

Review Article

Twin Deficiency of Calcium and Vitamin D Causes Chronic Pain Syndrome

Virendra Patil¹

Abstract

Background : Calcium and Vitamin D intake is crucial in bone and calcium metabolism. Low calcium intake is associated with several non-skeletal diseases and non-specific chronic musculoskeletal pain. Calcium is essential for the body, while Vitamin D plays an integral role in calcium homeostasis for maintaining optimum skeletal health. Almost 76% of Indians suffer from Vitamin D deficiency and insufficiency, which also leads to insufficient absorption of calcium, raising calcium deficiency in India.

Conclusion : To understand the clinical implications of the twin deficiency of calcium and Vitamin D, the present study aims to review and assess the role of calcium and Vitamin D in chronic non-specific musculoskeletal pains, the role of supplementation in treatment and prevention and offer treatment and prevention recommendations.

Key words : Calcium, Vitamin D, Chronic Pain, Musculoskeletal Pain, Calcium Deficiency.

Pain is a common complaint, which may be specific to some body part or diffused. There are several reasons causing pain, including tissue injury, an underlying health condition or an unknown etiology. Chronic non-specific musculoskeletal pain that occurs frequently is a pain that stays for over 3 months and is of idiopathic origin. Chronic pain affects the quality of life, significantly impacting the patient's physical activities, mental health and even social and economic life¹.

Vitamin D deficiency is highly prevalent and is associated with several skeletal symptoms of deficiency. Vitamin D increases the absorption of calcium. Both calcium and Vitamin D is crucial in bone and muscle metabolism¹.

Calcium is an essential nutrient for the body playing an important role in muscle contraction, activation of oocytes, development of strong bones and teeth, blood clotting, nerve impulse, controlling heartbeat, and fluid balance within the cells. Calcium is also important for maintaining general health².

Vitamin D plays an integral role in calcium homeostasis for maintaining optimal skeletal health. Calcium is essential for the proper mineralization of bone and strengthens bones. The classic function of

Editor's Comment :

- The twin deficiency of calcium and Vitamin D is a significant yet often overlooked cause of chronic pain syndrome.
- Ensuring adequate intake of both nutrients is essential for musculoskeletal health, pain management and overall well-being.

Vitamin D is to enhance the efficacy of the intestine in the absorption of calcium and phosphorus. An optimal level of Vitamin D is essential in increasing the efficiency of calcium absorption; its deficiency leads to the absorption of only 10% to 15% of dietary calcium³. It is suggested that the combined deficiency of Vitamin D and serum calcium raises the risk of fracture, increases the risk of falling and affects bone mineral density and muscle strength, leading to different pain syndromes. Besides, insufficient dietary calcium and Vitamin D intake can cause a high prevalence of osteoporosis among older persons⁴. Almost 76% of Indians suffer from Vitamin D deficiency and insufficiency in a study including 4624 individuals at 229 sites in 81 cities across the country, the prevalence most common among adults aged 18 to 30 years⁵. This leads to insufficient absorption of calcium associated with Vitamin D deficiency, thereby raising calcium deficiency in India.

The present review aims to study and explore the effect of twin deficiency of calcium and Vitamin D, the role of supplementation in treatment and prevention and provide treatment and prevention recommendations.

¹MD (Medicine), DM (Endocrinology), Department of Endocrinology, KEM, Mumbai 400012 and Corresponding Author

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MATERIALS AND METHODS

An English-language literature search was conducted using PubMed, Google Scholar and Cochrane database to identify relevant articles. The search terms included 'calcium deficiency,' 'vitamin D deficiency,' 'calcium and Vitamin D deficiency,' 'chronic non-specific musculoskeletal pain,' 'muscle cramps,' 'joint pains,' 'fractures,' and 'calcium and Vitamin D supplementation.' The literature search included case reports, case series, articles, systematic reviews, meta-analyses, and randomized controlled trials. Based on the selected articles, a backward citation search was also performed to search for relevant articles.

Deficiency of Calcium and Vitamin D :

Calcium and Vitamin D deficiencies lead to abnormal muscular functions such as non-specific pain and weakness. It has been observed in a study that patients with low back pain showed a low calcium intake. Several undetected cases of non-specific muscle pain and weakness are linked to low calcium or Vitamin D intakes. Muscle pain and weakness in many unrelated bone disorders are noted with low levels of Vitamin D in the body⁶.

A lack of Vitamin D attributes to skeletal mineralization defect, causing specific or generalized discomfort and aches and pain in joints and muscles. Sometimes, these symptoms also become the reason for misdiagnosing the condition with fibromyalgia, degenerative joint disease, arthritis, chronic fatigue syndrome, or even being dismissed as depression⁷.

Calcium Deficiency :

Calcium deficiency occurs due to inadequate calcium intake, which may cause bone thinning and weakening osteoporosis. If untreated, calcium deficiency can cause serious complications such as osteoporosis, hypertension, and cardiac arrhythmias. Muscle cramping, numbness, and tingling sensation are some of the earliest signs of calcium deficiency. Dry skin and brittle nails also indicate calcium deficiency. Increased menstrual symptoms and bone fractures result from calcium deficiency².

Calcium deficiency rarely gets manifested into clinically evident hypocalcemia. Ionized calcium is the main factor causing symptoms in patients with hypocalcemia. Calcium deficiency causes are classified into three major classes: dietary deficiency, calcium malabsorption and Vitamin D-dependent

deficiency. There has been growing evidence that sufficient calcium intake is crucial to alleviate deficiency symptoms, achieve optimal peak bone mass and minimize age-dependent bone loss⁸.

While low serum calcium levels can affect most organs and symptoms, the common symptom is increased neuromuscular irritability, including perioral numbness, tingling in the hands and feet, and muscle spasms. Postmenopausal women and individuals who avoid dairy products are at an increased risk of calcium deficiency⁹.

As we are aware that calcium is important for building bones and maintaining their strength. The weakening of the bones leads to osteoporosis, making the bones porous and fragile. Moderate calcium deficiency causes cramps, joint pains, abnormal growth, muscle cramps, numbness of the arms and/or legs, and brittle nails².

Vitamin D Deficiency :

In the absence of oral calcium intake, calcitriol cannot increase their intestinal absorption. Low dietary calcium and Vitamin D can lead to calcium deficiency, leading to secondary hyperparathyroidism. In the Indian population, twin deficiency of dietary calcium plus Vitamin D is responsible for causing osteomalacia in children and adolescents, while in adults, they lead to osteomalacia¹⁰.

A case series suggested that Vitamin D deficiency and inadequacy play a significant role in chronic pain and muscle spasm in the musculoskeletal system. It has also been observed that treating Vitamin D deficiency and inadequacy may improve symptoms in deficient individuals¹¹.

Studies have suggested that a low level of Vitamin D is related to the occurrence of both chronic and acute pain. Vitamin D results in anatomic, hormonal, neurological and immunological effects on pain manifestation. Hence, it plays an essential role in the etiology and maintenance of chronic pain stated and associated comorbidities. Vitamin D deficiency also leads to muscle weakness and pain in children and adults¹².

Other studies have indicated that Vitamin D deficiency plays a role in non-specific musculoskeletal pain. It is suggested that mild or early Vitamin D deficiency may lead to skeletal muscle pain, especially in the absence of gross musculoskeletal pathology. Besides, changes in serum calcium levels can also affect

muscle and nerve function. Vitamin D deficiency extended over long durations can also trigger hypocalcemia by disrupting calcium homeostasis. Besides, Vitamin D deficiency also enhances the susceptibility of tissues to inflammation¹³.

Various authors have hinted that Vitamin D deficiency could be a reason for initiating non-specific musculoskeletal pain, including low back pain. The nature of the pain associated with Vitamin D deficiency is characteristic, usually sensed in the bone or the muscle¹. In a study comparing adult OPD patients suffering from non-specific pain in the general body, back, tiredness and weakness were seen to be deficient in Vitamin D¹⁴. A positive relationship was noted between Vitamin D deficiency and skeletal pain, a link more notable in women than men¹⁵.

Current and Recommended Supplementation of Calcium and Vitamin D :

Calcium :

Calcium supplementation is essential for bone health, neuromuscular activity, blood coagulation and optimal cardiac function. It is an integral component of bone architecture and is needed for mineral deposition on bone throughout life. Calcium is absorbed in the small intestines with the help of Vitamin D. The best way to get calcium is through dietary supplements. Those who do not obtain adequate calcium through diet require supplements¹⁶.

Vitamin D :

Vitamin D is a critical nutrient for maintaining bone health. It regulates calcium absorption and stimulation of bone resorption, thus standardizing serum calcium concentration¹⁶. Vitamin D supplementation increased 25-hydroxy Vitamin D levels in the serum and therefore has the ability to correct the effects of Vitamin D deficiency¹².

Calcium and Vitamin D Intake in India :

Adequate calcium intake is necessary to maintain the skeletal mass attained and prevent any ongoing natural loss. India has a prevalence of calcium and Vitamin D deficiency, with the intake of dietary calcium, milk, milk products and cereals reducing drastically over half a century. Surveys have shown that dietary calcium intake (g/CU/day) has undergone a decline from 606 (1975-79) (recommended dietary allowance [RDA]-400) to 433 in the year 2011-2012 (RDA-600). The intake of milk and milk products (g/CU/day) has

reduced from 116 (1975-79) to 95 (2011-2012) (RDA-150). While the intake of calcium has been declining in India, the RDA in adult males and females (19-50 years) is 1,000 mg/daily, while in adult males, 51 to 70 years, 1,000 mg and females 51 to 70 years is 1,200 mg⁹. The decline has been observed across different age groups, including infants, children, adults, and pregnant and lactating women¹⁰. It was seen in a study that the calcium intake in urban India is 308 mg/day, while in rural India, it is 269 mg/day¹⁷.

Calcium and Vitamin D are essential for maintaining bone health, gaining bone mass, and preserving bone with progressing age¹⁰. Supplementation with Vitamin D and calcium reduces chronic non-specific musculoskeletal pain. It also has the potential to enhance physical activity capacity. Supplementation with Vitamin D and calcium and significant relief in painful conditions also improve the patient's physical, mental and social well-being¹.

In a case study of a patient with non-specific muscle pain that was aggravated if he lifted a heavy bag and progressively worsened, the pain subsided significantly after 3 days of calcium and Vitamin D supplementation. After 2 weeks, the patient was completely relieved of the pain. Non-specific muscular pain and weakness are related to the deficiency of calcium and Vitamin D in the body. The administration of these supplements is known to strongly improve the recovery of a patient with non-specific muscular pain and weakness⁶.

Low back pain is a commonly occurring problem. It has been suggested that chronic pain is more prevalent in older women than in men. The back pain in postmenopausal women is attributed to reduce bone mass, sarcopenia, vertebral fractures, and inflammation-deficiencies related to Vitamin D deficiency. Vitamin D supplementation is recommended as therapeutic medication to achieve euvitaminosis D in patients experiencing musculoskeletal pain. In order to manage the pain and weakness caused by Vitamin D deficiency, a holistic approach of appropriate sunlight exposure, Vitamin D plus calcium supplementation and appropriate physical exercise is recommended¹⁸.

Vitamin D should be given in suitable doses to those individuals who are deficient and 'at-risk' populations. It should be accompanied by appropriate age-related calcium administration. Calcium and Vitamin D supplementation in individuals suffering from chronic

non-specific muscular pain may lead to considerable relief in painful conditions. It may also improve physical activity capacity. With the substantial improvement in pain relief, a significant improvement in physical, mental and social well-being also ensues¹.

Treatment Recommendations :

It has been noted in previous studies that patients with persistent, non-specific musculoskeletal pain were at an enhanced risk of Vitamin D deficiency, which is frequently misdiagnosed¹⁹.

It is recommended that to be effective, calcium and Vitamin D supplementation should be targeted in an individual with documented or at-risk of calcium and Vitamin D insufficiencies. General supplementation in the community is not recommended²⁰. Most studies have recommended a combination of minimum doses of 1,200 mg calcium and 800 IU Vitamin D daily²¹.

Table 1 provides the Indian Council of Medical Research-National Institute of Nutrition (ICMR-NIN) 2020 recommendations for calcium and Vitamin D in Indians²².

Calcium carbonate supplements have the highest percentage of calcium amongst available calcium salts. Calcium carbonate has 40% elemental calcium, calcium citrate has 21%, calcium lactate has 13%, and calcium gluconate has 9% elemental calcium. Hence, the number of calcium carbonate tablets needed to maintain optimal daily intake is fewer, thus enhancing patient adherence. A cost-benefit analysis has also revealed that calcium carbonate is one of the less expensive carbonate products. Table 2 provides a comparative account of the different calcium salt supplements²³. The recommendation is to initiate the calcium/vitamin D supplement at a lower dose and gradually titrate the target intake amount over 1 to 2 months. Calcium carbonate products should be taken with a meal, unlike calcium citrate, which must be taken on an empty stomach or with a flood. Hence, the patient should be properly educated and counselled about using calcium supplementation¹⁶.

Table 2 — A comparative account of several calcium salt supplements²³

Calcium salts	Calcium (%)	Calcium (mg/g)
Calcium Carbonate	40	400
Calcium Citrate Malate	21	210
Calcium Acetate	25	253
Calcium Gluconate	9	93
Calcium Phosphate	38	383
Calcium Lactate	13	130
Calcium Orotate	20.6	152.44

CONCLUSION

Calcium and Vitamin D deficiency is common, and non-specific musculoskeletal pain and lower back pain are common complaints. On the basis of early signs of calcium deficiency, treated should/may be initiated to prevent long-term consequences. Prompt diagnosis and treatment can lead to the resolution of symptoms of chronic musculoskeletal pain and the prevention of osteomalacia, osteoporosis, and other possible long-term complications.

Early signs of calcium deficiency include muscle cramping, numbness, and tingling sensation, while dry skin and brittle nails also indicate calcium deficiency. While Vitamin D deficiency is responsible for low calcium absorption, it also leads to chronic pains, muscle cramping, joint pains, numbness and tingling sensation. Low levels of serum calcium do not lead to a clinical manifestation. Still, moderate calcium deficiency may lead to common symptoms such as neuromuscular irritability, muscle spasms, and tingling in the hands and feet. Calcium requirements in the body are the highest during periods of growth such as childhood, pregnancy, or breastfeeding.

Calcium intake has drastically declined in India over the last half-century. Studies have shown that dietary calcium intake declined from 606 (1975-79) (RDA-400) to 433 in the year 2011-2012 (RDA-600). Calcium supplementation is needed in individuals in whom dietary supplement is insufficient. The recommended daily allowance of calcium in the Indian population is 1,000 mg/day for adult males and females.

Table 1 — ICMR-NIN 2020 recommendations for calcium and Vitamin D in India

Supplement	RDA								
	Men	Women	Pregnant women	Lactating women	Infants	Children (1-3 years)	Boys/Girls (10-12 years)	Boys/Girls (13-15 years)	Boys/Girls (16-18 years)
Calcium	1,000 mg/d	1,000 mg/d	1,000 mg/d	1,200 mg/d	300 mg/d	500 mg/d	850 mg/d	1,000 mg/d	1,050 mg/d
Vitamin D	600 IU/D	600 IU/D	600 IU/D	600 IU/D	400 IU/d	600 IU/d	600 IU/d	600 IU/d	600 IU/d

Patil V. Twin Deficiency of Calcium and Vitamin D Causes Chronic Pain Syndrome.

Hence, a healthy lifestyle, optimal calcium and Vitamin D, and physical exercise from adolescence are important steps to prevent bone loss, muscle cramps, chronic pains and reducing the risk of fractures. Compliance and adherence are crucial in patients taking calcium and Vitamin D supplements.

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