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Role of Vitamin D in chronic low back pain in south Rajasthan: An Open-Label, Single-Arm Clinical Trial:

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ABSTRACT:

Objectives: *The purpose of the study is to evaluate how vitamin D supplementation affects the severity of pain, functional impairment, and vitamin D levels in individuals with CLBP.*

Study design: *An open-label, single-arm clinical trial*

Setting: *A tertiary care hospital's outpatient pain clinic*

Methods: *A total of 342 individuals were included in the study (CLBP for more than 3 months and plasma 25-hydroxyvitamin D3 levels of 30 ng/mL). For eight weeks, patients received 60,000 IU of oral vitamin D3 once a week as a supplement. At baseline, 2, 3, and 6 months after supplementation, VAS measurements of pain intensity and functional impairment were included as efficacy parameters. At baseline and eight weeks later, the levels of plasma 25 (OH) D3 were assessed.*

Results: *After taking vitamin D supplements, all 342 patients' serum vitamin D levels returned to normal. Of these, 84 patients had normal vitamin D levels and responded 69% to vitamin D therapy, while 258 patients had low vitamin D levels and responded 100% to vitamin D therapy for their LBP.*

Conclusion: *In addition to bringing levels back to normal, vitamin-D therapy in CLBP patients with vitamin-D deficiency may also reduce discomfort and enhance functional capacity. Controlled clinical trials in the future are necessary to verify the hypothesis.*

Key words: *persistent low back pain, vitamin D deficiency, screening, and supplementation.*

INTRODUCTION:

The clinical syndrome known as chronic low back pain (CLBP), which is characterised by pain that is located below the costal margins and above the inferior gluteal folds, may also be associated with leg pain or motor, sensory, or reflex impairments in the nerve root distribution [1] This is a much more frequent reason for medical consultation in the modern

day [2] and may cause impairment as well as interference with quality of life, work performance, and even societal economic losses [3]. Despite the availability of many medical facilities for testing and therapy, many people continue to experience morbidity from CLBP.

Numerous studies have linked persistent low back pain and vitamin D insufficiency. The cause of this is unknown, but certain connections have been suggested, including the possibility that hypovitaminosis D changes the way calcium and phosphorus are metabolised, making the skeleton a major source for preserving blood calcium levels. This could cause osteomalacia, worsen osteopenia, and increase the risk of osteoporosis. Histologically, osteomalacia is a common metabolic disease with varied clinical manifestations that is characterised by impaired bone mineralization. [4-7] As an osteomalacia-presenting symptom, CLBP is widely described.

India has a 50–90% vitamin D deficiency rate. A darker skin tone or consumption of a diet low in vitamin D may be the cause, as well as a change in lifestyle. The effectiveness of vitamin D in treating persistent low back pain has not yet been strongly supported by research. [3]

The purpose of this clinical trial was to find out how vitamin D affects the reduction of CLBP.

METHODS:

In order to determine the effectiveness of vitamin D supplementation in patients with CLBP, an open-label, single-arm clinical trial was conducted. The data reported in this paper comes from patients who were screened for inclusion in that experiment.

Study Design and Population: The population for this single-arm, open-label study was the pain clinic of an Indian public tertiary care hospital. From January 2019 to December 2020, patients were sought after.

The study site is in Rajasthan, a region of northwest India that has a hot, semi-arid environment with mild dry winters, hot, humid summers, and a medium amount of seasonal variation.

Inclusion Criteria: Patients with CLBP for at least three months who are either male or female, have leg discomfort, are not responding to medicine or physical therapy, and have low plasma levels of 25-hydroxyvitamin D3 (30 ng/mL) were eligible for the trial.

The baseline "pain-related questionnaire" was only to be completed by patients who could speak English, Hindi, or Mewari.

Exclusion criteria: Patients were excluded if they had signs of other neuropathy and painful conditions like diabetes, rheumatoid arthritis, symptomatic hip, knee, and ankle osteoarthritis,

epilepsy, psychiatric illnesses, substance abuse, metabolic bone disease (such as hypo- or hyperparathyroidism), chronic kidney disease, or medical or surgical conditions that affect vitamin D metabolism (such as gastric surgery, chronic liver disease, renal failure, intestinal malabsorption, systemic infection, cancer, etc.). Patients taking corticosteroids (Prednisolone reduces bone formation), bisphosphonates (Aldronate increases osteoclast apoptosis), PPIs (Omeprazole decreases calcium absorption), hormonal drugs (Medroxyprogesterone decreases protective oestrogen, causing more osteoclast activity), pregnant and lactating women, and women planning pregnancies were also excluded from the study. Patients who had taken vitamin D pills within the previous three months were also excluded from this trial.

Assessment of plasma 25-hydroxyvitamin D (25(OH)D3) levels: Using venous sampling, the level of serum 25-OH-vitamin D was determined. For the assessment of patients with deficiencies, this method offers a wide measuring range and good precision at the low end of detection. To avoid any circadian variation, all blood samples were obtained between 9:00 a.m. and 10:00 a.m. The patients were randomly divided into two sex groups (male and female) and three severity groups (10 ng/mL severe deficiency, 10–14.9 ng/mL moderate deficiency, and 15–22.4 ng/mL mild deficiency).

Procedure: 342 participants with nonspecific CLBP between the ages of 18 and 60 were enrolled in this study. A doctor conducted a baseline assessment of illness activity upon enrollment.

Treatment Regimen: For eight weeks, a pearl of vitamin D3 (60,000 IU) was given orally once per week. A clinical evaluation of pain was performed two months after vitamin D therapy started. The percentage of patients who experienced lasting pain alleviation was reported. At the beginning, two, three, and six months after supplementation, respectively, patient characteristics and outcome measures were gathered.

RESULTS:

A total of 342 CLBP patients visited the OPD in the years 2019 and 2020; of these, 194 (57%) women and 64 (18%) men had low levels of 25-OH vitamin D3. As shown in tables 1.1 (vitamin D levels) and 1.2, these patients were further divided into groups with mild (15–22.4 nmol/L), moderate (10–14.9 nmol/L), and severe (10 nmol/L) vitamin D deficiency.

After two months of treatment, the 25-OH-vit D3 level was once again measured weekly using venous sampling.

Table no. 1.1

	Low	normal	Total
Total number of patients	258	84	342
Total number of patients responded to vitamin d3	258	58	316

therapy			
Percentage of responders	100%	69.04%	92.39%

Table no. 1.2

All 342 patients normalised their serum level of vitamin D after this therapy, among whom 84 patients with a normal vitamin D level responded 69% with vitamin D therapy, whereas 258 patients with deficient vitamin D levels responded 100% in their LBP with vitamin D therapy, as shown in Tables 2.1 and 2.2.

Following supplementation, there was also a significant improvement in functional disability.

No adverse drug reactions were observed with oral vitamin-D supplementation in the study.

Table no. 2.1

	25-OH vitamin D3 level (nmol/L)	females	males
Normal	22.5-93.8	61	23
Mild	15-22.4	60	23
Moderate	10-14.9	34	8
Severe deficiency	<10	100	33

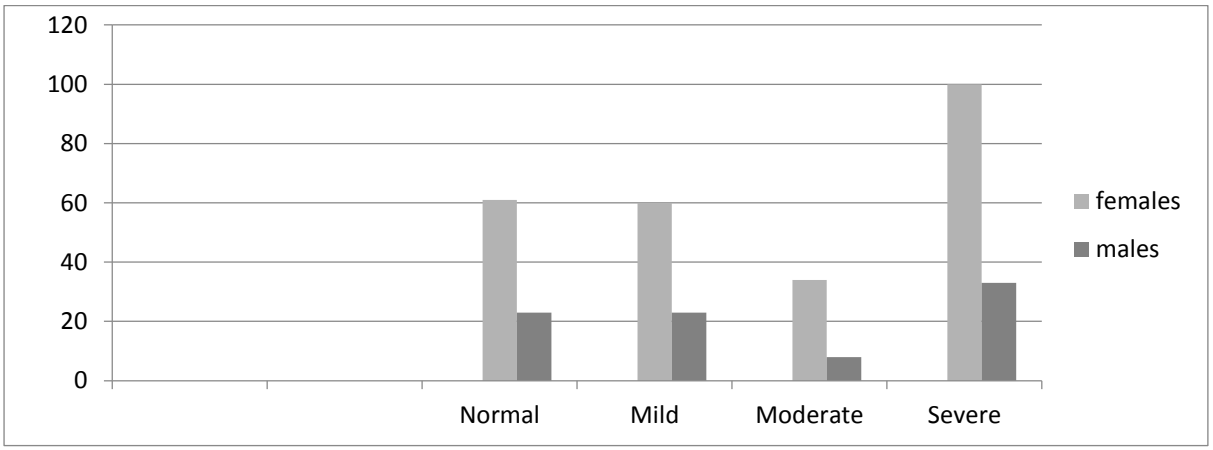
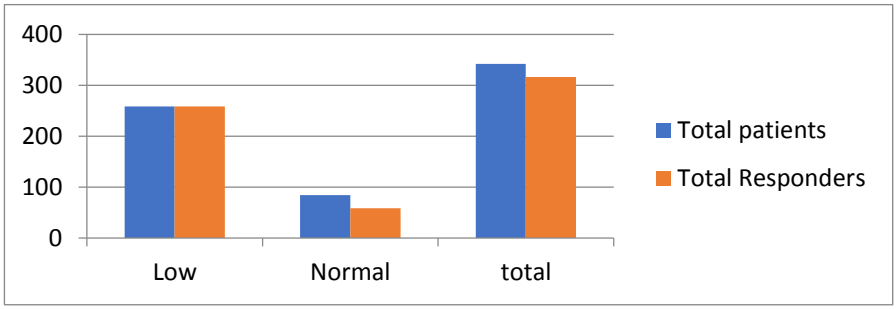


Table no. 2.2



DISCUSSION:

In this open-label, single-arm trial, we assessed the effectiveness of vitamin-D supplementation in deficient patients with CLBP in terms of providing pain relief. In the recruited patients, a higher prevalence of vitamin D deficiency was noted. Results displayed that all 342 patients attained normalised vitamin D levels after the supplementation. We also observed a significant reduction in pain with the vitamin-D supplementation at 2, 3, and 6 months, respectively.

Role of Vitamin D

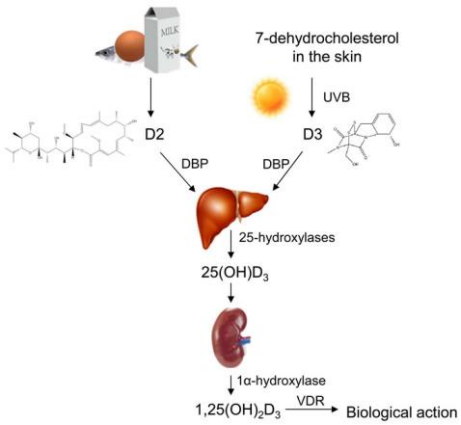
Vitamin D, or "sunshine vitamin," is one of the most penetratingly investigated nutrients of the 21st century. [3] which was originally revealed as an anti-rachitic agent capable of preventing a failure of bone mineralization. It plays a key role in the causation and progression of various chronic pain conditions and is linked to comorbidities by exerting anatomic, hormonal, neurological, and immunological impacts on pain expression.

Vitamin D Metabolism in Humans:

Ergocalciferol-D2 and cholecalciferol-D3 are the two forms of vitamin D, which is a fat-soluble vitamin. With the aid of endogenous 7-dehydrocholesterol, vitamin D3 is first synthesised from UVB radiation and, in small amounts, from food. A small portion of this is stored in adipose tissue, skeletal muscle, and many organs, and the rest of it is metabolised in the liver to 25-hydroxyvitamin D3 [25(OH)D3], which is then converted to 1a,25-dihydroxyvitamin D3 [1a,25(OH)2D3]. By attaching to its receptor and activating it, 1,25-dihydroxyvitamin D3 interacts with the retinoid X receptor (RXR) to form the VDR/RXR/cofactor complex, which then regulates gene transcription and takes on an active state. [9-13] The primary role of vitamin D is to stimulate the absorption of calcium and phosphorous from the gut and reabsorption from the kidney (PCT) when it works in tandem with PTH, as shown in figure 1.1.

An effective immunomodulator is vitamin D. Additionally, it controls inflammatory mediators, including interleukin, tumour necrosis factor, and macrophages, to have an anti-inflammatory impact.

Figure 1.1



Deficiency of Vitamin D

Individuals Predisposed to Developing Deficiencies:

Dark-skinned people According to Hollick et al., people with naturally darker skin tones may require three to five times the amount of sun exposure to synthesise the same amount of vitamin D as people with fairer skin tones [21-28]. Obese people (because vitamin-D stores are trapped in adipose tissue), hospitalised and institutionalised people, as well as people who regularly use sunblock and protective clothing, appear to be at an increased risk for vitamin D deficiency.

Effects of vitamin D deficiency:

Previous research has linked a lack of vitamin D to a variety of conditions, including fibromyalgia syndrome, rheumatic diseases, osteoarthritis, hyperesthesia, migraine headaches, chronic fatigue syndrome, and seasonal affective disorder.

In chronic pain patients, decreased vitamin-D levels have also been linked to increased cerebral sensitivity to mechanical stimulation. It has a significant impact on astrocyte detoxification pathways and hence has a neuroprotective effect. The proinflammatory mediators and macrophages that are suppressed by vitamin D lessen inflammation and pain.

Since skeletal muscle contains vitamin D receptors, myopathy, which manifests as diminished muscle strength, is also a result of the insufficiency and may occur before any discomfort.

The Connections Between Vitamin D and Pain

According to the theory that vitamin D is involved in musculoskeletal pain, the process is thought to start with hypocalcaemia brought on by insufficient vitamin D, which has a detrimental effect on bone metabolism and health. Even mild hypocalcaemia causes an

increase in parathyroid hormone (PTH), which can exacerbate osteoporosis and have a negative impact on bone architecture (osteoporosis).[16,17] PTH levels that are too high also prevent adequate bone mineralization, which results in a spongy matrix. This gelatin-like matrix has the ability to absorb fluid, expand, and put pressure on the periosteal tissues, which leads to pain because those tissues are heavily innervated with pain-sensing sensory fibres. [18,19,20]

Some data suggests that this abnormal bone metabolism, or osteomalacia, explains why many people with insufficient vitamin D may experience chronic bone pain**.**

Does vitamin D supplementation improve CLBP?

With hundreds of physiological functions in the human body, vitamin D is vital for overall health, according to Dr. Jagim. It is still a good idea to maintain adequate vitamin D levels since they are crucial for overall health, even though there may not be enough data to show a direct benefit of vitamin D supplementation in the treatment of chronic lower back pain.

The link between vitamin D deficiency and musculoskeletal pain, particularly in the neck and/or back, and/or muscular spasm has not been thoroughly studied.

The results of the limited studies have been mixed. Due to the high frequency of vitamin D deficiency among athletes and the hazards of stress fractures, sickness, and slowed muscle recovery, Sikora-Klak et al.7 have advised urgent treatment of vitamin D insufficiency and deficiency in sports. According to a quantitative meta-analysis8 of 19 randomised controlled trials with 3436 participants (1780 receiving vitamin D supplementation and 1656 receiving placebo), vitamin D supplementation resulted in a significantly greater mean decrease in pain score (the primary outcome) compared to placebo. Another study9 that followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and included 8 clinical trials, on the other hand, found that vitamin D supplementation was not any more effective for treating low back pain than a placebo, no intervention, or other non-pharmacologic or conservative interventions. However, that analysis had limitations because the overall quality of the evidence was "extremely low" as a result of the inclusion of studies with low methodological standards and small sample sizes. According to a retrospective study10, pain intensity increased as vitamin D deficiency increased in 98 patients with low back pain. However, the study's definition of vitamin D deficiency (84 patients) compared to the healthy group's (20 patients) (20 ng/mL and higher) did not accurately reflect the vitamin D-insufficient population, which was defined as blood levels of 20 to 30 ng/mL. One study11 discovered a link between low levels of vitamin D and ferritin and chronic neck pain, but it did not investigate the role of vitamin D deficiency in neck pain. It should be noted that the study population was skewed toward women, with 90% of the patients being women. [21,22,23,24]

The study's enrolled subjects had CLBP with or without radiculopathy, were taking any type of oral painkiller, and had a stable pain score over the previous three months.

Our results offer a plausible explanation and an argument for prescribing dietary supplements in addition to therapeutic medicine to help patients with musculoskeletal pain achieve normal Vitamin D levels. Screening for vitamin D levels in populations at risk is also crucial. It is advised to receive enough sun exposure, supplement with vitamin D and calcium, and engage in regular physical activity to reduce the morbidity brought on by the handicap brought on by improper vitamin-D homeostasis.

CONCLUSION:

Based on our clinical investigation, it is recommended that patients with chronic musculoskeletal pain and fatigue syndromes receive a sufficient intake of vitamin D. This recommendation should be more generally understood and implemented. This study demonstrates a positive response to vitamin D therapy in CLBP, which may operate by lowering pain and inflammation by regulating the excitability of sensory neurons and the presence of both anti- and pro-inflammatory cytokines. Contributing elements are frequently ambiguous or unknown. Vitamin D deficiency may contribute to and/or prolong the pain condition, even in cases where a particular aetiology has been identified. This possibility should not be discounted.

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AUTHORS CONTRIBUTION:

HL, AS, BR: Conceived and designed the study, conducted trial, provided research material, and collected organised data. HS: Provided manuscript. PS: Wrote initial and final draft. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity of index of manuscript.

CONFLICTS OF INTEREST:

There were no conflicts of interests between authors.

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