

## Review Article

# VITAMIN D AND ITS IMPLICATION IN NEUROFIBROMYALGIA

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### ABSTRACT

New and emerging roles of Vitamin D are being uncovered, except for its known traditional roles in bone mineralisation and calcium metabolism. Evidences associating it with cell proliferation and multiplication have linked with its potential role in cancer causation and treatment modality. Vitamin D is also finding its importance in mental disorders, proper immune functioning, and cognitive performances. Here we present a review article on association of Vitamin D with common but infrequently diagnosed cases non specific musculoskeletal pain, Neurofibromyalgia.

### INTRODUCTION

It is a long established fact that vitamins are essential to health. Among them, vitamin D is unique in its role because of the diverse sources available, new researches which are expanding our knowledge of the metabolic functions and physiologic needs. Normal physiological role of this vitamin is not limited to the traditional calcium and bone metabolism. New and promising fields of interest are arising towards its role in cancer, immune functions, cognitive functions, mental well being, and non-specific musculoskeletal pain, fibromyalgia.

#### Functions of vitamin D—traditional

Vitamin D is best known for its role in tightly regulating serum calcium levels by enhancing calcium absorption and increasing bone resorption, as part of a process involving parathyroid hormone (PTH). Vitamin D stimulates intestinal calcium absorption.<sup>1</sup> Without Vitamin D, only 10 to 15% of dietary calcium and about 60% of phosphorus are absorbed. Vitamin D sufficiency enhances calcium and phosphorus absorption by 30–40% and 80%, respectively.<sup>2,3</sup>

Thus, classic vitamin D deficiency results in bone demineralization, which can ultimately lead to rickets in children and osteomalacia or osteoporosis

in adults. As calcium also helps maintain muscle strength, vitamin D deficiency results in leg muscle weakness and an increase in falls in older people.

#### Functions of vitamin D—emerging

Extensive research is uncovering other non-traditional functions and benefits of vitamin D in the body. Significance of non-traditional roles emerged when it was discovered that cells other than the kidney could make the active form of vitamin D for their own use. In these cells, calcitriol acts to regulate gene expression. Those areas with the most substantiation are summarized below.

##### a. Cancer

Vitamin D insufficiency affects normal cellular proliferation and differentiation and may thus affect risk of cancer. Observational evidence suggests that people who get little or no exposure to sun tend to have higher rates of breast, colon and prostate cancer; some experts believe this is the result of marginal vitamin D status.<sup>4</sup> The strongest evidence for a

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protective effect of vitamin D against cancer is with colorectal cancer. Not only do rates of colorectal cancer rise with increasing distance from the equator, but higher serum 25(OH)D and higher vitamin D intakes are independently associated with lower risk.<sup>5,6</sup>

#### **b. Cognitive Performance**

Emerging evidence suggests vitamin D may play a role in cognitive performance. Cross-sectional studies in older adults show vitamin D deficiency is associated with low mood and worsened cognitive performance, as well as greater severity of dementia.<sup>7</sup>

#### **c. Immune Function**

Vitamin D insufficiency has been linked to an increased risk of tuberculosis and pneumonia, bacterial infections of the lungs and gingivitis. The active form of vitamin D<sub>3</sub>, calcitriol, is believed to mediate immunological effects by binding to nuclear vitamin D receptors present in most immune cells, which in turn increases expression of defensive genes.

#### **d. Periodontal Disease**

There is some evidence that poor vitamin D status is linked to higher risk of periodontal disease, a common chronic inflammatory disease leading to tooth loss. Studies have found that supplementation with vitamin D and calcium reduced tooth loss in older persons and it is also believed that vitamin D may also reduce periodontal disease through its anti-inflammatory effect.

#### **Vitamin D and Fibromyalgia**

The association between low levels of 25-hydroxyvitamin D and non-specific musculoskeletal pain, including fibromyalgia (FM), is although controversial.<sup>8-13</sup> The involvement of 1, 25-OH D in immune system regulation could therefore link muscle pain with vitamin D deficiency. FM and persistent nonspecific musculoskeletal pain have found that a low level of vitamin D in such disorder is common.<sup>14</sup>

Bhatty et al, in their study "Vitamin D deficiency in Fibromyalgia", done in Karachi based

hospital among 40 female patients diagnosed with FM, based on ACR criteria, reported 32 (80%) had vitamin D deficiency and 8 (20%) had vitamin D insufficiency.<sup>15</sup> Study of Plotnikoff et al reported that 93% of subjects had deficient levels of vitamin D, 28% of subjects were labelled as having severe deficiencies. Published works on vitamin D suggests that patients with nonspecific musculoskeletal pain should have their serum vitamin D levels measured regularly.

A significantly higher prevalence of low vitamin D concentrations in women with FM as compared with age matched female controls (42.5% vs 18.9%) was reported by Al Allaf and colleagues.<sup>14</sup> Badsha et al found that 74% of their patients with FM had a low vitamin D level.<sup>16</sup> It has also been suggested that up to 50% of Caucasian FM patients may have low levels of vitamin D, and these lower levels were observed more frequently in patients with anxiety and depression.<sup>11</sup>

According to Plotnikoff and Quigley, 93% of patients presenting with persistent nonspecific musculoskeletal pain had deficient levels of vitamin D, and 28% of subjects were labelled as having severe deficiencies.<sup>10</sup> The other aspect highlighted by these studies is, the age of patients. Most of the patients were of age less than 45 years, and had severe deficiency of vitamin D. Zuberi et al also found much younger patients than any previously reported in populations at risk of vitamin D deficiency. Similarly in Plotnikoff's study on 150 patients, 55% were younger than 30 years of age.<sup>10</sup> These data on serum vitamin D levels in young people raise some concern about their food choices and even the amount of time they spend in the sunshine. Alternatively, patients with fibromyalgia could be vitamin D deficient due to pain, poor mobility or associated depression potentially leading to less time spent outdoors, or high rates of adiposity leading to decreased synthesis of vitamin D.

#### **Vitamin D and its Therapeutic Role in FM**

Abokrysha et al, reported effective treatment with high-dose vitamin D could lead to resolution of almost all symptoms of FM in their patients.<sup>17</sup> The

patients were treated with either oral or injectable forms of vitamin D3 for eight weeks. Patients were seen at follow-up one month after treatment with vitamin D injection or two months after treatment with vitamin D tablets. All patients had normal calcium levels and normal vitamin D levels at follow-up. The treated patients had improved clinically with significant improvement on different items of new clinical FM diagnostic criteria apart from cognitive symptoms. Badsha et al, in their study stated that treatment with vitamin D resulted in clinical improvement in 90% of their patients with FM.<sup>16</sup>

In conclusion, vitamin D deficiency should be taken into account in the differential diagnosis of patients with musculoskeletal pain or FM and as a possible modality of treatment for the same.

## CONCLUSION

Vitamin D has remained mysterious among all known vitamins with its unique biochemical properties and functions. As numerous researches are still ongoing to establish its association with different diseases and as treatment modalities, Vitamin D status should be considered as an important diagnostic parameter when necessary.

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