ISSN 2394–806X (Print), ISSN 2454-5139 (Electronic)
IJHRMLP, Vol: 03 No: 01 January, 2017
Printed in India




**ORIGINAL PAPER**

# Study of Vitamin-D status in patients with low backache

***Borah Papori[1], Begum Firdushi[2], Khakhlari Arjun R[3], Kayal Ashok K[4], Goswami Munindra[5]***

***Received** on November 07, 2016; **editorial approval** on December 02, 2016*

**ABSTRACT**

***Introduction:*** *Apart from its established role in calcium homeostasis, studies have found vitamin D to be very much important for the normal maintenance and functioning of the muscles and nerves.* ***Aims:*** *i) To study the vitamin D levels in patients of low back ache ii) compare it with a control population.* ***Methods****: The study was designed as a case control study, with 100 cases and 100 controls. Patients with complaint of low backache were included in the study. A sample of venous blood was collected for vitamin D estimation.* ***Results****: In this study mean vitamin D level in the case group was found to be 29.19 ng/ml and in the control group 38.45ng/ml. P- value was found to be <.0001. Vitamin D deficiency and insufficiency was found more in females than males in both groups. 77.5% of the female patients and 45% of male patients had below normal vitamin D levels.* ***Conclusion****: There is a high possibility that vitamin D deficiency has a role to play in the aetiology of low backache.*

***Keywords****: Hypovitaminosis D, myopathy, pro-inflammatory, skeletal, supplementation.*

## INTRODUCTION

Low backache is one of the most common presenting complaints of patients visiting the Neurology, Neurosurgery and Orthopedics Outdoor clinics. The definition of chronic low back pain has been standardized and is defined as a clinical syndrome characterized with pain localized in the area below the costal margins and above the inferior gluteal folds.[1] Low back pain is experienced by most individuals at some point of time and is one of the commonest health reasons given for work loss.[2] In upto 80% of the patients the exact cause cannot be ascertained by the physician.[3] In the diagnosed cases, lumbar Prolapsed Intervertebral Disc Lesion (PIVD) comes out as the most common etiology. PIVD may be caused by osteoporosis which may in turn be the outcome of vitamin D deficiency.

The role of vitamin D in healthy development of bones is well established. Research on this important nutrient is now concentrated on its non-classical actions. Studies have found this vitamin to be very much important for the normal maintenance and functioning of the muscles and nerves and Vitamin D deficiency has been linked with myopathy, aches and pains in many studies.[4] Studies have also shown that vitamin D deficiency is associated with increased incidence of inflammation being directly linked with anti-inflammatory cytokines.[5, 6]

Till the last century vitamin D deficiency was not thought to be prevalent by the physicians or contribute to a disease process except for rickets and osteomalacia. But recent studies carried on in different parts of the world have reported a high prevalence of vitamin D deficiency in different study populations.[7-9] India though is located in the tropical zone, receiving ample amount of sunlight, the prevalence of vitamin D deficiency has been found to be very high in all age groups and both sexes.[10-11] Besides studies showing vitamin D deficient status among patients suffering from low back ache, chronic musculoskeletal pain or other neurological diseases in comparison to controls,[12-14] there are research works which have shown that supplementation of vitamin D results in alleviation of symptoms in these disease processes.[15]

So vitamin D deficiency may either play a proinflammatory role or by virtue of its role in calcium homeostasis, deficient status of

**Address for correspondence:**
[1]Assistant Professor **(Corresponding Author)**
Department of Neurology,
**Mobile**: +9194351 12184
**Email**: drpapori@gmail.com
[2]Assistant Professor, Department of Biochemistry
[3]Assistant Professor, Department of Anesthesiology
[4]Professor, Department of Neurology
[5]Professor & HOD, Department of Neurology
Gauhati Medical College & Hospital, Guwahati, Assam, India

this vitamin may cause skeletal deformities in the vertebral column resulting in pain. Taking the findings of these research studies into consideration and also noting the high prevalence of vitamin D deficiency in patients of low back pain visiting the OPDs ,and alleviation of pain brought about by vitamin D supplementation, this study was planned to study the vitamin D levels in patients of low back ache and compare it with a control population under a standard protocol, so that the practical findings can be tabulated and presented for the benefit of the patient population.

## METHODS

**Study Design and duration:** The study was designed as a case control study to be completed within a period of one year.

**Study population:** A total number of 100 patients irrespective of gender and age, who visited neurology OPD with complaints of back pain was selected as cases after considering the exclusion and inclusion criteria. Similarly 100 controls were selected from the attendants of the patients, volunteers in the department of Neurology and Biochemistry .Informed consent was taken both from the cases and controls.

**Place and time of study:** The study was conducted in the department of Neurology and Central Clinical Laboratory, Biochemistry Section of Gauhati Medical College & Hospital from December 2015 to September 2016.

**Inclusion Criteria: Cases:** Patients attending Neurology OPD with complaints of low backache. Controls: (1) Healthy attendants of the patients. (2) Volunteers in the department of Neurology and Biochemistry not suffering from backache.

**Exclusion Criteria:** Cases:

1. Patients who had a mechanical cause for the backache.
2. Patients suffering from infectious diseases like Tuberculosis.
3. Patients with known renal impairment or chronic liver disease .
4. Patients suffering from Primary/ Metastatic bone disease.
5. Patients suffering from autoimmune disease.
6. Patients taking vitamin D supplements, using sun blocks.
7. Patients on drugs like antitubercular drugs.
8. Pregnant & lactating women.

Controls: (1) Persons taking vitamin D supplements, using sun blocks (2) Pregnant & lactating women.

**Study Methodology:** Cases were selected from among the patients who visited neurology OPD with complaints of backache. After obtaining informed consent from the patient a thorough history was taken and general as well as neurological examination done. The required data and the relevant examination findings were noted down in a questionnaire. The patients were then sent to Central Clinical Laboratory-Biochemistry Section, where a venous blood sample was collected for vitamin D, Calcium and Phosphorus estimations.

**Analysis of samples:** The venous blood samples were promptly centrifuged and serum was separated and stored at -20°C until the time of analysis. Serum 25(OH)D was estimated using the Vitros 25(OH)D total reagent pack on the Vitros ECiQ Immunodiagnostic System.A competitive immunoassay technique is used which involves the release of the 25(OH)D in the sample from the binding protein using a low ph denaturant and the subsequent competition of the free 25(OH)D with HRP labelled 25(OH)D reagent for the monoclonal anti-vitamin D bound to the wells. Calibration of the reagent was done every 28 days and one level of control was run with each batch of assay. Calcium and phosphorus was estimated in Vitros 4600 Chemistry System using dry slide technology and reflectance spectrophotometry.

**Definition of vitamin D levels** [16]*:*

i) Vitamin D deficient – 25(OH)D < 20 ng/ml.

ii) Vitamin D insufficient – 25(OH)D – 20-<30 ng/ml.

iii) Vitamin D normal – 25(OH)D- 30-100 ng/ml.

**Statistical Analysis***:* Data are presented as mean ± standard deviation. Student's t test was used to compare the data. Pearson's coefficient was calculated to study the correlation between vitamin D and calcium and vitamin D and phosphorous. P<0.05 was considered significant.

## RESULTS & OBSERVATIONS:

**Table 1** Demographic and biochemical profile of study cases and controls

| | CASES(n=100) | | CONTROLS(n=100) | | |
|---|---|---|---|---|---|
| | Mean ± SD | Range | Mean ± SD | Range | p-value |
| Age(years) | 46.99 ± 14.54 | 17-77 | 35 ± 12.43 | 21- 43 | <.0001*** |
| Male : Female | 60 : 40 | - | 56 : 44 | - | - |
| Body mass index (kg/m$^2$) | 23.09 ± 4.12 | 16.5-32.5 | 21.6 ± 3.24 | 16.07-29.5 | 0.0049** |
| 25 OH Vit D(ng/ml) | 29.19 ± 15.92 | <8-94.4 | 38.45 ± 13.21 | 13.8-81 | <0.0001*** |
| Calcium (mg/dl) | 9.08 ± 0.69 | 7.1-10.7 | 9.26 ± 0.56 | 7.9-10.3 | 0.0442* |
| Phosphorous (mg/dl) | 3.91 ± 0.59 | 2.7-5.2 | 3.68 ± 0.45 | 2.9-4.7 | 0.0022** |

***-Extremely significant,**-Very significant, *Significant*

**Table 2** Vitamin D status in cases and controls

| | | Male | Female | Total |
|---|---|---|---|---|
| Deficient | Cases | 12 | 13 | 25 |
| | Controls | 2 | 1 | 3 |
| Insufficient | Cases | 15 | 18 | 33 |
| | Controls | 5 | 19 | 24 |
| Normal | Cases | 34 | 8 | 42 |
| | Controls | 42 | 31 | 73 |

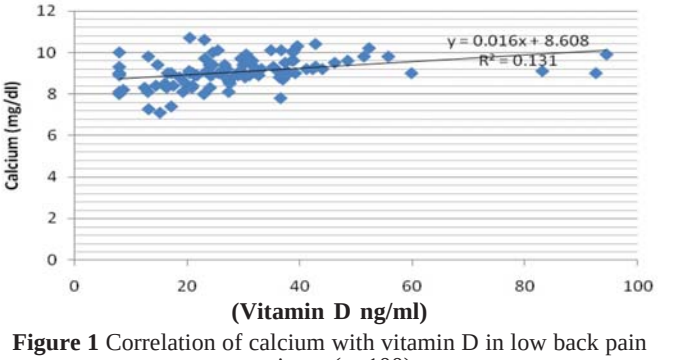


**Figure 1** Correlation of calcium with vitamin D in low back pain patients (n=100)

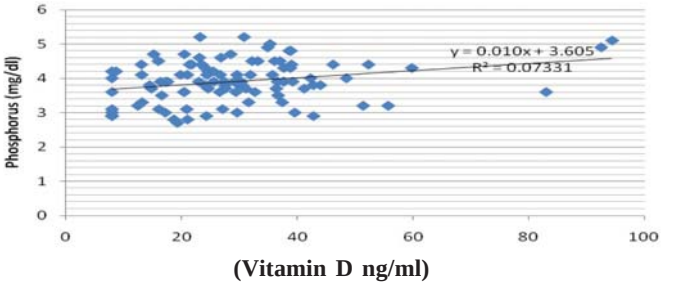


**Figure 2** Correlation of phosphorous with vitamin D in low back pain patients (n=100)

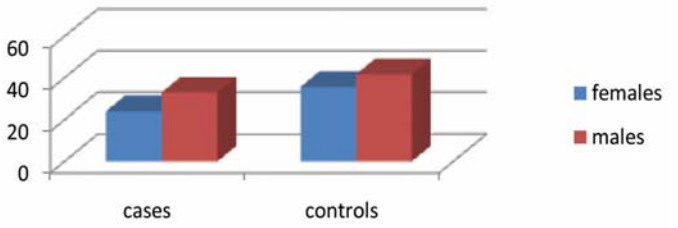


**Figure 3** Comparison of Vitamin D levels between males and females in both cases and controls.

## DISCUSSION

Low backache is the most common reason for medical consultation. It is a leading cause of disability and interferes with the quality of life and work performance. In many cases anatomic defect as a cause is not detected. In cases where anatomic defect is the cause of low backache, the anatomic defect may be the outcome of vitamin D deficiency resulting in deranged calcium-phosphorous metabolism.[17-19] however chronic pain is one of the many conditions which have been recently associated with vitamin D deficiency. Also vitamin D being responsible for calcium homeostasis and bone metabolism, it is highly possible that low vitamin D levels may result in muscle weakness and abnormalities in bone metabolism leading to back pain.[20]

Before 2000, vitamin D deficiency was not known and doctors also did not consider it as a cause of any medical problem. But with changes in the life style of people limiting outdoor activity, and with availability of new technology to measure vitamin D, vitamin D deficiency has emerged as a global phenomenon. Several Neuronal cells, and muscle cells have been found to express vitamin D receptors. This explains that vitamin D plays a role in the normal metabolism and function of these cells. Measurement of total 25-OH Vitamin D, because of its long life and it being the major circulating form , provides the best assessment of a person's vitamin D status. A serum level of 40-60 ng/ml is believed to be optimum for skeletal and non-skeletal functions and levels upto 100ng/ml is considered safe.[21]

In the present study the case group consisted of more males than females, in the ratio of 6:4. As was hypothesized that low levels of vitamin D may be responsible for low backache, it was found that the level of vitamin D in case group subjects was significantly low with a p-value of $< 0.001$, when compared with the control group. As expected in hypovitaminosis D, calcium level was also found to be significantly low in the case group when compared with control group,(9.08 vs 9.26,p=0.0442).Recent studies have come up with similar findings of significantly low vitamin D levels in patients suffering from chronic low backache.[22-24] Studies done on other cases of chronic pain have also come forward with similar findings.[25-27] Also there are follow up studies which have reported that more than 90% of patients with pain and muscle weakness responded to treatment with vitamin D supplement.[15,28] Schreuder et al, in a study reported a positive effect of vitamin D supplementation in patients with non-specific musculoskeletal pain.[29]

In this study vitamin D deficiency and insufficiency was found to be more in females as compared to males both in the case and control group. 77.5% of the female patients suffering from low backache had below normal vitamin D levels, whereas 45% of male patients had low levels of vitamin D. In the control group percentage of low vitamin D levels in females was 43.48 and males was 12.96. However the mean vitamin D levels did not differ significantly between males and females in both the study groups. In most studies the status of vitamin D has been noted to be low in females as compared to males. This may be considered the result of females mainly remaining indoors limiting their exposure to sunlight. However data on sun exposure though collected could not be properly analysed. Also regarding diet 95% of the study participants, both case and control were non-vegetarians, ruling out the diet related deficiency of vitamin D. Consensus has not been established regarding levels of vitamin D in males and females, as there are studies where vitamin D deficiency has been found to be more in males in comparison to females.[23,30]

The role of vitamin D in different disease processes has recently received great interest with the discovery of vitamin D receptors in many tissues of the body. A number of studies have suggested a link between low levels of vitamin D and higher incidence of chronic pain in different patient populations like rheumatology patients, women with low back pain during child bearing period, patients with non-specific musculoskeletal pain and with lumbar spinal stenosis.[25-27] Furthermore studies on association of latitude and season of the year with pain have provided indirect evidence of the importance of low vitamin D levels on the aetiology of pain.[31-32] More specifically hypovitaminosis D has been linked to chronic low back pain in many studies conducted in different parts of the world. The exact pathogenic mechanism of low back pain in patients with low vitamin D levels has not been arrived at, but several hypotheses have been laid forward. High levels of inflammatory markers have been found in people with low vitamin D levels, signifying that vitamin D is anti-inflammatory .[33,34] People with low vitamin D levels are more susceptible to inflammation in the vertebral end plates resulting in low backache. Also adequate levels of vitamin D are necessary for the continuous regeneration of nerve cells. Chronic vitamin D deficiency has been found to result in osteoporosis, osteomalacia, and increased risk of falls.[35] In a study by TH Kim et al, it was found that severe back pain and leg pain was associated with higher incidence of osteoporosis and higher level of bone resorption marker (serum CTx).[36]

Studies have not only revealed a high prevalence of vitamin D deficiency in patients presenting with chronic low backache but several of such follow-up studies have shown that replacement therapy with vitamin D in patients suffering from chronic low backache of unknown aetiology and with low levels of vitamin D resulted in remarkable relief of symptoms.

## CONCLUSION

In conclusion it can be said that this study revealed a significant difference of vitamin D levels between cases of low backache and normal controls, with chronic low backache patients having low levels of the vitamin. Vitamin D deficiency was also found to be more in females as compared to males. So although the exact pathogenic mechanism implicating low vitamin D in low backache is still not clear, vitamin D measurement can be made a part of the investigation protocol and clinicians may try with replacement therapy in low vitamin D status patients for alleviation of symptoms.

**Conflict of interest**: None declared.

**Ethical clearance**: Taken.

**Source of support:** We acknowledge the support provided by Ortho Clinical Diagnostics India Pvt Ltd in conducting the study in the form of free supply of reagents required for the study.

**Declarations**: (1) The Article is original with the author(s) and does not infringe any copyright or violate any other right of any third parties; (2) The Article has not been published (whole or in part) elsewhere, and is not being considered for publication elsewhere in any form, except as provided herein; (3) All author (s) have contributed sufficiently in the Article to take public responsibility for it and (4) All author (s) have reviewed the final version of the above manuscript and approve it for publication.

## REFERENCES

1. Dionne CE, Dunn KM, Croft PR, Nachemson AL, Buchbinder R, Walker BF, et al. A consensus approach towards the standardization of back pain definitions for use in prevalence studies. Spine 2008;33:95-103.
2. Wadell G, Burton AK. Occupational health guidelines for the management of low back pain at work: evidence review. Occupational Medicine 2000;51(2):124-35.
3. Deyo RA. Diagnostic evaluation of LBP-reaching a specific diagnosis is often impossible. Arch Intern Med 2002;162:1444-7.
4. Ali JMM. Vitamin D deficiency in outpatient department: eastern province of KSA experience. Rawal Med J 2010;35:221-3.
5. Schleithoff SS, Zittermann A, Tenderich G et al. Vitamin D supplementation improves cytokine profiles in patients with congestive heart failure: a double-blind randomized, placebo-controlled trial. Am J Clin Nutr 2006;83:754-9.
6. D'Ambrosio D, Cippitelli M, Cocciolo MG, Mazzeo D, Di Lucia P, Lang R et al. Inhibition of IL-12 production by 1,25-dihydroxyvitamin D3. Involvement of NF-kappa B down regulation in transcriptional repression of the p40 gene J Clin Invest 1998;101:252-62.
7. Holick MF, Chen TC. Vitamin D deficiency: a worldwide problem with health consequences. Am J Clin Nutr 2008;87:1080S-6S.
8. Arabi A, El Rassi R, El-Hajj Fuleihan G. Hypovitaminosis D in developing countries-prevalence, risk factors and outcomes. Nat Rev Endocrinol 2010;6:550-61.
9. Van der Meer IM, Middelkoop BJ, Boeke AJ, Lips P. Prevalence of vitamin D deficiency among Turkish, Moroccan, Indian and sub-Sahara African populations in Europe and their countries of origin: An overview. Osteoporos. Int 2011;22:1009–21.
10. Harinarayan CV, Joshi SR. Vitamin D status in India-Its implications and Remedial Measures. J Assoc Physicians India 2009;57:40-8.
11. Zargar AH, Ahmad S, Masoodi SR, Wani AI, Bashir MI, Laway BA et al. Vitamin D status in apparently healthy adults in Kashmir valley of Indian subcontinent. Postgrad Med J 2007;83(985):713-6.
12. Plotnikoff GA, Quigley JM. Prevalence of severe hypovitaminosis D in patients with persistent, nonspecific musculoskeletal pain. Mayo Clin Proc 2003;78(12):1463-70.
13. McCarty DE, Reddy A, Keigley Q, Kim PY, Cohen S, Marino AA. Nonspecific pain is a marker for hypovitaminosis D in patients undergoing evaluation for sleep disorders: a pilot study. Nat Sci Sleep 2013;5:37-42.
14. Al Faraj S, Al Mutairi K. Vitamin D deficiency and chronic low back pain in Saudi Arabia. Spine (Phila Pa 1976) 2003;28(2):177-9.
15. Rao Ch R, Maruthi W. Study of Beneficial Role of Vitamin D in Chronic Low Back Pain. Paripex-Indian J of Research 2015;4(7):68-70.
16. Holick MF, Binkley NC, Bischoff-Ferrari HA, Gordon CM, Hanley DA, Heaney RP et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2011;96(7):1911-30.
17. Atherton K, Berry DJ, Parsons T, Macfarlane GJ, Power C, Hyppönen E. Vitamin D and chronic widespread pain in a white middle-aged British population: evidence from a cross-sectional population survey. Annals of the Rheumatic Diseases 2009;68(6):817–22.
18. Benson J, Wilson A, Stocks N, Moulding N. Muscle pain as an indicator of vitamin D deficiency in an urban Australian Aboriginal population. Medical Journal of Australia 2006;185(2):76–7.
19. Lotfi A, Abdel-Nasser AM, Hamdy A, Omran AA, El-Rehany MA. Hypovitaminosis D in female patients with chronic low back pain. Clinical Rheumatology 2007;26(11):1895–1901.
20. Simonelli C. The role of vitamin D deficiency in osteoporosis and fractures. Minn Med 2005;88:34-6.
21. Bischoff-Ferrari HA, Giovannucci E, Willett WC, Dietrich T, Dawson-Hughes B. Estimation of optimal serum concentrations of 25-hydroxyvitamin D for multiple health outcomes. Am J Clin Nutr 2006;84(1):18-28.
22. Lodh M, Goswami B, Mahajan RD, Sen D, Jajodia N, Roy A. Assessment of vitamin D status in Patients of Chronic Low Back Pain of Unknown Etiology. Ind J Clin Biochem 2015;30(2):174-9.
23. Ghai B, Bansal D, Kapil G, Kanukula R, Lavudiya S, Sachdeva N. High Prevalence of Hypovitaminosis D in Indian Chronic Low Back Patients. Pain Physician 2015;18:E853-E862.
24. Kalra S, Kalra B, Khandelwal SK. Vitamin D status in patients with musculoskeletal symptoms in Haryana. Indian J Med Nutr Nutraceut. 2012;1:50-3.
25. Plotnikoff GA, Quigley JM. Prevalence of severe hypovitaminosis D in patients with persistent, non-specific musculoskeletal pain. Mayo Clin Proc 2003;78:1463-70.
26. Stoll D, Dudler J, Lamy O, Hans D, So A, Krieg MA et al. High prevalence of hypovitaminosis D in a Swiss rheumatology outpatient population. Swiss Med Wkly 2011;141:W13196.
27. Lofti A, Abdel-Nasser AM, Hamdy A, Omran AA, El-Rehany MA. Hypovitaminosis D in female patients with chronic low back pain. Clin Rheumatol 2007;26:1895-1901.
28. Jalili A, Bahrabadi M, Zare S. Prevalence of vitamin D deficiency in Nonspecific Musculoskeletal Pain . Shafa Orthopedic Journal 2015;2(4):e4052.
29. Schreuder F, Bernsen R, van der Wouden JC. Vitamin D supplementation for non-specific musculoskeletal pain in non-western immigrants: a randomized controlled trial. Ann Fam Med 2012;10:547-55.
30. Yetley EA. Assessing the vitamin D status of the US Population. The Am J of Clin Nutr 2008;88(2):558S-564S.
31. Mitsikostas DD, Tsaklakidou D, Athanasiadis N, Thomas A. The prevalence of headache in Greece: correlations to latitude and climatological factors. Headache 1996;36(3):168-73.
32. Zeng QY, Chen R, Xiao Y et al. Low prevalence of knee and back pain in southeast China; the Shantou COPCORD study. Journal of Rheumatology 2004;31(12):2439-43.
33. Zhang Y, Leung DY, Richers BN, Liu Y, Remigio LK, Riches DW et al. Vitamin D inhibits monocyte/macrophage proinflammatory cytokine production by targeting MAPK phosphatase. J Immunol 2012;188(5):2127-35.
34. Lacativa PGS, Farias ML. Osteoporosis and inflammation. Arq Bras Endocrinol Metab 2010;54(2):123-32.
35. Bischoff-Ferrari HA, Dawson-Hughes B, Willett WC, Stachelin HB, Bazemore MG, Zee RY et al. Effect of vitamin D on falls: a metaanalysis. JAMA 2004;291:1999-2006.
36. Kim TH, Lee BH, Lee HM, Lee SH, Park JO, Kim HS et al. Prevalence of Vitamin D deficiency in patients with lumbar spinal stenosis and its relationship with pain. Pain Physician 2013;16(2):165-76.