviews have reported heterogeneity in RCT evidence and that, across the population, supplementation would not reliably reduce chronic pain outcomes without selecting for the deficiency at baseline.[10-12] This nuance resolves the apparent conflict in cross-sectional observational studies. Upon observational association of vitamin D being low in many people with pain, this does not mean that for everyone enhancement of pain will occur with supplementation at a population level, or even at an individual level with documented vitamin D deficiency, since a sufficient baseline level exists or pain's mechanism is unrelated to vitamin D biology.

Additionally, large high-quality meta-analyses assessing related musculoskeletal domains and outcomes have cautioned about broad expectations for musculoskeletal benefits from supplementation. That is, the pooled evidence, which merged all musculoskeletal endpoints (falls, fracture risk, Bone Mineral Density (BMD), and generalized musculoskeletal outcomes),

reported limited clinically meaningful effects of vitamin D alone overall in adult populations.[13] Therefore, our results—a strong inverse correlation observed in a clinic cohort selected for deficiency—warrant an approach to supplementation that is better characterized as targeted rather than universal. Assessment and treatment of deficiency should be made in individuals, particularly in cases of unexplained pain where other causes have been excluded.

Several recent single-site interventional studies and meta-analyses demonstrate pain improvement among certain subgroups (fibromyalgia, chronic widespread pain, or severely deficient members), again emphasizing the significance of baseline deficiency and pain phenotype.[14,15] Our observation that mean VAS scores were higher in severely deficient patient subgroups supports the potential subgroup signals. It suggests that future RCTs should preselect for deficiency and incorporate standardized dosing and validated pain-related outcomes.

The identification of female sex and reduced sunlight as independent predictors aligns with previous observational studies that have characterized demographic and lifestyle determinants of hypovitaminosis D and musculoskeletal pain.[16,17] Moreover, recent Mendelian and contemporary population studies suggest that population-wide supplementation will likely not yield substantial reductions in pain and depression; however, identifying members of the severely deficient subgroup for targeted correction may offer some improvement, underscoring the rationale for our targeted recommendation.[18]

Limitations: The cross-sectional design of this study does not permit causal inference. Whether low vitamin D causes pain, or whether pain-related behavior (i.e., less outdoor activity) causes low vitamin D, cannot be determined. We attempted to control for common confounders, but residual confounding is a possibility. Our sample was clinic-based and may not translate to a community sample. Finally, although our CLIA assay is widely used and recommended, variability between laboratories is known to occur; as a result, absolute values for 25(OH)D may differ from one laboratory to another.

Clinical and research implications: According to our data and the literature at the time of submission, it may be reasonable to routinely assess vitamin D in patients with unexplained chronic musculoskeletal pain, particularly when risk factors for deficiency are present (female sex, low sunlight exposure, higher BMI). Future interventional studies should enroll participants with documented deficiency, stratify participants by pain phenotype, apply standardized repletion protocols, and apply mechanistic biomarkers (PTH, inflammatory markers) to elucidate the pathways by which vitamin D may affect nociception. Taken together, our results add to the body of evidence that vitamin D deficiency is prevalent in people with musculoskeletal pain, and vitamin D repletion trials focused on patients with documented deficiency represent the next highest-value step.

Conclusion

This study reports a high prevalence of vitamin D deficiency among patients presenting with chronic musculoskeletal pain. There was also a notable negative relationship between serum 25(OH)D concentrations and pain severity. Deficiency was predominant among females and those with low sunlight exposure, two identifiable and modifiable lifestyle risk factors. These findings reiterate the accumulating evidence that vitamin D provides a contributory role in the pathophysiology of musculoskeletal pain. While causality cannot be inferred from this cross-sectional design, the overall association does lend support to routine evaluation of vitamin D status in patients experiencing chronic or unexplained musculoskeletal pain.

Given the inconsistent results from intervention trials, a targeted correction of vitamin D deficiency—testing and treating only those who are confirmed deficient—appears to be the most warranted overall approach. Future, larger, prospective randomized studies must be undertaken to determine whether correction of vitamin D deficiency results in clinically meaningful reductions in pain intensity or improvements in functional status. In summary, Vitamin D deficiency remains a relatively unrecognized yet potentially modifiable dietary risk factor for musculoskeletal pain and should be included as part of a comprehensive pain assessment algorithm, especially in those at risk.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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