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Vitamin D Deficiency in North Indian Orthopaedic Patientspresenting with Non Specific Chronic Musculoskeletal Pain.

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Abstract

Purpose- Vitamin D deficiency may present with unexplained musculoskeletal pain and weakness before developing frank symptoms of osteomalacia. The aim of our study is to find the prevalence of vitamin D deficiency in patients presenting with chronic non specific musculoskeletal pain not attributable to any other condition to the orthopaedic outpatient department.

Material & Methods:- The study was conducted at a tertiary level medical college facility in northern India in the orthopaedic department between January 2019 and June 2020. All the patients presenting in the orthopaedic outpatient department between 10 years to 80 years of age with unexplained chronic musculoskeletal pain and general fatigability were included in the study. Vitamin D levels, Serum Calcium, phosphorus and alkaline phosphatase were done for all the patients.

Results:- The total no of patients in our study were 604 patients out of which 250 were males (41.4%) and 354 females (58.6%). Median value of vitamin D in our study was 11 ng/ml and median age of our patients was 28 years. The vitamin D deficiency was seen in 83.4% cases and insufficiency in 8.3% cases . Most of the subjects having vit D deficiency were in the age group of 21-40 years (83.46%) which was stastically significant and higher than other age groups ($p<0.05$). There was no stastically significant difference with regard to sex and BMI in any other patient group.

Conclusion:-. Based on our study we would recommend screening and treatment for vitamin D deficiency for all patients presenting with chronic generalized nonspecific musculoskeletal pain.

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Dietary counseling, fortification of foods and exposure to sunshine should be encouraged to eliminate this problem.

Keywords- Vitamin D deficiency, musculoskeletal pain, osteomalacia,

Introduction

Vitamin D has always been considered a vital nutrient for bone health. In recent times it has also emerged to have an important role in extra skeletal diseases such as in diabetes, cancer, cardiovascular, autoimmune and infectious diseases **[1, 2].** Vitamin D also functions as a hormone to regulate musculoskeletal health and to maintain calcium homeostasis [**3, 4].** Severe Vitamin D deficiency causes osteomalacia in adults and rickets in children. Vitamin D receptors are also present in skeletal muscle cells and have an important role in muscle function. Chronic non specific muscle pain is said to be unexplained when there are no clinical or investigational findings to explain its occurrence. Such kind of pain can cause disability and decreased quality of life for the patient (5). The aim of our study is to study the prevalence of vitamin D deficiency in patients presenting with such unexplained chronic generalised non specific musculoskeletal pain.

Material & Methods:

Present study was an observational study done at a tertiary level medical college facility in northern India in the Orthopedics department between January 2019 and June 2020. All the patients presenting in the Orthopedics outpatient department from 10 years of age to 80 years with unexplained chronic musculoskeletal pain and general fatigability were included in the study. Thorough history based on their clinical features and physical examination was done to rule out any other cause of chronic musculoskeletal pain.

Pathological tests such as Vitamin D, Serum Calcium, Phosphorus, Alkaline phosphatase along with haemogram, renal and hepatic function tests were done. Ethical clearance was
taken from ethical committee of the institute and written informed consent from the patient was also taken.

Exclusion criteria: Patients with chronic diseases like diabetes mellitus, cancer, hepatic, renal, thyroid or parathyroid gland disorders and dermatological disorders were excluded. Patients on hormone replacement therapy, glucocorticoids, bisphosphonates, teriparatide, Vitamin D and anticonvulsants were also excluded.

From each study subject, 10 ml blood sample was drawn without venostasis. In lab serum was separated after centrifugation at 3000 rpm for 15 min at 4- 8 degrees C. Vitamin D levels were measured by ARCHITECT 25-OH vitamin D chemiluminescence microparticle immunoassay (CMIA) (ABBOTT, USA).The subjects were classified as vitamin D deficient, insufficient or sufficient on the basis of 25(OH) D concentrations of <= 20 ng/ml, 21-30 ng/ml and 31-100 ng/ml respectively, according to recent consensus (6,7,8). Data is presented as number and proportion. Chi square and student t test was used to compare qualitative and quantitative variables. A p-value of <0.05 was taken to be statistically significant.

Results

The total no of patients in our study were 604 consisting of 250 (41.4%) males and 354 females (58.6%). Median age of our patients was 28 years with a minimum age of 10 years and a maximum of 80 years. The total no of patients with vitamin D deficiency were 554 out of which 228 (41.2%)

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were males and 326 (58.8%) patients were female (Figure 1). However there was no statistically significant difference between the male and female gender in the deficiency group (p-value = 0.69).
Table 1 shows distribution of Vitamin D deficiency in study subjects. A total of 505 subjects (83.44%) had vitamin D deficiency, 50(8.28%) had insufficiency and 50 (8.28%) had sufficient level of vitamin D. The overall deficiency of vitamin D was present in approximately 92% of the patients. Median value of vitamin D was 11ng/ml. The lowest value of vitamin D was 4 ng/ml and the maximum value was 105 ng/ml. Median value of S. Ca was 9.36 mg/dl and phosphorus was 3.41 mg/dl.

Age wise distribution and results of the patients has been shown in Table 2. Most of the subjects having vitamin D deficiency were in the age group of 21-40 years (83.46%) and minimum were in the age group <20 years (25.86%) (Figure: 2). Difference in the age groups was statistically significant (p- value=0.022). Vitamin D deficiency was 94 % in Muslims and 89.6% in Hindus which was also statistically significant (p value=0.048).
Table 3 shows laboratory values of Vitamin D, Serum Calcium, phosphorus and alkaline phosphatase level in patient groups having deficient, insufficient and sufficient levels of vitamin D. There was no statistically significant difference in body mass index (BMI) of the patients with and without Vitamin D deficiency (p-value= 0.347). Median Vitamin D levels was 10ng/ml in the deficiency group which was significantly lower (p-value =0.00001) than the sufficient group (41ng/ml).

Discussion

Vitamin D deficiency is present in pandemic proportions throughout the world including India [9, 10]. Vitamin d deficiency is present as a silent disease in all age groups (80-90%) irrespective of sex, ethnicity, religion and geographical location [11]. Indian diet is mostly vegetarian having less calcium and protein, cooking methods involving heating or frying further decreases vitamin D levels in food [1].
Severe Vitamin D deficiency (VDD) leads to various musculoskeletal problems most commonly manifesting as rickets in children and osteomalacia in adults. Subclinical deficiency of Vitamin D may also cause severely impaired muscle function and weakness even before the manifestation of biochemical signs of bone disease [12].
Vaishya et al have also highlighted that subclinical Vitamin D deficiency is present in nearly 70-100% of healthy Indian population[13]. McBeth et al conducted a study in 3075males over 40 years of age. They found that low vitamin D levels was a significant factor for musculoskeletal non specific pain even after taking into account factors like physical inactivity, depression, alcoholism, smoking and high body mass index[14]. Khalid et al studied 261 patients and 100 controls and found a positive association between low vitamin D levels and widespread musculoskeletal pain, anxiety and depression[15]. In our study we focused on patients with unexplained musculoskeletal pain and weakness. These patients may be having early or subclinical symptoms of Vitamin D deficiency before manifestation of frank disease.

In our study of 604 patients we found a high prevalence of vitamin D deficiency (92%) between 10 and 83 years of age. Plotnikoff et al studied 150 patients between 10 to 65 years of age presenting with nonspecific musculoskeletal pain and found 93% deficiency of Vitamin D[16].
Many studies all over the world have also reported an association between vitamin D deficiency and nonspecific musculoskeletal symptoms. Hsiao et al in their metanalysis of observational studies

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found that patients with severe Vitamin D deficiency (< 10 ng/ml) had more chances of having chronic widespread pain syndrome [17]. In our study the median value of vitamin D was also10 ng/ml in the severely deficient patient group (83.4 %).
Humeira et al (18) also found myalgias or non specific muscle pain to be associated with low levels of Vitamin D <20 ng/ml in Arab countries having adequate sunlight. Vitamin D deficiency was found in74% of their 139 patients. They also reported amelioration of symptoms in 90% of these patients with vitamin D therapy. Yong et al (5) in their metanalysis of chronic widespread pain syndrome inferred that Vitamin d supplementation decreased pain and improved the quality of life of Vitamin D deficient patients. Mokta et al (19) looked for proximal muscle weakness in 99 patients. They found Vitamin D deficiency (<30ng/ml) as a major and reversible cause for weakness in these patients.
Pal et al (20) also found vitamin D deficiency to be 91.3% in their study of general orthopaedic patients. The severely deficient group (61.2%) had a median value of 14.5ng/ml Vitamin D. In our study only patients who had complaint of chronic non specific musculoskeletal pain were included from the orthopaedic outpatient. 83.4% of our subjects had severely Vitamin D deficiency and had a median value of 10ng/ml (interquartile range 8 -12.7).

Preeti et al (2) in their paper stated that children between 6-18 yrs had 93% Vitamin D deficiency (VDD) which was higher than any other age group. In our study we also found younger population (21-40) yrs to have higher percentage (>80%) of VDD compared to other age groups (p-value=0.022).
Plotnikoff et al (16) also did not find any significant difference in Vitamin D deficiency between the young and old population. Pal et al (20) however found elderly population to be at higher risk for vitamin d deficiency (VDD).
In our study 41.4% males and 58.6% females were deficient but the difference was not stastistically significant. Pal et al (20) also did not find any significant difference between male and female population. Plotnikoff et al (16) found that young women of childbearing age were at disproportionately higher risk of VDD.

High BMI has been reported to be a risk factor for VDD in many studies (21). Pal et al (20) also found inverse relation between BMI and Vitamin D Deficiency. However in our study the median BMI was only 25 and was not a significant predictor of VDD. Non obese patients are also at high risk for Vitamin D deficiency according to our study.
Kalra et al (22) also did a single centre crosssectional study on 234 females in Haryana presenting with musculoskeletal symptoms. They reported Vit D deficiency as high as 94% in these females with severe deficiency of 55% only. The average age of the patients was 45 years. VDD was only 66.7% reported in healthy asymptomatic postmenopausal women from the same centre compared to 94% in the symptomatic group. These high levels of vitamin D deficiency are consistent with 92% deficiency as noted in our study of symptomatic patients. However the number of patients (604) in our study is higher and study includes both males and female population of all age groups compared to their study of 234 postmenopausal females. Also 83.44 % of our patients had severe Vitamin D deficiency as compared to 55% reported by Kalra et al (22).

In a study by Ramakrishna et al(23) of asymptomatic healthy young adults only 49.3% of them had Vitamin D deficiency while in our study of symptomatic patients approximately 92.3% of young adults had Vitamin D deficiency. Beloyartseva et al (24) found 79% vitamin D deficiency in 2119

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healthy adults of average age 42.7 years spread over 18 cities in India. These asymptomatic healthy young adults may be considered as historical control groups since our study lacks the presence of a healthy control group for studying Vitamin D levels. Also the number of elderly group > 60 years which had 26 % sufficiency of Vitamin D was only 27 out of 604 which could have given disproportionate results. These shortcomings in our study can be rectified by having a comparable number of elderly patients to the young patients and also having a healthy control group for comparison of vitamin D levels.

Conclusion

Vitamin D deficiency appears to be present as a silent disease in all age groups irrespective of sex, ethnicity, religion and geographical location. Based on our study we would recommend screening and treatment for vitamin D deficiency for all patients presenting with chronic generalised non specific musculoskeletal pain. Looking at the data from earlier published reports our study appears to be the largest one studying Vitamin D deficiency in patients of chronic non specific musculoskeletal pain in the Indian population. However large scale studies with controls before and after supplementation needs to be conducted before we arrive at a final recommendation. Public awareness, dietary counselling, fortification of foods and exposure to sunshine should be encouraged to eliminate this problem.

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Abbreviations: Vitamin D deficiency-VDD.

References :

1. G Ritu, Gupta A. Vitamin D deficiency in India: prevalence, causalities and interventions. Nutrients. 2014 Feb 21;6(2):729-75. doi: 10.3390/nu6020729. PMID: 24566435; PMCID: PMC3942730.
2. Kamboj P, Dwivedi S, Toteja GS. Prevalence of hypovitaminosis D in India & way forward. Indian J Med Res. 2018 Nov;148(5):548-556. doi: 10.4103/ijmr.IJMR_1807_18. PMID: 30666982; PMCID: PMC6366270.
3. Harinarayan CV, Joshi SR. Vitamin D status in India – Its implications and remedial measures. *J Assoc Physicians India* 2009; *57*: 40-8.
4. Khadilkar AV. Vitamin D deficiency in Indian adolescents. *Indian Pediatr* 2010; *47*: 755-6.
5. Yong WC, Sanguankeo A, Upala S. Effect of vitamin D supplementation in chronic widespread pain: a systematic review and meta-analysis. Clin Rheumatol. 2017 Dec;36(12):2825-2833. doi: 10.1007/s10067-017-3754-y. Epub 2017 Aug 15. PMID: 28812209.
6. Dawson-Hughes B, Heaney RP, Holick MF, Lips P,Meunier PJ, Vieth R, *et al.* Estimates of optimal Vitamin D status. *Osteoporos Int* 2005; *16* : 713-6.
7. Grant WB, Holick MF. Benefits and requirements of Vitamin D for optimal health: A review.

Altern Med Rev 2005;*10* : 94-111.

8. Hollis BW. Circulating 25-hydroxyvitamin D levels indicative of Vitamin D sufficiency: Implications for establishing a new effective dietary intake recommendation for Vitamin D. *J Nutr* 2005; *135*: 317-22.
9. Beloyartseva M, Mithal A, Kaur P, et al. Widespread vitamin D deficiency among Indian health care professionals. Arch Osteoporos. 2012; 7(1–2):187–192-7.
10. Khadgawat R, Brar KS, Gahlo MeT. High prevalence of vitamin D deficiency in Asian-Indian patients with fragility hip fracture: a pilot study. JAPI. 2010;58(Sep-tember):539–542
11. Aparna P, Muthathal S, Nongkynrih B, Gupta SK. Vitamin D deficiency in India. *J Family Med Prim Care*. 2018;7(2):324-330.
12. Glerup H, Mikkelsen K, Poulsen L, Hass E, Overbeck S, Andersen H, Charles P, Eriksen EF. Hypovitaminosis D myopathy without biochemical signs of osteomalacic bone involvement. Calcif Tissue Int. 2000 Jun;66(6):419-24. doi: 10.1007/s002230010085. PMID: 10821877.
13. Vaishya R, Vijay V, Agarwal AK, Jahangir J. Resurgence of vitamin D: Old wine in new bottle. J Clin Orthop Trauma. 2015 Sep;6(3):173-83. doi: 10.1016/j.jcot.2015.02.002. Epub 2015 Mar 26. PMID: 26155053; PMCID: PMC4488032.
14. McBeth J, Pye SR, O'Neill TW, Macfarlane GJ, Tajar A, Bartfai G, Boonen S,Bouillon R, Casanueva F, Finn JD, Forti G, Giwercman A, Han TS, Huhtaniemi IT,Kula K, Lean ME, Pendleton N, Punab M, Silman AJ, Vanderschueren D, Wu FC; EMAS Group. Musculoskeletal pain is associated with very low levels of vitamin D in men: results from the European Male Ageing Study. Ann Rheum Dis. 2010 Aug;69(8):1448-52. doi: 10.1136/ard.2009.116053. Epub 2010 May 24. PMID: 20498201.
15. Abdul-Razzak KK, Mayyas FA, Al-Farras MI. Vitamin D as potential antidepressant in outpatients with musculoskeletal pain. *Int J Clin Pharmacol Ther*. 2018;56(9):400-410.
16. Plotnikoff GA, Quigley JM. Prevalence of severe hypovitaminosis D in patients with persistent, nonspecific musculoskeletal pain. *Mayo Clin Proc*. 2003;78(12):1463-1470. doi:10.4065/78.12.1463
17. Hsiao MY, Hung CY, Chang KV, Han DS, Wang TG. Is Serum Hypovitaminosis DAssociated with Chronic Widespread Pain Including Fibromyalgia? A Meta-analysis of Observational Studies. Pain Physician. 2015 Sep-Oct; 18(5):E877-87. PMID: 26431141.
18. Badsha H, Daher M, Ooi Kong K. Myalgias or non-specific muscle pain in Arab or Indo-Pakistani patients may indicate vitamin D deficiency. Clin Rheumatol. 2009 Aug; 28(8):971-3. doi: 10.1007/s10067-009-1146-7. Epub 2009 Mar 10. PMID: 19277814.
19. Mokta J, Balraj, Mokta K, Ranjan A, Joshi I, Garg M. High Prevalence of Hypovitaminosis D in Patients Presenting with Proximal Muscle Weakness: A Sub- Himalayan Study. J Assoc Physicians India. 2017 Nov;65(11):55-58. PMID:29322711.
20. Pal CP, Kumar H, Kumar D, Mittal V, Deshwar G, Altaf D, Verma S. Prevalence of vitamin D deficiency in orthopaedic patients - A single centre study. J Clin Orthop Trauma. 2016 Oct-

Annals of R.S.C.B., ISSN:1583-6258, Vol. 25, Issue 4, 2021, Pages. 8159 - 8167
Received 05 March 2021; Accepted 01 April 2021.

Dec; 7(Suppl 2):143-146. doi: 10.1016/j.jcot.2016.06.009. Epub 2016 Oct 15. PMID: 28053375; PMCID: PMC5197054.

21. Bogunovic L, Nguyen J, Lane JM, et al. Hypovitaminosis D in patients scheduled to undergo orthopaedic surgery: a single-center analysis. J Bone Jt Surg Am. 2010;92: 2300–2304.
22. Kalra S, Kalra B, Khandelwal SK, et al. Vitamin D status in patients with musculo-skeletal symptoms in Haryana, India. J Med Nutr Nutraceut. 2012;1(January–June (1)):50–53.
23. Ramakrishnan, S.; Bhansali, A.; Bhadada, S.K.; Sharma, R.; Walia, R.; Ravikiran, M.; Shanmugasundar, G.; Ravikumar, P. Vitamin D status and its seasonal variability in healthy young adults in an Asian Indian urban population. *Endocr. Pract.* **2011**, *17*, 185–191.
24. 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.

TABLE: 1 Vitamin D status of patients:

Vitamin D status	No.(%)
Deficiency (vitamin D <20ng/ml)	504(83.44%)
Insufficiency (vitamin D <20- 30ng/ml)	50(8.28%)
Sufficiency (vitamin D >30ng/ml)	50(8.28%)
Total	604

Table: 2 Demographic profile of Vitamin D deficiency

		Deficiency (vitamin D <20ng/ml)	Insufficiency (vitamin D <20-30ng/ml)	Sufficiency (vitamin D >30ng/ml)
Age group	< 20 year(174)	45(25.86%)	11(6.32%)	7(4.02%)
	21-40 year(284)	237(83.46%)	25(8.80%)	22(7.74%)
	41-60 year(119)	97(81.52%)	8(6.72%)	14(11.76%)
	>60 year(27)	15(55.56%)	5(18.52%)	7(25.92%)
Gender	Male (250)	219(87.6%)	19(7.6%)	22(8.8%)

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	Female (354)	295(83.33%)	31(8.76%)	28(7.91%)
Religion	Hindu (318)	250(78.62%))	35(11%))	33(10.38%)
	Muslim (286)	254(88.82%)	15(5.24%)	17(5.94%)

Table: 3 Laboratory characteristics of study subjects (Median and Interquartile range)

Characteristic	Deficiency (vitamin D <20ng/ml)	Insufficiency (vitamin D <20-30ng/ml)	Sufficiency (vitamin D >30ng/ml)
BMI* (Kg/m2)	25.16(22-28)	26.67(25-28.5)	25.41(21.5-28)
Vitamin D(ng/ml)	10(8-12.7)	23(21.3-24.8)	41(36-50.3)
Calcium(mg/dl)	9.26(9-9.7)	9.48(9.2-9.5)	9.33(9.1-9.8)
Phosphorous(mg/dl)	3.1 (2.7- 4.2)	3.23 (3.1-4.7)	3.41(2.9-4 .1)
Alkaline Phosphtase(IU/l)	96 (75-106)	88 (78-104)	85 (70-110)

*BMI-Body mass index

Figure 1- Male and female patient distribution of VDD.

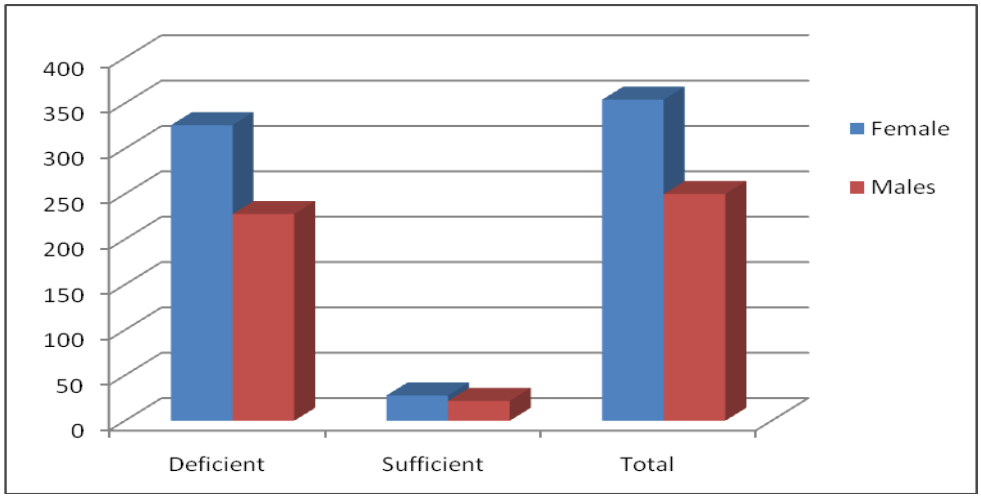

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Figure 2- Age distribution of Vit D deficiency