

Prevalence of Vitamin D Deficiency in Nonspecific Musculoskeletal Pain

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Abstract

Background: Vitamin D deficiency is common in all age groups throughout the world, and results in abnormalities in calcium, phosphorus and bone metabolism that can lead to muscle weakness, osteomalacia and osteopenia.

Objectives: This study was designed to investigate the prevalence of vitamin D deficiency in patients with nonspecific pain for whom no specific causes such as trauma, infection, tumor, and inflammatory disorders could be identified.

Patients and Methods: This cross-sectional study included 438 patients with nonspecific musculoskeletal pain seen at our clinic. After evaluating their vitamin D status, we treated two groups of patients: those with vitamin D deficiency (< 20 ng/mL) and those with insufficiency (20 - 29 ng/mL). We treated our patients with 50,000 units of vitamin D every week for 6 - 8 weeks. After treatment we evaluated pain relief of patient and level of 25 hydroxi vitamin D.

Results: A total of 438 patients (52 men and 386 women) participated in the study. There was no statistically significant correlation between sex and symptoms. Deficiency was more frequent in females but the difference compared to males was not statistically significant. Approximately half of the patients (47%) comprised the vitamin D-deficient group. Most patients (86.5%) had insufficient or deficient levels (< 30 ng/mL) of vitamin D. The most prevalent vitamin D status in men was insufficiency, whereas the most prevalent status in women was deficiency. Spearman's correlation coefficient showed weak positive correlations between vitamin D status and the number of pregnancies ($r = 0.14$). More than 90% of our patients reported that pain and muscle weakness responded to treatment after 3 weeks.

Conclusions: Because osteomalacia is a common cause of persistent, nonspecific musculoskeletal pain, screening all patients with these symptoms for hypovitaminosis D should be standard practice in clinical care.

Keywords: Musculoskeletal Pain, Prevalence, Vitamin D, Vitamin D Deficiency

1. Background

Vitamin D deficiency is common throughout the world, and can result in abnormalities in calcium, phosphorus and bone metabolism. These abnormalities lead to muscle weakness, osteomalacia and osteopenia (1, 2).

The major source of vitamin D in humans is endogenous production by sunlight. A limited number of foods contain vitamin D such as fish oil, salmon and fortified foods (3, 4).

Vitamin D that is ingested or produced in skin is transferred to the liver, where it is hydroxylated to the most frequent metabolite, 25 hydroxi (OH) vitamin D. For the active form of vitamin D to be produced, 25 OH vitamin D must be further hydroxylated to 1, 25 (OH) 2 vitamin D in the kidneys (5). Hydroxylation in the kidneys is regulated by many factors and enhanced by parathyroid hormone, hypocalcemia and hypophosphatemia (6).

The active form of vitamin D [1, 25 (OH) 2 vitamin D] performs many functions involved in gene transcription via a vitamin D receptor in the nucleus (7). Via this nuclear receptor the active form of vitamin D in the small intestine increases calcium absorption from 10% - 15% to 30%

- 40% and increases phosphorus absorption from 60% to 80% (4). One of the most important functions of vitamin D is to maintain calcium and phosphorus within normal levels, which are important for neuromuscular functioning and bone metabolism (8, 9).

Although 1, 25 (OH) 2 vitamin D is the active form of vitamin D, it may be normal in vitamin D-deficient persons. The best way to evaluate vitamin D status in patients is to measure 25 OH vitamin D (10).

According to the endocrine society, a serum level of 25 OH vitamin D of 20 ng/mL or less indicates vitamin D deficiency; 21 - 29 ng/mL indicates insufficiency and a concentration of 30 ng/mL or higher is considered sufficient (11). These criteria apply to both children and adults. It is believed that the optimum serum level of 25 OH vitamin D for skeletal and nonskeletal functions is 40 - 60 ng/mL, and that up to 100 ng/mL is safe (12).

A serum concentration of 25 OH vitamin D of at least 20 ng/mL is required to maintain parathyroid hormone (PTH) within the normal range and this hormone is required for bone and muscle functioning and to prevent

osteomalacia (13). Vitamin D insufficiency can result in secondary hyperparathyroidism, increased bone resorption and increased low-energy trauma fracture (14). In secondary hyperparathyroidism, serum calcium levels are maintained by the resorption of calcium from bone and increased phosphorus loss in the kidneys (15). Osteoclastic activity, which is stimulated by PTH, can result in decreased bone mineral density and osteopenia (16).

Increased phosphorus loss due to secondary hyperparathyroidism leads to an inadequate Calcium/Phosphorus (Ca/P) ratio and mineralization defects in the skeleton. In children the growth plate is open and produces cartilage to be mineralized, so this mineralization defect can lead to rickets (17, 18). In adults the growth plate is closed and mineral levels in the skeleton are adequate to prevent deformity. As a result, mineralization defects can lead to osteomalacia which often remains undiagnosed. Osteomalacia causes diffuse or localized pain and muscle weakness.

2. Objectives

The present study was designed to investigate the prevalence of vitamin D deficiency in patients with nonspecific diffuse or localized pain for whom no specific causes such as trauma, infection, tumor, and inflammatory disorders could be identified.

3. Patients and Methods

This cross-sectional study included 438 patients with nonspecific musculoskeletal pain who were seen at the orthopedic surgery clinic of Shahid Mohammadi hospital, affiliated with Hormozgan university of medical sciences in Bandar Abbas, Iran, from March to October 2014.

This study was approved by ethic committee of our university. These patients did not respond to usual treatment modes such as nonsteroidal anti-inflammatory drugs or physiotherapy. We used "vitamin D" to refer to vitamin D2 (ergocalciferol) and vitamin D3 (cholecalciferol) (Figure 1). 25 hydroxy vitamin D and 1, 25 dihydroxy vitamin D include vitamin D2 and D3 metabolites (19).

After taking personal data and number of pregnancies in women, the patient's history and physical examination was recorded. X-ray and laboratory tests for exclusion of specific causes of pain such as trauma, tumor, infection or inflammatory causes and 25 OH vitamin D were requested. The inclusion criterion (in addition to nonspecific musculoskeletal pain that did not respond to the usual treatments) was absence of any of the following: anatomical abnormalities, injuries such as fractures, tumors, trauma, infection or inflammatory disease. The above-mentioned differential diagnosis was ruled out by laboratory tests and X-ray. Patients with history of trauma, surgery or specific cause of pain were excluded from the study. The patients' symptoms were categorized as low back pain, unilateral knee pain, bilateral knee pain, bilateral knee pain and low back pain, miscellaneous pain and diffuse pain. Patients with diffuse pain had pain at more than two sites. After

evaluating their vitamin D status, we divided the patients into vitamin D deficient (< 20 ng/mL), insufficient (20 - 29 ng/mL) and sufficient groups (30 - 100 ng/mL).

All patients in the vitamin D deficient and insufficient groups were treated with 50,000 IU vitamin D every week for 6 weeks in the insufficient group and 8 weeks in the deficient group. After treatment, patients were evaluated clinically for relief of pain and the level of vitamin D was measured. All statistical analyses were performed using SPSS version 20 (IBM Corporation, Armonk, NY) software.

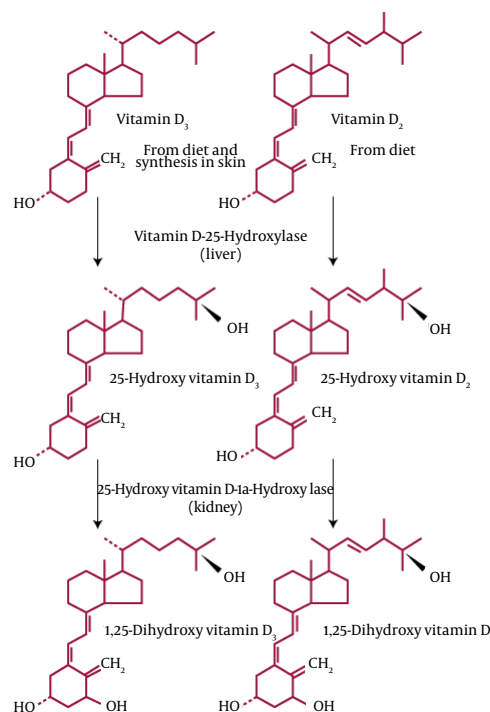


Figure 1. Vitamin D2 and D3 and Hydroxylation to the Active Metabolite

4. Results

A total of 438 patients (52 men and 386 women) participated in the study. Mean age was 37.8 (\pm 15.6) years (range 2 - 78 years); 11.9% of the participants were men and 88.1% were women. Mean age in men was 27.9 \pm 20.2 years, and mean age in women was 39.17 \pm 14.4 years. The age difference between sexes was statistically significant ($P < 0.05$).

In the entire sample of patients, the average vitamin D concentration was 16 \pm 13.7 ng/mL. This value was slightly higher in men (16.27 \pm 11.3 ng/mL) than in women (15.97 \pm 14 ng/mL), but the difference was not significant.

The prevalence of vitamin D deficiency was 47% (308 cases), and mean age in this subgroup was 34.6 \pm 13.8) years. The prevalence of vitamin D insufficiency was 39.5% (173 cases); mean age in this subgroup was 38.7 \pm 16.5 years. The prevalence of vitamin D sufficiency was 13% (57 cases), with a mean age in this subgroup of 46.7 \pm 15.4 years. The positive correlation between age and vitamin D status was weak but statistically significant ($r = 0.26$, $P < 0.001$).

Table 1. Distribution of Vitamin D Status in Men and Women in the Present Sample^a

Gender	Vitamin D Status			Total
	Deficient	Insufficient	Sufficient	
Male	38.5	48	13.5	100
Female	48.7	38.3	13	100
Total	47	39.5	13.5	100

^aData are presented as percent.

Table 2. Correlation Between Vitamin D Status and Pregnancy^a

Vitamin D Status	Pregnancies	Live Born	N
Deficient	2.64	2.31	188
Insufficient	3.09	2.72	148
Sufficient	4.46	3.76	50
Total	3.05	2.65	386

^aValues are presented as mean number.

Table 3. Correlation Between Symptom Categories and Sex^a

Gender	LBP	UKP	BKP	BKP/LBP	Mis P	Dif P	Total
Male	11.5	11.5	26.9	1.9	13.6	34.6	100
Female	20.2	13.2	24.1	6.2	3.6	32.7	100
Total	19.2	13.0	24.4	5.7	4.8	32.9	100

Abbreviations: BKP, bilateral knee pain; Dif P, diffuse pain; LBP, low back pain; Mis P, miscellaneous pain; UKP, unilateral knee pain.

^aData are presented as percent.

Table 1 shows the frequency of each vitamin D status in men and women. Overall, vitamin D status was less than sufficient (29 ng/mL) in 86.5% of the patients.

The most prevalent vitamin D status in men was insufficiency, whereas the most prevalent status in women was deficiency. However, the differences between sexes in the frequency distribution of each type of vitamin D status were not statistically significant.

The number of pregnancies reported by women in this study ranged from 1 to 13, with a mean of 2.6 ± 2.7 . The mean number of live born children was 2.3 ± 2.3 . Spearman's correlation coefficient showed weak positive correlations between vitamin D status and the number of pregnancies ($r = 0.14$) and between vitamin D status and the number of live born children ($r = 0.15$) ($P < 0.05$). Table 2 shows the associations between vitamin D status and the number of pregnancies and live born children.

The most frequent symptom in both women and men was diffuse pain and the most frequent symptom in this group was knee pain.

More than 60% of patients had knee pain (unilateral, bilateral, bilateral + lower back pain, and patients with diffuse pain who had knee pain). There was no statistically significant difference between women and men in the frequency distribution of different symptoms (Table 3).

5. Discussion

Almost half of our patients (45%) were vitamin D deficient and 39.5% had vitamin D insufficiency. In 86.5% of our participants, serum vitamin D levels were below the amount considered sufficient. Plotnikoff et al. (20), in a cross-sectional study between 2000 and 2002 of 150 patients with persistent, nonspecific musculoskeletal pain, found that 93% (140/150) of the participants had deficient levels of vitamin D. In a study by McCarty et al. of 153

patients with nonspecific musculoskeletal pain, 54% of patients had vitamin D deficiency (21). In a study of 360 patients with low back pain in Saudi Arabia, Al Faraj et al. founds that 83% of patients had abnormally low levels of vitamin D (22).

Gannage-Yared and coworkers (23) studied the relationship between hypovitaminosis D and some lifestyle factors such as style of clothing and dwelling on 316 Lebanese volunteers (99 men and 217 women between 30 - 50 years). They measured serum calcium, phosphor, albumin, alkaline phosphatase, 25 OH vitamin D, PTH, osteocalcin, and urinary free deoxypyridinoline (DPD). They assessed vitamin D intake of their population. Mean level of vitamin D was 9.7 ± 7.07 ng/mL. hypovitaminosis D [25 OH vitamin D < 12 ng/mL] affected 72.8% of their population. According to endocrinology society (25 OH vitamin D < 20 ng/mL have deficiency and between 20 - 30 ng/mL are insufficient) more than 90% of their population had hypovitaminosis D. They found reverse relationship between 25 OH vitamin D and PTH and free DPD, and weak positive relationship with osteocalcin. They found 25 OH vitamin D was higher in men, in urban subjects and in nonveiled women (23).

Influence of clothing has been studied in Saudi Arabia and Kuwait (24, 25). Deficiency was more common in veiled women compared to nonveiled women.

We treated our patients with 50,000 units of vitamin D every week for 6 - 8 weeks. More than 90% of our patients reported that pain and muscle weakness responded to treatment after 3 weeks.

Osteomalacia is a common cause of persistent, nonspecific musculoskeletal pain. Screening all patients with this type of pain for hypovitaminosis D should be standard practice in clinical care. We found that women, despite childbearing and breastfeeding, had the same mean concentration of vitamin D as men. Patients in the vita-

min D sufficient group were older than those in the insufficient and deficient groups. This result suggests that younger persons in our setting, who use more measures to avoid exposure to sunlight or have different life style or dietary habits, are more prone to vitamin D deficiency.

Because of life style and dietary habits and the low vitamin D content in the diet, osteomalacia is common. In addition to calcium metabolism and bone turn-over, vitamin D contributes in lowering the risk of overall mortality, cancer, diabetes, autoimmune disease, cardiovascular disease, hypertension, sleep disorders and musculoskeletal disorders (26-31). Future research should be done to determine the prevalence of vitamin D deficiency in the general population. This would be a first step toward measures to improve public health care for musculoskeletal functioning, cardiovascular, autoimmune and neoplastic disease. Because of the high prevalence of vitamin D deficiency in patients with nonspecific musculoskeletal pain, we suggest that vitamin D should be measured in all patients with musculoskeletal pain. Because the habitual diet consumed by our participants does not cover the recommended vitamin D requirements, we suggest that foods such as milk, yogurt or cereals should be fortified with vitamin D.

A potential limitation of our study is the difference in the number of women and men who participated. This makes it difficult to compare the findings in the two sexes.

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Footnote

Authors' Contribution: Study concept and design: Mehrdad Bahrabadi and Alireza Jalili; analysis and interpretation of data: Shahram Zare, and Alireza Jalili; drafting of the manuscript: Alireza Jalili, and Mehrdad Bahrabadi; critical revision of the manuscript for important intellectual content: Alireza Jalili.

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