VOLUME - 10, ISSUE - 02, FEBRUARY - 2021 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper | Physical Medicine And Rehabilitation

ASSESSMENT OF THE RELATIONSHIP BETWEEN VITAMIN D LEVEL AND NON-SPECIFIC MUSCULOSKELETAL PAIN: A HOSPITAL BASED OBSERVATIONAL STUDY

Dr Shipra Chaudhary DNB (PMR) Associate Professor Physical Medicine and Rehabilitation ABVIMS & DR RML hospital New Delhi.

Dr Nikhil Agarwal* MD Physical Medicine and Rehabilitation *Corresponding Author

Dr Neha Singh Voluntary Research Fellow Department of Orthopaedic University of Alabama Birmingham, Alabama, USA.

ABSTRACT The prevalence of Vitamin D deficiency in India ranges from 50% to 94% in different age groups. Primary objective of the study was to determine the prevalence of vitamin D deficiency among adults with non-specific complaints of musculoskeletal pain/tiredness/weakness with no other symptoms or medical comorbidities. The normal reference range of our laboratory for serum 25(OH)D level is 30–100 ng/ml. Out of the entire cohort of 400 patients, only 12% (n=48) had sufficient serum vitamin D levels (>30 ng/mL) .T he mean± S.D. value of serum vitamin D for the study population was 20.61 ±11.67 (median =20; range= 2.4-124). More than half of the study sample (n=222; 55.5%) analyzed had deficient serum Vit D levels (≤20 ng/ml) and almost a third of the sample (n=130; 32.5%) had insufficient serum Vit D levels (21-30 ng/ml). This study also documented statistically significant results between serum vitamin D levels in patients with different sunlight exposure (p=0.032). This study confirms a high prevalence of vitamin D deficiency in people with diffuse musculoskeletal pain in apparently healthy urban Indians and advocates the supplementation of vitamin D in such patient population.

KEYWORDS : Vitamin D ,Musculoskeletal pain

INTRODUCTION

Vitamin D is a fat-soluble vitamin that is made available to our body by natural and fortified food items and as a dietary supplement. It is also synthesized endogenously by the skin in the presence of sunlight. Vitamin D obtained from sun exposure, foods, and supplements is biologically inert and must undergo two hydroxylations in the body for activation. The first hydroxylation, which occurs in the liver, converts vitamin D to 25-hydroxyvitamin D [25(OH)D], also known as "calcidiol." The second hydroxylation occurs primarily in the kidney and forms the physiologically active 1,25-dihydroxyvitamin D [1,25(OH)2D], also known as "calcitriol".

The prevalence of Vitamin D deficiency in India ranges from 50% to 94% in different age groups.[1]The deficiency of Vitamin D has further been implicated in various skeletal and extra-skeletal manifestations including common types of cancer, autoimmune diseases, cardiovascular diseases and diseases of infectious etiology.Vitamin D deficiency in adults is commonly associated with skeletal mineralization defects, increased risk of falls, proximal muscular weakness and widespread musculoskeletal pain.

A meta-analysis of twelve observational studies with 1854 participants noted inconclusive results, with significantly increased odds of vitamin D deficiency associated with chronic widespread pain, but no difference in mean 25(OH)D levels between people with and without chronic widespread pain. [2] Multiple reviews of randomized controlled trials have also reported inconsistent conclusions about improvement in chronic pain on vitamin D supplementation. [3] Given the limited evidence and inconsistent conclusions from previous studies much is still left to explore with regards to widespread musculoskeletal pain and its association with vitamin D deficiency. With the present study we, therefore, aim to determine the prevalence of vitamin D deficiency among patients with diffuse musculoskeletal pain.

METHODOLOGY

It was a prospective, observational study conducted at the outpatient clinic of department of Physical Medicine and Rehabilitation at a tertiary care hospital in New Delhi. Primary objective of the study was to determine the prevalence of vitamin D deficiency among adults with non-specific complaints of musculoskeletal pain/tiredness/weakness with no other symptoms or medical comorbidities.

A total of 400 participants satisfying the inclusion and exclusion criteria were enrolled in the study. The inclusion criteria were age over 18 years, idiopathic diffuse musculoskeletal pain, generalized weakness & fatigue and willingness to participate in study. The exclusion criteria were unwillingness to participate in the study; localized pain attributed to trauma, arthritis or infection; diffuse musculoskeletal pain due to any systemic comorbidity; patients treated with Vitamin D in the last 3 months or with history of corticosteroid intake (for a duration of 3 months in the last year), patients with chronic diseases, pregnant or breastfeeding and post-menopausal patients. The determination of serum 25-hydroxyvitamin D levels was done by radioimmunoassay for all the participants. Blood samples were collected between 0800 and 1000 hours, following fasting for ≥8 h. The samples were obtained from the antecubital vein.

The normal reference range of our laboratory for serum 25(OH)D level is 30–100 ng/ml. In this study serum 25(OH)D levels less than or equal to 20 ng/mL were considered as "deficient", the levels between 21 ng/ml and 30 ng/mL were considered as "insufficient", levels greater than 30 ng/mL were considered as "sufficient" and levels greater than 150 ng/ml were considered "toxic".

RESULTS

Out of the entire cohort of 400 patients, only 12% (n=48) had sufficient serum vitamin D levels More than half of the study sample (n=222; 55.5%) analyzed had deficient serum Vit D levels and almost a third of the sample (n=130; 32.5%) had insufficient serum Vit D levels. The mean age of the population studied was 32.37 years (S.D. =7.7, Median= 32 years) with almost 2/3rd female participants (n=259; 64.8%). On further evaluation it was observed that the maximum number of participants with deficient serum vitamin D levels were in the age group of 40-50 years (Table 1)

The mean± S.D of serum calcium was 9.08 ± 0.66(median =9.1; range= 7-10.2). Almost 2/3rd of the study population had adequate amount of daily calcium intake (n=258, 64.5%). In

the subset of study population with sufficient serum vitamin D levels, slightly better results were seen in patients with adequate daily calcium intake (Table 2) with the results being statistically significant (p=0.000)

Most participants (n=271; 67.8%) in the study admitted to spending more than 15 minutes in sunlight per day. Only 1 participant acknowledged spending less than 5 minutes per day in sunlight. Overall, the patients with sunlight exposure of more than 25 minutes in a day had better reserves of serum vitamin D with the results being statistically significant at p=0.03 (Table 2)

Table 1

	DEFICIENT/Vit D ≤ 20 ng/ml (N=222) n %	INSUFFICIENT/Vit D= 21-30 ng/ml (N=130) n %	SUFFICIENT/Vit D >30 ng/ml (N=48) n %	Total participants (N=400) n %	P value*
Age (in years)					
18-30	88 50.9%	65 37.6%	20 11.6%	173 43.2%	0.179
31-40	101 57.4%	55 31.2%	20 11.4%	176 44.0%	
41-50	33 64.7%	10 19.6%	08 15.7%	51 12.8%	
Gender					
Male	57 40.4%	69 48.9%	15 10.6%	141 35.2%	0.000
Female	165 63.7%	61 23.6%	33 12.7%	259 64.8%	

Table 2

	DEFICIENT/Vit D ≤ 20 ng/ml (N=222) n %	INSUFFICIENT/Vit D= 21-30 ng/ml (N=130) n %	SUFFICIENT/Vit D >30 ng/ml (N=48) n %	Total participants (N=400) n %	P value*
Sun Exposure (mins)					
<5	1 100%	0 0%	0 0%	001 0.2%	0.032
5 -15	84 65.6%	28 21.9%	16 12.5%	128 32%	
16-25	76 51.7%	58 39.5%	13 8.8%	147 36.8%	
>25	61 49.2%	44 35.5%	19 15.3%	124 31%	
RDA (Calcium)					
Adequate	154 59.7%	65 25.2%	39 15.1%	258 64.5%	0.000
Inadequate	68 47.9%	65 45.8%	9 6.3%	142 35.5%	
BMI (kg/m^2)					
<18.5	25 11.3%	22 16.9%	1 2.1%	48 12%	0.236
18.5-24.9	91 41%	52 40%	22 45.8%	165 41.2%	
25-29.9	43 19.4%	20 15.4%	10 20.8%	73 18.2%	
>30	63 28.4%	36 27.7%	15 31.2%	114 28.5%	

P value considered significant at <0.05
Statistical test involved -Chi square test

DISCUSSION

Vitamin D association and implication in diffuse musculoskeletal pain has been a subject of great debate with inconclusive results. Hypovitaminosis D is a global problem which is noted with almost the same frequency in both tropical and colder areas. It was presumed that populations living near the equator where there is abundant sunlight would be immune to vitamin D deficiency. But sadly, this is not the case! More than 50% and up to 80% of children and adults in the tropical nations like Middle East, India, Brazil, and South East Asia have been reported to be vitamin D deficient or insufficient. The high prevalence of hypovitaminosis D in these populations could be attributed to several factors, including extensive skin coverage, increased skin melanin content, lack of vitamin D supplementation and dietary fortification, and inadequate sunlight exposur. In the Indian sub-continent, multiple studies have reported a prevalence of 70%-100% in diverse subsets [1,4] of population ranging from apparently healthy young soldiers with adequate dietary intake of calcium and regular exercise schedule [5] to healthcare professionals studied from all over India [6]. Congruous results were seen in this study too with a prevalence rate of 88% for hypovitaminosis D. This study is an addendum of already existing prevalence studies and was aimed at getting an insight into role played by hypovitaminosis D in adult Indian population in the northern part of the country.

This study focused on adults with idiopathic diffuse musculoskeletal pain and a majority of them were found to have insufficient levels of vitamin D. Similar results were reported by Gregory et al who documented that younger patients had higher prevalence of hypovitaminosis D and that age was directly proportional to the serum vitamin D levels. [7] Another study of Asian adults in United Kingdom reported 82% prevalence of hypovitaminosis D with levels less than 12 ng/ml (or 30 nmol/L) during summer with the prevalence increasing to 94% during the winter season. [8] Holick MF also reported a higher prevalence of 84% in a population of black adults in Boston with serum vitamin D levels less than 20 ng/ml. [9]

This study reported more male participants with vitamin D insufficiency and more female participants with Vitamin D deficiency and sufficiency. However, when combined more male participants had hypovitaminosis D than their female counterparts (F=87.3%, M=89.3%). Similarly, various Indian prevalence studies on hypovitaminosis D have reported more female participants with vitamin D deficiency than the male participants [10]. The reason for more male participants with insufficient reserves of serum vitamin D in this study could be attributed to more participants being from upper-lower socio-economic status with less availability of vitamin D fortified food.

The mean serum vitamin D level in this study was 20.61 ±11.67 ng/mL which was lower than the normal range. These results may be explained by the fact that this study was conducted in an urban city where residents live in over-crowded space and have limited exposure to sunlight. Lack of space also plays a detrimental effect on outdoor activities. Additionally, the air pollution in city like New Delhi restricts the exposure of ultraviolet rays to the skin and interferes in its synthesis. [4] Similar low mean values for serum vitamin D have been documented across India by multiple researchers Shukla et al [11] who reported a mean of 21.47 ± 14.4 in a retrospective analysis of an urban cohort, Manoharan et al [12] who reported a mean value of 24.19 ng/mL [95% CI = 22.23ng/mL - 26.16ng/mL] in males and a mean value of 24.15 ng/mL [95% CI =21.95 ng/mL - 26.35 ng/mL] in females. Even globally low mean value for serum vitamin D has been documented in people from different ethnic groups by Plotnikoff et al [7] and Cidem M et al [13] who reported a mean of 10.7 ± 4.6 ng/mL in study population deficient in serum vitamin D.

In this study statistically significant results were seen for prevalence of hypovitaminosis D in patients with adequate daily intake of Calcium with p=0.000. Similar significant association was observed by Ferreira at al [14] in a study on premenopausal women and by Mithal A et al [15] in a study on hospital staff in a different northern Indian city.

In this study although no statistically significance was observed between different serum vitamin D levels for patients with different BMI groups (p=0.236), but higher levels of serum vitamin D were observed in patients with normal BMI and those who were overweight. Vitamin D is a fat-soluble vitamin so higher levels would be expected in patients with higher BMI but morbidly obese people could also have hypovitaminosis D on account of reduced sun exposure (when compared with their lean counterparts); decrease in 25(OH)D concentrations due to negative feedback from an increased 1,25(OH)D concentration in obese individuals; sequestration of vitamin D within adipose tissue and volumetric dilution. Contrary to the results of this study, Selvarajan S et al [10] observed a significant difference in Vitamin D level among people with normal BMI (22.18 [19.61–24.76] ng/ml) as compared to those with high BMI (13.65 [7.82–19.48] ng/ml.

This study also documented statistically significant results between serum vitamin D levels in patients with different sunlight exposure (p=0.032).. Analogous observations were made by Mithal A et al [15] who measured an average sunlight exposure time of 11 min per day in their study subjects, and a strong correlation between the duration of sunlight exposure and 25(OH)D levels, strengthening the fact that adequate sun exposure is necessary to maintain vitamin D levels.

CONCLUSION

Adults with hypovitaminosis D are often misdiagnosed as having fibromyalgia, chronic fatigue syndrome, or myositis and treated inappropriately with nonsteroidal anti-inflammatory agents or antidepressants. This study confirms a high prevalence of vitamin D deficiency in people with diffuse musculoskeletal pain in apparently healthy urban Indians and advocates the supplementation of vitamin D in such patient population.

LIMITATIONS

The patient group analyzed in the study—patients with "persistent, nonspecific musculoskeletal pain"—is by definition an amalgamation of multiple physical and emotional issues. In the absence of a concurrent comparison group, this study says nothing about whether vitamin D deficiency is more common in such patients than in the population at large or whether it has any role in causation. Therefore, it is imperative that a confirmatory case-control study followed by an evaluation of the effects of vitamin D repletion should be undertaken before proposing vitamin D supplementation for management of nonspecific musculoskeletal pian.

REFERENCES

1. Aparna P, Muthathal S, Nongkynrih B, Gupta SK. Vitamin D deficiency in India. J Family Med Prim Care. 2018;7(2):324-330.
2. Hsiao MY, Hung CY, Chang KV et al. Is serum hypovitaminosis D associated with chronic widespread pain including fibromyalgia? A meta-analysis of observational studies. Pain Physician 2015;18, E877–E887.
3. Wu Z, Malihi Z, Stewart AW, Lawes CM, Scragg R. The association between vitamin D concentration and pain: a systematic review and meta-analysis. Public Health Nutr. 2018 Aug;21(11):2022-2037.
4. Ritu G, Gupta A. Vitamin D deficiency in India: prevalence, causalities and interventions. *Nutrients*. 2014;6(2):729-775.
5. Tandon N., Marwaha R.K., Kalra S., Gupta N., Dudha A., Kochupillai N. Bone mineral parameters in healthy young Indian adults with optimal vitamin D availability. Natl. Med. J. India. 2003; 16:298–302.
6. Beloyartseva M., Mithal A., Kaur P., Kalra S., Baruah M.P., Mukhopadhyay S., Bantwal G., Bandgar T.R. Widespread vitamin D deficiency among Indian health care professionals. Arch. Osteoporos. 2012; 7:187–192.
7. Plotnikoff G.A., Quigley J.M. Prevalence of Severe Hypovitaminosis D in Patients With Persistent, Nonspecific Musculoskeletal Pain. Mayo Clin Proc. 2003; 78:1463-1470.
8. Pal BR, Marshall T, James C, Shaw NJ. Distribution analysis of vitamin D highlights differences in population subgroups: preliminary observations from a pilot study in UK adults. J Endocrinol. 2003; 179:119-129.
9. Holick MF. Vitamin D: the underappreciated D-lightful hormone that is important for skeletal and cellular health. Curr Opin Endocrinol Diabetes. 2002; 9:87-98.
10. Selvarajan S, Gunaseelan V, Anandabaskar N, et al. Systematic Review on Vitamin D Level in Apparently Healthy Indian Population and Analysis of Its Associated Factors. Indian J Endocrinol Metab. 2017;21(5):765-775.
11. Shukla K, Sharma S, Gupta A, Raizada A, Vinayak K. Current Scenario of Prevalence of Vitamin D Deficiency in Ostensibly Healthy Indian Population: A Hospital Based Retrospective Study. Indian J Clin Biochem. 2016;31(4):452-457.
12. A Manoharan, P Selvaraj, P Vasanthamani. Vitamin D level among patients with non specific musculoskeletal pain attending tertiary care hospital in Tamil Nadu. Int J Orthop Sci 2016;2(4):94-96.
13. Cidem M, Karacan L, Beytemur O, Kara S. Prevalence and risk factors for vitamin D deficiency in patients with widespread musculoskeletal pain. Turk J Med Sci (2017) 47: 728-731.
14. Ferreira Tda S, Rocha TM, Klein MR, Sanjuliani AF. Vitamin d deficiency is associated with insulin resistance independent of intracellular calcium, dietary calcium and serum levels of parathormone, calcitriol and calcium in premenopausal women. Nutr Hosp. 2015 Apr 1;31(4):1491-8.
15. Arya V, Bhambri R, Godbole MM, Mithal A. Vitamin D status and its relationship with bone mineral density in healthy Asian Indians. Osteoporos Int. 2004 Jan;15(1):56-61. doi: 10.1007/s00198-003-1491-3.