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# Combatting Fatigue and Bone Pain: The Impact of Vitamin D Treatment in the General Practice Setting

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**Abstract**

Vitamin D deficiency is a global health problem associated with chronic musculoskeletal pain. Addressing this deficiency is vital for managing pain and fatigue syndromes. Objective: To assess if treating vitamin D deficiency in patients with persistent unspecific pain of the muscular and skeletal system reduces symptoms. Methods: This study involved 80 patients in Tripoli, Libya, suffering long-term, unexplained bone and muscle pain receiving treatment at primary health care centers. Vitamin D levels were measured, injections were administered to those with deficiencies, followed by blood levels and pain severity assessments. Eighty participants (18 men, 62 women) were studied. Mean serum vitamin D levels increased from 8.4 to 36.1 post-treatment. The average age was 38.9 ± 7 years (range 18-70). Pre-treatment levels were 11.1 in men and 7.6 in women, rising to 28.9 in men and 38.5 in women. A significant reduction in chronic non-specific bone pain was noted, with serum levels improving from 8.4 ± 7.4 to 36.11 ± 5.1 (79) = -16.6, $p<0.001$. Participants with chronic fatigue and muscle pain had low vitamin D levels, which significantly improved after treatment. More research is needed to determine how optimal vitamin D levels can reduce fatigue, chronic bone pain, and muscle weakness. Routine vitamin D deficiency testing should be standard for individuals with chronic pain, particularly those experiencing bone pain and fatigue. Public education on the importance of vitamin D, its natural food sources, and the benefits of sunlight exposure is crucial for increasing levels.

**Keywords:** Vitamin D deficiency, Chronic pain, Musculoskeletal pain, Fatigue, Intervention studies.

## INTRODUCTION

Vitamin D deficiency is a prevalent issue affecting populations worldwide, particularly in sunny regions where higher vitamin D levels might be expected. Alarmingly, studies suggest that between 44% and 95% of individuals in many countries such as Saudi Arabia, Egypt, and India are vitamin D deficient, with many having circulating levels of serum 25(OH)D lower than the critical limit of 20ng/mL (Holick, 2007; Lotfi et al., 2007).

This deficiency is often exacerbated by cultural practices that limit sun exposure, particularly for women who cover most of their skin with clothing (Micka, 2014). Additionally, dietary habits significantly contribute to vitamin D levels, because many people do not consume enough vitamin D foods, which can lead to various health complications, including chronic pain syn-

dromes and other systemic diseases (Sichert-Hellert et al., 2006).

The implications of vitamin D deficiency extend beyond musculoskeletal health, with research suggesting its involvement in the pathogenesis of numerous disorders, including cardiovascular diseases, autoimmune conditions, and metabolic disorders (Pittas et al., 2006). Furthermore, Vitamin D deficiency is often linked to unspecific symptoms such as fatigue and generalised myalgia, which can lead to misdiagnosis of conditions like fibromyalgia or chronic fatigue syndrome (Holick, 2003).

Given the complex role of vitamin D in health, this study aims to investigate the correlation between vitamin D levels and chronic pain, focusing on how addressing vitamin D deficiency may alleviate symptoms and improve overall health outcomes.

## MATERIALS AND METHODS

### Study design

A cross-sectional vitamin D study was conducted on 80 adults (age range: 21-65 years) attending the Arada Polyclinic for non-specific musculoskeletal pain and fatigue. Chronic conditions that affect vitamin D absorption, such as hepatic and renal disease, or drugs such as steroids and antiepileptic drugs that can affect vitamin D levels, were excluded from the study.

### Data collection

The methodology included a comprehensive questionnaire that collected demographic information, medical history, and symptoms related to fatigue and musculoskeletal pain.

### Study duration and follow-up

The study, conducted from January to September 2019, began with the collection of data on vitamin D deficiency levels over the first three months. Patients followed up four weeks after receiving their initial treatment dose and continued to be monitored for three additional months to complete their treatment course.

### Serum 25(OH) D measurement

Blood samples were analyzed for serum 25-hydroxyvitamin D (25(OH)D) levels, the primary indicator of vitamin D status due to its 2-3 week half-life, reflecting skin synthesis and diet absorption. At the visit's end, a 5 mL blood sample was collected from each participant. All tests for 25-OH vitamin D were done in the clinical lab using an ELISA kit. Participants were classified by vitamin D levels, with deficiency set as a serum concentration below 20 ng/ml.

### Vitamin D treatment

Patients were advised to receive an intramuscular injection of active vitamin D3 at a dose of 200,000 IU on the same day their suboptimal serum vitamin D levels were confirmed. They were instructed to return for a follow-up after four weeks, during which their symptom improvement would be assessed, and a second dose of vitamin D3 would be administered. The treatment regimen consists of three monthly doses of 200,000 IU intramuscular injection (IM).

### Sunlight and diet questionnaire

The study aimed to link vitamin D deficiency with symptom prevalence, considering factors like skin pigmentation, which affects vitamin D synthesis by influencing UVB ray absorption. Participants reported their sun exposure habits, which are vital for vitamin D production, with recommendations of 5-30 minutes of sun exposure at least twice a week. Regarding dietary habits, participants categorized their consumption of vitamin D-rich foods (e.g. fish and milk) as never, yes, or specify-

ing the frequency. Additionally, the regular use of multivitamin supplements containing vitamin D was noted.

**Data management and analysis**

Questionnaire and clinical data were entered into a Microsoft Access database and analyzed using SPSS version 16. Quantitative data were reported as mean ± SD and qualitative data were shown as counts and percentages.

An independent samples t-test with $p < 0.05$ compared results before and after treatment, while serum vitamin D and bone pain changes were evaluated using a paired t-test. Patients were informed about the study's objectives, especially regarding vitamin D levels, and encouraged to attend follow-ups. Informed consent was collected from all participants, ensuring voluntary participation and data confidentiality.

## RESULTS

A study of eighty patients with fatigue and musculoskeletal pain revealed significant vitamin D deficiency in the entire cohort. The demographic analysis showed that the predominant age group was 18 to 30 years, accounting for 30% of the participants (Table 1).

**Table (1):** Distribution of study participants by age group

| Age group by years | No | (%) |
|---|---|---|
| 18-30 | 24 | 30% |
| 31-40 | 20 | 25% |
| 41-50 | 18 | 22.5% |
| 51-60 | 16 | 20% |
| 61-70 | 2 | 2.5% |
| Total | 80 | 100% |

Notably, there was a higher prevalence of female patients, with 62 out of the 80 participants being female. It also evaluated the distribution of patients with various comorbid conditions, especially diabetes and hypertension. A key aspect of the research was to assess the link between low serum vitamin D and vitamin-rich food intake, such as seafood and dairy. Patients consuming sufficient amounts of these foods had higher serum vitamin D than those who did not. Additionally, sunlight exposure for over an hour daily significantly raised serum vitamin D levels.

An evaluation of patients' knowledge regarding natural sources of vitamin D revealed that only 26 participants were aware of the importance of sunlight as a source. A mere 10 patients recognized dietary sources of vitamin D. The predominant type of pain reported was nonspecific musculoskeletal pain, affecting 55% of the patients (Table 2).

To assess the impact of vitamin D treatment on patients' symptoms, a t-test was employed, yielding statistically significant results ($t = -16.6$). Mean serum vitamin D levels rose from 8.4 ng/mL to 36.4 ng/mL after treatment, demonstrating the effectiveness of supplementation for deficiency symptoms. Results are in Table 3.

**Table (2):** Impact of Vitamin D Treatment on Demographic Parameters: A Comparative Analysis

| Variables | Distribution details | No. | Percentage change % | Pre-treatment mean | Post-treatment mean |
|---|---|---|---|---|---|
| Gender | Male | 18 | 22.5 | 11.1 ±5.9 | 28.9 ±1.2 |
| | Female | 62 | 77.5 | 7.6 ±4.0 | 38.5 ±1.5 |
| | Total | 80 | 100 | 8.4 ±4.7 | 36.4 ±1.5 |
| Daily exposure to sunlight | One hour | 32 | 40% | 11.6 ± 5.3 | 35.6 ± 1.8 |
| | Less than 1 hour | 48 | 60% | 6.3 ±2.8 | 36.9 ± 1.2 |
| | Total | 80 | 100 | 8.4 ±4.7 | |
| Usages of sunscreen | Yes | 12 | 15% | 5.5 ± 2.8 | 36.2 ± 6.3 |
| | No. | 68 | 85% | 8.9 ± 4.8 | 36.4 ± 1.6 |
| | Total | 80 | 100% | 8.4 ±4.7 | 36.4 ±1.5 |
| Multivitamin supplements | Yes | 18 | 22.5% | 14.8 ± 4.6 | 38.4 ± 1.6 |
| | No. | 62 | 62.5% | 6.6 ± 2.8 | 35.8 ± 1.4 |
| | Total | 80 | 100% | 8.4 ±4.7 | 36.4 ±1.5 |
| Dairy products intake | Non | 18 | 22.5 | 5.6 ±3.2 | 35.9 ±1.2 |
| | weekly | 48 | 60 | 8.6 ±3.8 | 36.5 ±1.4 |
| | Daily | 14 | 17.5 | 11.2 ±7.1 | 36.3 ±1.9 |
| | Total | 80 | 100 | 8.4 ±4.7 | 36.4 ±1.5 |
| Seafood Consuming | Non | 18 | 22.5 | 4.6 ± 2.1 | 34.8 ± 1.3 |
| | Once | 38 | 47.5 | 8.0 ± 3.7 | 35.8 ± 1.5 |
| | >Once | 24 | 30 | 12 ±5.1 | 38.4 ± 1.6 |
| | Total | 80 | 100 | 8.4 ±4.7 | 36.4 ±1.5 |
| Chronic bone pain | Chronic nonspecific bone pain | 44 | 55% | 8.4± 5.1 | 36.7± 1.5 |
| | Leg pain | 16 | 20% | 9.4± 5.6 | 37.1± 1.6 |
| | Back pain | 20 | 22% | 7.6± 2.9 | 35.1± 1.3 |
| | Total | 80 | 100% | 8.4± 4.7 | 36.4± 1.5 |

**Table (3):** T-test applied to investigate if chronic pain improvement after vitamin D Treatment:

| T-test | Treatment | No. | Mean | + SD | P value | t | df |
|---|---|---|---|---|---|---|---|
| | before | 80 | 8.46 | 4.77 | | | |
| | After | 80 | 36.40 | 15.14 | 0.001 | -16.6 | 79 |

*M*= mean
*SD*= standard deviation
The result showed that the amount of $t_{(79)}$ is (t= -16.6) and the result was statistically significant $p < 0.001$, which is less than 0.05. Thus, the findings are statistically different.

## DISCUSSION

Recent research has focused on vitamin D deficiency and its effects on fatigue and musculoskeletal pain. This study focused on the improvement in chronic bone pain and fatigue following vitamin D fortification and treatment of vitamin D deficiency. Several studies have shown a strong correlation between low levels of vitamin D and an increase in the severity of fatigue symptoms. For example, a retrospective observational study of 98 patients demonstrated that improvement in fatigue was significantly more common in those who received vitamin D supplementation versus placebo, with rates of 72% versus 50% ($P < 0.01$) (Nowak et al., 2016).

This finding is consistent with other studies that have reported similar improvements in fatigue symptom scores following the normalisation of vitamin D levels with supplementation (Khan et al., 2010). The mechanisms underlying these improvements are complex. Vitamin D is essential for various physiological functions, including immune response and muscle regulation (Holick, 2011). A study of 174 adults found that supplementing deficient vitamin D significantly reduced fatigue severity, indicating its role in energy metabolism and muscle performance. (Roy et al., 2014). In

addition, vitamin D receptors are present in various tissues, including skeletal muscle, which may explain the observed improvements in muscle pain and weakness following treatment (Vasquez et al., 2004). In addition, our study showed that the prevalence of vitamin D deficiency is particularly high in certain populations, such as women and those with limited sun exposure. This finding is consistent with our previous study and other studies that have reported marked vitamin D deficiency due to lifestyle or clothing choices (Al-Graiw et al., 2020; Hatun et al., 2005; Mallah et al., 2011). Studies indicate that conservative clothing choices among adolescent girls in Turkey are linked to lower vitamin D levels, while men, who generally participate in more outdoor activities, tend to have higher levels of this essential nutrient (Hatun et al., 2005).

This gender difference in vitamin D status may worsen the prevalence of fatigue and musculoskeletal pain in women. Research shows that over 90% of female patients with low vitamin D experienced relief from pain and muscle weakness after treatment (Jalili et al., 2015; Shipton & Shipton, 2015). Thus, vitamin D deficiency is a significant contributor to fatigue and musculoskeletal pain, and normalizing vitamin D levels through supplementation can alleviate these symptoms. Routine screening for vitamin D deficiency in patients reporting fatigue and pain is essential, prompting healthcare providers to prioritize vitamin D status in managing these common issues (Jalili et al., 2015).

Vitamin D is vital for muscle function and pain relief. This might explain why women suffering from pain and fatigue often improve with increased vitamin D levels (Bertone-Johnson & Manson, 2012). Our study demonstrated that vitamin D supplementation significantly elevated levels from 8.4 ng/mL to 36.4 ng/mL across all patient groups, highlighting its effectiveness in alleviating deficiency-related symptoms. Indeed, Vitamin D, as explained by Di Molfetta et al. (2024), helps alleviate fatigue by reducing oxidative stress and inflammation, which are major contributors to fatigue. It does this by lowering levels of oxidative molecules and inflammatory cytokines, regulating neurotransmitters such as dopamine and serotonin, and improving mitochondrial function in the muscles, thereby increasing energy production and overall well-being.

## CONCLUSION

Addressing low vitamin D levels, especially in women, is crucial for alleviating these health concerns. The current study underscores the importance of vitamin D in managing fatigue and musculoskeletal pain symptoms and highlights the need for proper diet and sunlight exposure to maintain adequate vitamin D levels.

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## ETHICS AND CONSENT

All trial participants were informed about the study's goals and procedures, including vitamin D levels at various stages. They were urged to attend follow-ups to monitor changes. Informed consent was obtained to confirm their understanding, voluntary participation, and assurance that data would be used solely for research.

**Duality of interest:** The authors declare that they have no duality of interest associated with this

manuscript.

**Author contributions:** Contribution was equal between authors**.**

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