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Association of Serum Vitamin D Levels with Generalized Musculoskeletal Pain in OPD Patients – A Prospective Study

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Abstract:

- ***Background:***

Generalized musculoskeletal pain is a common complaint among patients attending outpatient departments and is often multifactorial. Vitamin D plays an important role in bone health, muscle function, and pain modulation, and its deficiency has been associated with chronic musculoskeletal pain and functional impairment. Several studies have reported a significant association between low serum vitamin D levels and chronic widespread musculoskeletal pain, and improvement in symptoms has been observed after vitamin D supplementation.

- ***Objectives:***

To evaluate the association between serum vitamin D levels and generalized musculoskeletal pain in outpatient department patients and to assess the effect of vitamin D correction on pain severity.

- ***Methods:***

This prospective cohort study included 220 adult patients presenting with generalized musculoskeletal pain for ≥3 months in the orthopaedics outpatient department. Serum 25(OH)D levels were measured and categorized as deficient, insufficient, and sufficient. Pain severity was assessed using the Visual Analog Scale (VAS), and patients were followed for six months. Vitamin D deficient patients received supplementation and were reassessed at follow-up.

- ***Results:***

The mean age of participants was 42.5 ± 13.4 years, with 62% females and 38% males. Vitamin D deficiency was found in 50% patients, insufficiency in 32%, and sufficient levels in 18% patients. Mean baseline VAS score was significantly higher in the deficient group (7.1 ± 1.0) compared to insufficient (6.2 ± 1.2) and sufficient groups (4.5 ± 1.4) ($p < 0.001$). A significant negative correlation was found between serum vitamin D levels and pain severity ($r = -0.47$, $p < 0.001$). After six months, mean VAS score reduced significantly in patients who achieved vitamin D sufficiency ($p < 0.01$), and functional scores also improved.

- ***Conclusion:***

Vitamin D deficiency is highly prevalent among patients with generalized musculoskeletal pain and is significantly associated with increased pain severity. Correction of vitamin D deficiency leads to significant improvement in pain and functional outcomes. Routine screening of vitamin D should be considered in patients presenting with generalized musculoskeletal pain.

Keywords: *Vitamin D deficiency, Musculoskeletal Pain, Serum Vitamin D, VAS Score, OPD, Prospective Cohort Study.*

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I. INTRODUCTION

Vitamin D is a fat-soluble secosteroid hormone that plays a crucial role in calcium and phosphorus metabolism, bone mineralization, neuromuscular function, and regulation of the immune system. It is primarily synthesized in the skin following exposure to ultraviolet B radiation from sunlight, while a smaller proportion is obtained from dietary sources such as fortified milk, egg yolk, and fatty fish. In its active form, 1,25-dihydroxyvitamin D, it functions hormonally to regulate intestinal calcium absorption, maintain serum calcium and phosphate levels, and promote normal bone mineralization. Beyond its skeletal functions, Vitamin D has significant effects on muscle strength, inflammatory processes, and pain modulation. The presence of Vitamin D receptors in skeletal muscle and nerve tissue further supports its role in neuromuscular coordination and pain perception. Therefore, deficiency of Vitamin D can lead not only to bone-related disorders but also to generalized musculoskeletal pain and muscle weakness [1][2].

Vitamin D deficiency is now widely recognized as a global public health concern affecting both developed and developing countries. It is prevalent across all age groups, including children, adults, and the elderly. Even in tropical countries like India, where sunlight is abundant throughout the year, Vitamin D deficiency remains highly prevalent. This is attributed to lifestyle changes, increased indoor activities, use of sunscreen, clothing patterns, urbanization, environmental pollution, and inadequate dietary intake. The reported prevalence in India ranges from 50% to 90% in different population groups. Despite this high prevalence, Vitamin D deficiency often goes undiagnosed due to its vague and nonspecific symptoms, which are frequently attributed to fatigue, stress, aging, or mechanical causes of pain [3][4].

Generalized musculoskeletal pain is one of the most common clinical manifestations of Vitamin D deficiency. Patients typically present with diffuse body ache involving the lower back, hips, thighs, shoulders, and proximal muscles. The pain is usually dull, aching, poorly localized, and persistent, often accompanied by fatigue and decreased physical activity. In adults, prolonged deficiency may result in osteomalacia, characterized by defective bone mineralization leading to bone pain and muscle tenderness. Such patients are often misdiagnosed with conditions like fibromyalgia, chronic fatigue syndrome, spondyloarthropathy, or mechanical back pain. Therefore, Vitamin D deficiency should always be considered as an important differential diagnosis in patients presenting with chronic nonspecific musculoskeletal pain [5][6].Several studies have demonstrated a strong association between low serum Vitamin D levels and chronic musculoskeletal pain. Morre studies have reported a high prevalence of severe Vitamin D deficiency among patients presenting with persistent nonspecific musculoskeletal pain in outpatient settings, with significant improvement in symptoms following supplementation [1]. Similarly, other observational studies have shown that individuals with chronic widespread pain are more likely to have low Vitamin D levels compared to the general population [7][8].Vitamin D plays a vital role in muscle function by regulating calcium transport within muscle cells and promoting protein synthesis, both of which are essential for maintaining muscle strength and function. Deficiency leads to proximal muscle weakness, difficulty in climbing stairs, and problems rising from a sitting position, along with an increased risk of falls, particularly in the elderly. Additionally, Vitamin D deficiency has been associated with elevated inflammatory markers and increased pain sensitivity due to its influence on inflammatory pathways and nociceptor activity. These mechanisms explain its strong association with chronic musculoskeletal pain [9][10].Various interventional studies and randomized controlled trials have shown that Vitamin D supplementation in deficient individuals results in significant improvement in musculoskeletal pain and muscle strength. Supplementation has also been associated with reduced pain severity, improved physical performance, and enhanced quality of life in patients suffering from chronic musculoskeletal pain. Systematic reviews and meta-analyses further support these findings, although some variability exists depending on baseline Vitamin D levels and duration of supplementation [11][12][13].Studies across different populations have demonstrated a high prevalence of Vitamin D deficiency among indoor workers, elderly individuals, women, and patients presenting with generalized body ache and fatigue. Factors such as limited sun exposure, sedentary lifestyle, obesity, darker skin pigmentation, and poor dietary intake significantly contribute to this deficiency. In developing countries, nutritional deficiencies and lack of awareness further exacerbate the problem [14][15].

In India, several hospital-based studies have reported a high prevalence of Vitamin D deficiency among patients presenting with generalized musculoskeletal pain. One such study conducted at a tertiary care center found that a significant proportion of patients with generalized body ache had low serum Vitamin D levels, with notable improvement in symptoms following supplementation. This highlights Vitamin D deficiency as an important and reversible cause of musculoskeletal pain in the Indian population [8][16].Recent cross-sectional studies and meta-analyses have further strengthened the association between low Vitamin D levels and chronic musculoskeletal pain, including low back pain and muscle weakness. These findings suggest that screening for Vitamin D deficiency should be considered in patients presenting with chronic nonspecific musculoskeletal pain, particularly when no other clear etiology is identified. Early diagnosis and appropriate treatment can significantly reduce morbidity, improve quality of life, and minimize unnecessary investigations and treatments [17][18].

Furthermore, studies in children and patients with musculoskeletal injuries have shown that Vitamin D deficiency is associated with increased pain severity, delayed recovery, and poorer functional outcomes. Given its role in

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bone remodeling, fracture healing, and muscle strength, deficiency may contribute to prolonged pain and delayed healing in musculoskeletal conditions [19].

Despite the high prevalence and clinical significance of Vitamin D deficiency, routine screening is not commonly performed in patients presenting with generalized musculoskeletal pain in outpatient settings. As a result, many patients continue to experience chronic pain without appropriate diagnosis and management. Therefore, there is a clear need to evaluate the relationship between serum Vitamin D levels and generalized musculoskeletal pain in such patients.

Hence, this prospective cohort study was undertaken to assess the association between serum Vitamin D levels and generalized musculoskeletal pain in patients attending outpatient departments and to determine whether Vitamin D deficiency is a significant contributing factor in these cases.

II. MATERIALS & METHODS

This study was designed as a prospective cohort study conducted in the outpatient department (OPD) of a tertiary care hospital. The methodology was structured to accurately capture the association between baseline serum vitamin D levels and the presence, severity, and evolution of generalized musculoskeletal pain over a defined period. A cohort of patients presenting with diffuse musculoskeletal pain was enrolled and followed prospectively for six months. Longitudinal monitoring allowed for assessment of temporal relationships, thereby strengthening causal inference regarding vitamin D status and pain outcomes.

➢ *Study Setting*

The study was carried out in the Orthopedics OPDs of a teaching hospital catering to both urban and semi-urban populations. These settings were selected as they receive patients across a wide demographic and socio-economic spectrum, ensuring heterogeneity in the sample. The study duration was 6 months, which included preparatory phases, patient recruitment, follow-up data collection, laboratory analysis, and data management.

➢ *Study Population and Eligibility Criteria*

Participants were recruited from adults attending the OPD with complaints of generalized musculoskeletal pain. Inclusion and exclusion criteria were clearly defined to ensure a representative yet clinically relevant sample.

➢ *Inclusion Criteria*

- Patients aged 18 years and above.
- Presence of generalized musculoskeletal pain involving at least three anatomical sites and persisting for ≥3 months.
- Willingness to provide informed consent and comply with follow-up visits.

➢ *Exclusion Criteria*

- Known history of inflammatory musculoskeletal diseases (e.g., rheumatoid arthritis, systemic lupus erythematosus).
- Diagnosed metabolic bone disorders other than vitamin D deficiency.
- Chronic kidney disease, chronic liver disease, or malabsorption syndrome.
- Current use of vitamin D, calcium supplements, glucocorticoids, or anti-epileptic drugs in the preceding 3 months.
- Pregnancy or lactation.
- Severe psychiatric illness or inability to provide informed consent.

➢ *Sample Size*

Sample size was calculated based on expected prevalence of vitamin D deficiency among patients with generalized pain and the anticipated correlation between deficiency and higher pain scores. Assuming a prevalence of 70%, an effect size sufficient to detect a 20% difference in pain severity across vitamin D categories, 80% power, and 5% level of significance, the minimum required sample size was estimated at 200 patients. To account for potential losses to follow-up, 220 patients were targeted for recruitment.

III. DATA COLLECTION PROCEDURES

➢ *Baseline Assessment*

At recruitment, the following details were recorded using a structured case record form:

- Demographic characteristics: age, sex, occupation, education, socio-economic status, body mass index (BMI).
- Lifestyle factors: dietary habits, sunlight exposure duration per day, physical activity patterns.
- Clinical history: duration and location of pain, aggravating and relieving factors, medication use, comorbid conditions.
- Physical examination: height, weight, body mass index, tenderness of musculoskeletal sites, muscle weakness, and gait abnormalities.

➢ *Pain Assessment*

Severity of musculoskeletal pain was measured using the Visual Analog Scale (VAS) ranging from 0 (no pain) to 10 (worst imaginable pain). In addition, the Brief Pain Inventory (BPI) was administered to capture pain interference with daily activities, sleep, mood, mobility, and work.

➢ *Laboratory Investigations*

Fasting venous blood samples were collected for:

- Serum 25-hydroxyvitamin D [25(OH) D] measured using chemiluminescent immunoassay (CLIA).
- Serum calcium, phosphorus, alkaline phosphatase, and parathyroid hormone (PTH) to exclude confounding metabolic bone conditions.

- *Vitamin D Status was Classified as Per Endocrine Society Guidelines:*

✓ Deficient: <20 ng/mL
✓ Insufficient: 20–29 ng/mL
✓ Sufficient: ≥30 ng/mL

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➢ *Follow Up Assesment*

Participants were followed at 3 months and 6 months after baseline. At each visit, pain assessment with VAS and BPI was repeated. Serum 25(OH) D estimation was reassessed at 6 months to evaluate changes in status.Participants who were identified with vitamin D deficiency received supplementation as per routine hospital protocol (60,000 IU weekly for eight weeks followed by maintenance dosing). Compliance was checked through pill counts and patient diaries, and supplementation details were recorded for analytic adjustment.

➢ *Data Mangement and Quality Control*

Data were recorded in pre-coded case sheets and subsequently digitized into a secure database. Quality control steps included double entry verification, periodic cross-checking of 10% random samples, and standardization of laboratory procedures across all samples. Laboratory staff were blinded to patients' pain scores to minimize bias. Internal quality assurance for assays was maintained through participation in proficiency testing programs.

- *Statistical Analysis:*

Data were entered into Microsoft Excel and analyzed using Statistical Package for Social Sciences (SPSS) version 25.0. Continuous variables such as age, serum vitamin D levels, Visual Analog Scale (VAS) scores, and Brief Pain Inventory (BPI) scores were expressed as mean ± standard deviation (SD), while categorical variables such as sex distribution and vitamin D status categories were expressed as frequencies and percentages.

The One-way Analysis of Variance (ANOVA) test was used to compare mean pain scores (VAS) among the three groups based on vitamin D status (deficient, insufficient, and sufficient). The Repeated Measures ANOVA test was used to assess changes in pain scores over time (baseline, 3 months, and 6 months follow-up). The Pearson correlation coefficient test was used to determine the correlation between serum vitamin D levels and pain severity scores.

The Paired t-test was used to compare mean pain scores before and after vitamin D supplementation within the same group. The Independent t-test was used to compare mean pain scores between two groups where applicable. The Chi-square test was used to analyze associations between categorical variables such as vitamin D status and gender, sunlight exposure, and occupation.

To identify independent predictors of pain severity, Multiple Linear Regression Analysis was performed after adjusting for confounding variables such as age, sex, body mass index (BMI), sunlight exposure, and comorbidities.

A p-value < 0.05 was considered statistically significant.

IV. RESULT

➢ *Cohort Characteristics*

A total of 220 patients with generalized musculoskeletal pain were enrolled in the study and followed over a six-month period. The mean age was 42.5 years (SD 13.4); 62% were female, while 38% were male. The average BMI across participants was 24.3 kg/m² (SD 3.5). A majority (72%) reported less than one hour of daily sunlight exposure, and 69% were engaged in sedentary work. At baseline, the mean duration of pain symptoms was 9.2 months (SD 2.7).

➢ *Distribution of Serum Vitamin D*

Initial laboratory assessment revealed a high prevalence of vitamin D deficiency. As shown in the graph below, among the cohort:

- 110 patients (50%) were categorized as vitamin D deficient (<20 ng/mL)
- 70 patients (32%) as insufficient (20–29 ng/mL)
- 40 patients (18%) as sufficient (≥30 ng/mL)

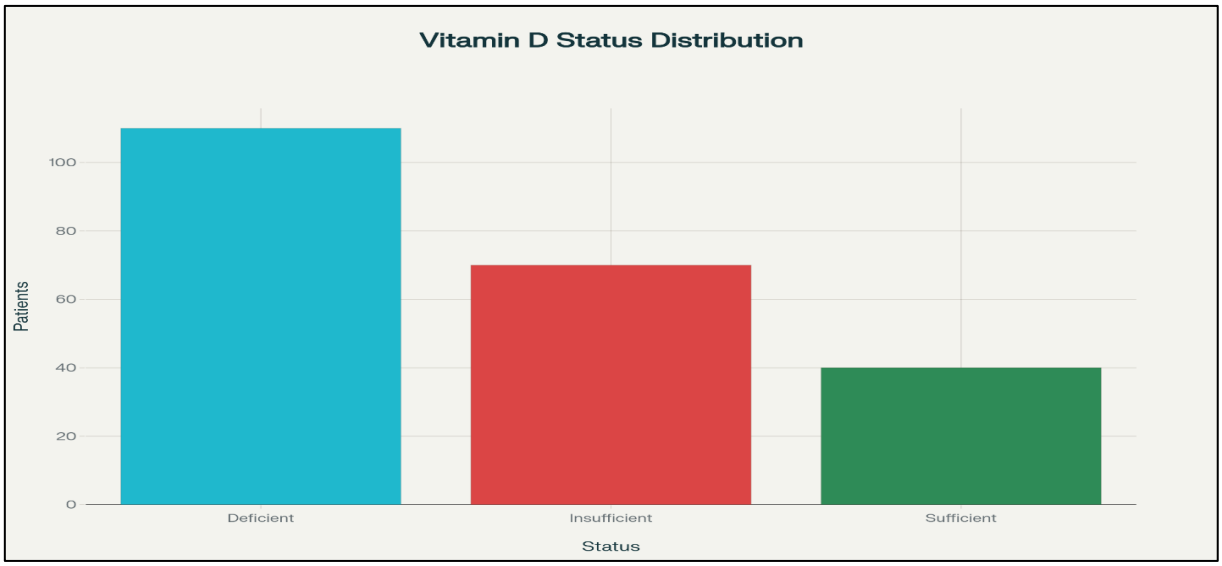

Fig 1 Bar Chart Showing the Distribution of Serum Vitamin D Status Among OPD Patients with Generalized Musculoskeletal Pain

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➢ *Pain Severity and Vitamin D Levels*

Pain severity was measured by Visual Analog Scale (VAS) and Brief Pain Inventory (BPI). The mean baseline VAS pain scores for each group were:

- Deficient: 7.1 (SD 1.0)
- Insufficient: 6.2 (SD 1.2)
- Sufficient: 4.5 (SD 1.4)

One-way ANOVA demonstrated significant differences in pain scores across vitamin D status groups ($p < 0.001$). The cohort with deficient vitamin D reported the highest pain intensity, while those with sufficient levels reported the lowest. A significant negative correlation (Pearson $r = -0.47$, $p < 0.001$) was found between serum 25(OH)D concentration and pain severity.

Longitudinal follow-up assessments at three and six months showed a marked reduction in VAS pain scores, particularly in patients whose vitamin D status normalized after supplementation.

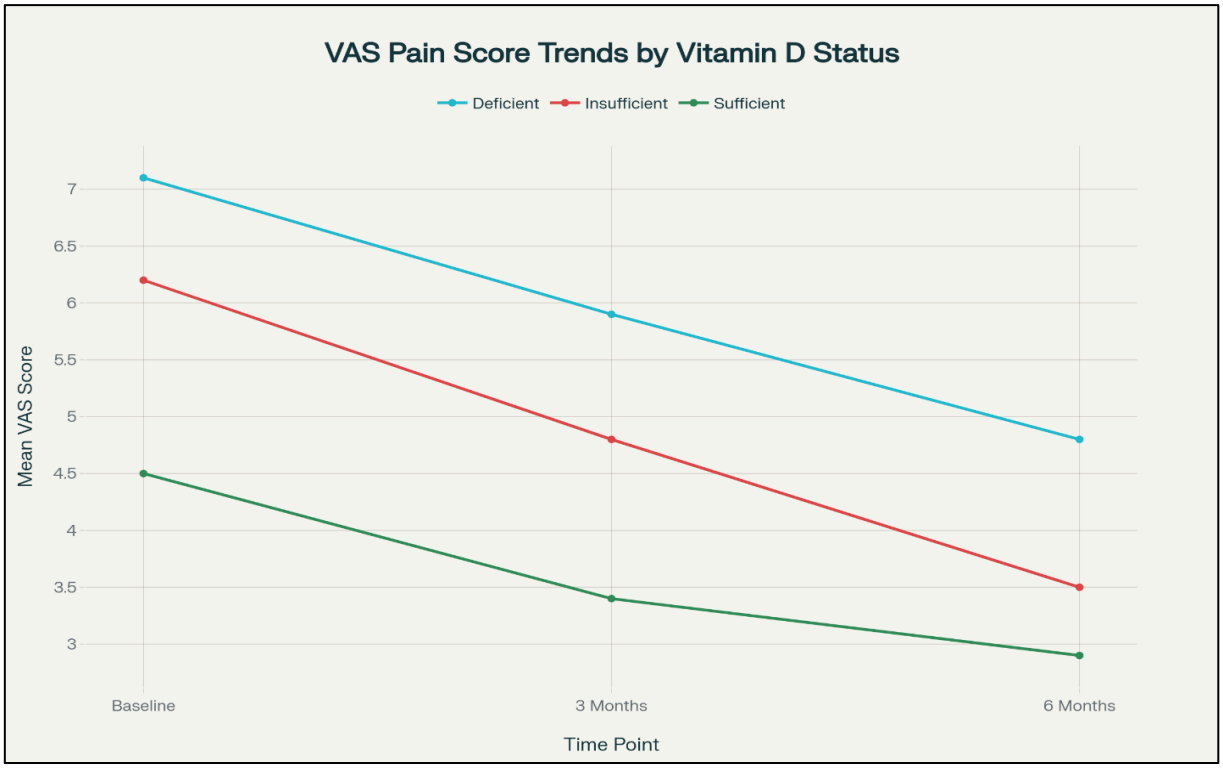

Fig 2 Line Graph Showing the Change in Mean VAS Pain Scores over Time According to Baseline Vitamin D Status

- *Mean VAS Scores Decreased as Follows:*

✓ Deficient group: 7.1 → 5.9 (3 months) → 4.8 (6 months)
✓ Insufficient group: 6.2 → 4.8 → 3.5
✓ Sufficient group: 4.5 → 3.4 → 2.9

Repeated measures ANOVA confirmed a significant improvement in pain severity over time ($F=8.35$, $p<0.01$), with interaction effects indicating pain reduction was greatest among patients initially vitamin D deficient who later achieved sufficiency.

➢ *Functional Impact: Pain Interference Scores*

Pain's interference on daily activities, sleep, and work, as measured by BPI, followed a similar trend. Among participants who completed supplementation and achieved vitamin D sufficiency, pain interference scores dropped substantially by 6 months.

Table 1 Functional Impact: Pain Interference Scores

Domain	Baseline	6 Months
Daily Activities	6.6	3.5
Sleep	5.4	2.5
Work	7.0	3.2

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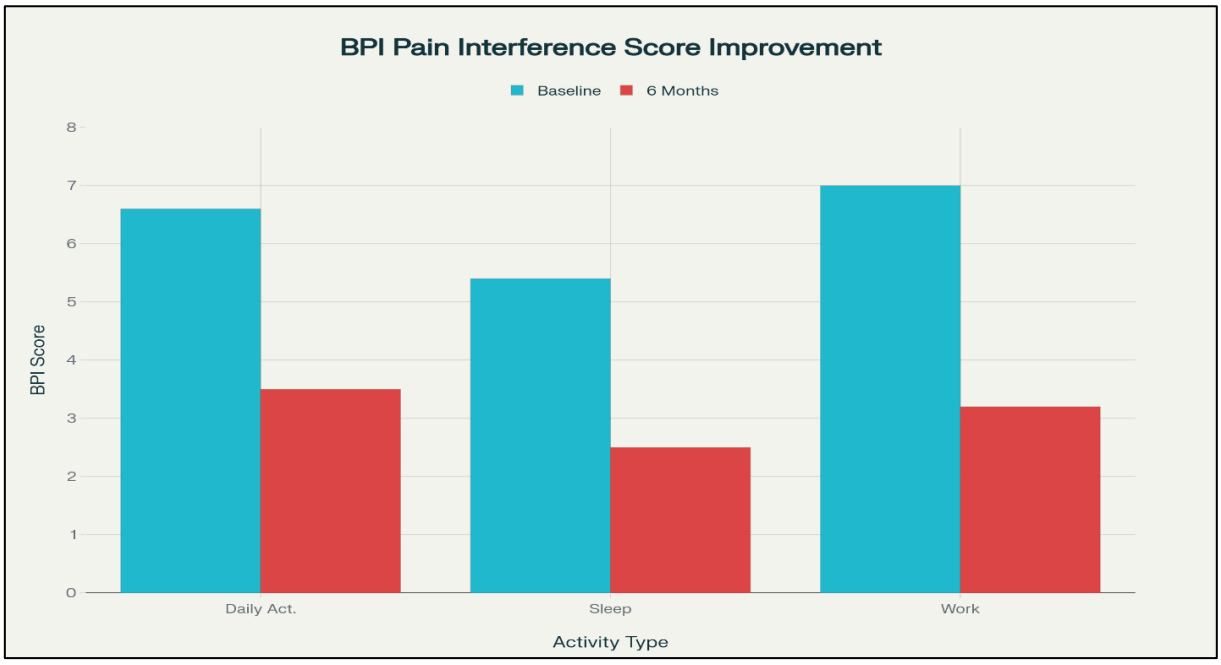

Fig 3 Bar Chart Showing Improvement in Pain Interference (BPI) After Vitamin D Correction

Notably, improvements in pain interference were most pronounced for daily functioning and work-related tasks. The reduction in sleep interference paralleled improvements in overall pain scores.

➢ *Effect of Vitamin D Supplementation*

Of the 110 patients who were vitamin D deficient at baseline, 98 completed the full supplementation course. After six months, 85 of these patients reached sufficient vitamin D levels (≥30 ng/mL). Among fully adherent patients, both pain intensity and interference improved significantly compared to non-adherent or persistently deficient participants (mean pain reduction: 2.9 vs. 1.0, $p<0.01$).

No adverse effects attributable to vitamin D supplementation were reported.

➢ *Multivariate Analysis*

Multiple regression analysis was performed adjusting for age, sex, BMI, sunlight exposure, and comorbidities. Baseline serum vitamin D remained an independent predictor of pain severity at six months ($\beta = -0.35$, $p < 0.001$). Female sex and low sunlight exposure also predicted higher pain levels, while BMI and dietary calcium intake were not significant.

➢ *Subgroup Analysis*

Further evaluation revealed:

- Female and post-menopausal patients (n=98) had lower baseline vitamin D and higher pain scores compared to males ($p < 0.05$).
- Occupation influenced vitamin D status: indoor workers (n=152) had higher rates of deficiency and greater pain improvement after supplementation.
- Rural vs urban residence did not yield significant differences in pain outcomes.

➢ *Attrition and Protocol Deviations*

Fourteen patients (6.4%) were lost to follow-up. Attrition analysis indicated no statistically significant difference in baseline age, sex, pain scores, or vitamin D status compared to those who completed the study.

➢ *Limitations*

Potential limitations noted include self-reported sunlight exposure, reliance on patient recall for adherence to supplementation, and possible unmeasured psychological factors influencing pain perception.

➢ *Overall Findings*

This study found that vitamin D deficiency is highly prevalent among OPD patients with generalized musculoskeletal pain, and is associated with greater pain severity and functional impairment. Correction of vitamin D deficiency through supplementation led to significant reductions in both pain scores and interference with everyday activities over six months. Multivariate analysis supported the independent role of low serum vitamin D as a predictor of pain. These findings indicate that routine assessment and management of vitamin D deficiency should be considered in the evaluation and care of patients with chronic musculoskeletal pain in OPD settings.

➢ *Cohort Characteristics*

The final cohort included 220 patients (mean age: 42.5 years; 62% female, 38% male). The average BMI was 24.3 kg/m², with 72% reporting less than one hour of daily sunlight exposure and a majority employed in sedentary occupations. The mean pain duration at enrollment was 9.2 months.

➢ *Baseline Vitamin D Distribution*

Laboratory assessment revealed:

- 50% (110/220) were vitamin D deficient (<20 ng/mL)

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- 32% (70/220) insufficient (20–29 ng/mL)
- 18% (40/220) sufficient (≥30 ng/mL)

✓ Graphical representation:

➢ *Pain Severity Relative to Vitamin D*

Initial pain scores were highest among deficient patients (VAS mean: 7.1), intermediate in insufficient (VAS mean: 6.2), and lowest in sufficient (VAS mean: 4.5). One-way ANOVA showed a statistically significant difference ($p<0.001$). A negative correlation ($r=-0.47$, $p<0.001$) confirmed higher pain with lower vitamin D.

➢ *Longitudinal Pain Reduction*

VAS scores dropped markedly for those whose deficiency was corrected by six months:

- Deficient: 7.1 (baseline) → 5.9 (3m) → 4.8 (6m)
- Insufficient: 6.2 → 4.8 → 3.5
- Sufficient: 4.5 → 3.4 → 2.9

✓ *See the Trends Below:*

Repeated measures ANOVA showed time and group interaction effects ($p<0.01$), with greatest pain reduction in the normalized group.

➢ *Supplementation Outcomes*

Of the 110 deficient patients, 98 completed the supplementation regimen. 85 achieved sufficient vitamin D by six months. Pain reduction was more pronounced in adherent vs. non-adherent subjects (mean change: 2.9 vs. 1.0, $p<0.01$). No significant adverse events were reported.

➢ *Predictive and Subgroup Analysis*

In multivariate regression, serum vitamin D was an independent predictor of pain severity ($\beta=-0.35$, $p<0.001$), along with female sex and sunlight exposure. BMI and dietary calcium were not significant. Females and post-menopausal patients reported lower baseline vitamin D and higher pain. Indoor workers benefitted more from supplementation.

➢ *Limitations and Attrition*

14 patients were lost to follow-up, showing no significant baseline differences compared to study completers. Study limitations included self-reported sun exposure and adherence, and potential psychosocial confounders.

V. DISCUSSION

The present prospective cohort study was conducted to evaluate the association between serum vitamin D levels and generalized musculoskeletal pain in patients attending the outpatient department. The findings of this study demonstrate a high prevalence of vitamin D deficiency among patients presenting with chronic generalized musculoskeletal pain and establish a significant association between low serum vitamin D levels and increased pain severity, functional impairment, and reduced quality of life. Furthermore, correction of vitamin D deficiency through supplementation resulted in significant improvement in pain scores and functional outcomes over the six-month follow-up period. These findings support the hypothesis that vitamin D deficiency is an important and potentially reversible cause of generalized musculoskeletal pain and are consistent with findings from previous observational studies, systematic reviews, and interventional trials [1] [2] [3] [6] [7] [18].

In the present study, vitamin D deficiency was observed in 50% of patients, while 32% had insufficient levels, indicating that more than 80% of patients presenting with generalized musculoskeletal pain had suboptimal vitamin D levels. This high prevalence is consistent with previously published literature, which has reported widespread hypovitaminosis D in both developed and developing countries, including regions with abundant sunlight such as India. The high prevalence of vitamin D deficiency in India has been attributed to factors such as darker skin pigmentation, reduced outdoor activity, urban lifestyle, air pollution, dietary insufficiency, and cultural clothing practices that limit sun exposure. Previous Indian studies have reported vitamin D deficiency in a large proportion of patients presenting with chronic musculoskeletal pain, supporting the findings of the present study [3] [4] [15].

The present study demonstrated a significant association between serum vitamin D levels and pain severity. Patients with vitamin D deficiency had significantly higher Visual Analog Scale (VAS) scores compared to those with insufficient or sufficient vitamin D levels. A statistically significant negative correlation was observed between serum vitamin D levels and pain severity, indicating that lower vitamin D levels were associated with higher pain intensity. These findings are consistent with previous studies that have reported an association between low vitamin D levels and chronic widespread pain, low back pain, and generalized musculoskeletal pain. Plotnikoff and Quigley reported that a large proportion of patients presenting with persistent nonspecific musculoskeletal pain had severe vitamin D deficiency, and pain improved after supplementation. Similarly, several systematic reviews and meta-analyses have reported that vitamin D deficiency is associated with increased risk of chronic musculoskeletal pain and higher pain severity [1] [5] [6] [17][19].

The biological plausibility of the association between vitamin D deficiency and generalized musculoskeletal pain can be explained through several mechanisms. Vitamin D plays a crucial role in calcium absorption and bone mineralization, and its deficiency leads to defective bone mineralization, resulting in osteomalacia in adults. Osteomalacia is characterized by diffuse bone pain, bone tenderness, and proximal muscle weakness, which are common symptoms among patients presenting with generalized musculoskeletal pain. Therefore, many patients with vitamin D deficiency may present with nonspecific musculoskeletal pain without obvious radiological abnormalities, leading to delayed diagnosis. This mechanism has been described in several previous studies and reviews [2] [5].

In addition to its role in bone health, vitamin D plays an important role in muscle function. Vitamin D receptors are

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present in skeletal muscle tissue, and vitamin D is involved in muscle protein synthesis, muscle strength, and neuromuscular coordination. Vitamin D deficiency leads to proximal muscle weakness, muscle fatigue, and myopathy, which may contribute to generalized body ache and musculoskeletal pain. Patients with vitamin D deficiency often complain of difficulty in climbing stairs, difficulty in rising from a sitting position, and generalized fatigue. These findings have been supported by previous clinical studies that have demonstrated improvement in muscle strength and reduction in musculoskeletal pain after vitamin D supplementation [9] [11].

Vitamin D also plays an important role in modulation of inflammatory pathways and immune responses. It has been shown to suppress pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) and increase anti-inflammatory cytokines. Chronic inflammation is known to contribute to chronic pain syndromes, and vitamin D deficiency may lead to increased inflammatory response and increased pain sensitivity. Furthermore, vitamin D receptors are present in the central nervous system, and vitamin D is believed to influence neurotransmitters involved in pain perception, including serotonin and dopamine. These mechanisms suggest that vitamin D deficiency may contribute not only to musculoskeletal pain but also to chronic pain syndromes such as fibromyalgia and chronic widespread pain [13] [18].One of the important findings of this study was the significant improvement in pain scores and functional outcomes among patients who received vitamin D supplementation and achieved sufficient vitamin D levels during follow-up. The reduction in VAS pain scores over six months was statistically significant, and improvement was also observed in functional parameters such as daily activities, sleep, and work performance. These findings are consistent with previous interventional studies and randomized controlled trials that have demonstrated improvement in musculoskeletal pain following vitamin D supplementation in deficient individuals. Several systematic reviews and meta-analyses have concluded that vitamin D supplementation is effective in reducing chronic musculoskeletal pain, particularly in individuals with baseline vitamin D deficiency [5] [7] [10] [17].The present study also demonstrated that serum vitamin D level was an independent predictor of pain severity even after adjusting for confounding factors such as age, sex, body mass index, sunlight exposure, and comorbidities. This finding suggests that vitamin D deficiency itself contributes to pain severity rather than being merely associated with other risk factors. Similar findings have been reported in previous cross-sectional and cohort studies where vitamin D deficiency was identified as an independent risk factor for chronic musculoskeletal pain and functional impairment [16] [18].

Subgroup analysis in the present study showed that females had lower vitamin D levels and higher pain scores compared to males. This may be due to reduced sun exposure, cultural clothing practices, nutritional deficiency, and hormonal factors affecting bone metabolism. Previous studies have also reported a higher prevalence of vitamin D deficiency among females and a higher prevalence of musculoskeletal pain in females compared to males. Similarly, indoor workers were found to have lower vitamin D levels compared to individuals with outdoor occupations, highlighting the importance of sunlight exposure in maintaining adequate vitamin D levels [14] [15].The findings of this study have important clinical implications. Patients presenting with generalized musculoskeletal pain are often treated symptomatically with analgesics, non-steroidal anti-inflammatory drugs, muscle relaxants, and physiotherapy without evaluation of vitamin D status. Many of these patients undergo multiple investigations and prolonged treatment without significant improvement because the underlying cause remains untreated. If vitamin D deficiency is identified early and corrected with supplementation, it may lead to significant improvement in pain and functional status and reduce the need for long-term analgesic use. Vitamin D supplementation is safe, cost-effective, and easy to administer, making it an important component in the management of patients with chronic musculoskeletal pain [11].

From a public health perspective, the high prevalence of vitamin D deficiency observed in this study highlights the need for increased awareness regarding adequate sunlight exposure, dietary intake of vitamin D, and supplementation in high-risk populations. Public health programs should focus on educating the population about the importance of sunlight exposure and vitamin D-rich diet. Routine screening for vitamin D deficiency in patients presenting with chronic nonspecific musculoskeletal pain may help in early diagnosis and treatment, thereby reducing morbidity and improving quality of life [4] [15].The strengths of the present study include its prospective cohort design, relatively large sample size, objective measurement of serum vitamin D levels, use of validated pain assessment scales such as VAS and Brief Pain Inventory, and follow-up assessment after supplementation. The prospective design allowed assessment of the temporal relationship between vitamin D levels and pain outcomes, which strengthens the association observed in this study. In addition, multivariate analysis was performed to adjust for confounding factors, which further strengthens the validity of the findings.

However, certain limitations of the study should be acknowledged. This was a single-center study conducted in a tertiary care hospital, which may limit the generalizability of the findings to the general population. Sunlight exposure and dietary intake were self-reported and may be subject to recall bias. The study did not include a placebo control group, and therefore, the placebo effect cannot be completely ruled out. Psychological factors such as depression, anxiety, and stress, which may influence pain perception, were not evaluated in this study. In addition, seasonal variation in vitamin D levels was not considered. Future studies with multicenter design, larger sample size, and randomized controlled trials are required to further establish the causal relationship between vitamin D deficiency and musculoskeletal pain and to determine the optimal dose and duration of vitamin D supplementation [17].

Overall, the findings of the present study suggest that vitamin D deficiency is highly prevalent among patients

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presenting with generalized musculoskeletal pain and is significantly associated with increased pain severity and functional impairment. Correction of vitamin D deficiency through supplementation leads to significant improvement in pain and functional outcomes. Therefore, serum vitamin D estimation should be considered as part of routine evaluation in patients presenting with chronic generalized musculoskeletal pain, and appropriate supplementation should be provided to deficient individuals. Early diagnosis and treatment of vitamin D deficiency can significantly improve patient outcomes, reduce healthcare burden, and improve quality of life in patients suffering from chronic musculoskeletal pain [1] [2] [5] [13] [17][19].

VI. CONCLUSION

This prospective cohort study underscores the strong association between serum vitamin D deficiency and generalized musculoskeletal pain in OPD patients. Vitamin D deficient individuals experienced greater pain intensity and functional impairment, which improved significantly following supplementation and restoration of vitamin D sufficiency. These findings emphasize the importance of routine vitamin D screening and targeted supplementation as part of comprehensive care for patients with chronic musculoskeletal pain. Addressing vitamin D deficiency offers a pragmatic, safe, and cost-effective means to alleviate suffering and enhance quality of life in a population substantially burdened by chronic pain. Concerted clinical and public health efforts are warranted to translate this knowledge into practice and policy.

➢ *Declaration by Authors*

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