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Correlation of Vitamin D Levels with Cardiac Function in Patients with Dilated Cardiomyopathy

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Abstract

Introduction: Vitamin D affects immune activation, which is plays a role in the pathogenesis of cardiomyopathy. In the present study we aim to identify correlation between vitamin D levels and echocardiographically determined heart function in patients with dilated cardiomyopathy (DCMP).

Methodology: Cases included patients diagnosed to have DCMP and admitted in our indoor admission ward from January 2019 till December 2019. At the same time, age and gender matched controls were included, which were patients of other medical illnesses admitted in the same hospital. All study participants underwent echocardiography, vitamin D and other biochemical estimations.

Results: During the study period we included 33 cases of DCM and 35 controls. Meanage, gender distribution and BMI was similar for the two study groups. Serum calcium levels were found to be significantly lower in the cases as compared to controls (8.1 ± 1.7 vs 9.8 ± 0.9 mg/dl, $p < 0.05$). 25(OH)D3 was also found to be significantly lower among cases as compared to controls (13.8 ± 3.2 vs 32.8 ± 6.4 ng/dl, $p < 0.01$). We observed that the stroke volume, left ventricular ejection fraction and left ventricular fractional shortening had a significant positive correlation with serum 25 (OH) D3 levels. On the other hand, left ventricular end-diastolic diameter and left ventricular end-systolic diameter had a significant negative correlation with serum 25 (OH) D3 levels.

Conclusions: Our results show that patients with DCMP had lower vitamin D levels than controls, and vitamin D deficiency had a significant correlation with echocardiographic parameters.

Keywords: Vitamin D; Cardiomyopathy; Echocardiography.

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Introduction

Vitamin D not only plays a crucial role in mineral homeostasis and skeletal health but also regulates body immune response as it is a steroid and immunomodulatory hormone.[1] Vitamin D deficiency is well known to be associated with skeletal diseases such as rickets, osteomalacia and osteoporosis. In addition, there is limited evidence which suggests a plausible role of vitamin D in the causation of cardiovascular disease. Due to the presence of vitamin D receptors in various tissues of the cardiovascular system, its deficiency leads to increased inflammation, resulting in various cardiovascular pathology. By signalling inflammatory cascades, vitamin D deficiency has been shown to cause loss of collagen, fibrosis, increased oxidative stress, increased inflammation, increased sensitivity to infections and decreased protective mechanisms.[2]

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Cardiomyopathies (CMPs) represent a heterogenic group of heart muscle disease. In this the heart muscle can be affected as a primary pathologic process or secondarily as a result of a systemic disease. CMPs can be classified due to their morphology into dilated CMP (DCMP), hypertrophic CMP (HCMP), restrictive CMP (RCMP), arrhythmogenic right ventricular CMP (ARVC) and undefined CMP.[3] As immune activation plays an important role in the pathogenesis of CMP, vitamin D is thought to be one of the etiological agents for CMP. In the present study we aim to identify correlation between vitamin D levels and echocardiographically determined heart function in patients with DCMP.

Methodology

Study Design and Sample Population: The present case control study was conducted at a tertiary level teaching hospital in Navi Mumbai. Cases included patients diagnosed to have DCMP and admitted in our indoor admission ward from January 2019 till December 2019. At the same time, age and gender matched controls were included, which were patients of other medical illnesses admitted in the same hospital. DCMP was diagnosed according to American Heart Association Scientific Statement on the Classification of Cardiomyopathy.[4] We excluded patients with comorbid conditions like ischemic pathology (e.g. coronary artery disease and tachyarrhythmia), those on chemotherapy, cytotoxic drugs, anticonvulsants or any drugs interfering with vitamin D metabolism, hyperparathyroidism, diagnosed with infections (e.g. viral myocarditis), autoimmune diseases (e.g. systemic lupus erythematosus, scleroderma, and dermatomyositis), chronic liver and renal disease andperipartum cardiomyopathy. The study was approved by the Institutional Ethics Committee and an informed written consent was obtained from the study participants.

Echocardiographic protocol: All study subjects were explained the purpose of the study and underwent transthoracic two-dimensional-guided M-mode echocardiography. Echocardiography was performed using a 2.5-MHz probe. The images were acquired in parasternal long and short axis as well as in apical four- and two-chamber projections. Left atrial and LV dimensions and function were assessed by standard methods, and LV volumes and LV ejection fraction (LVEF) were calculated by the Simpson's method, averaging values from three consecutive cardiac cycles.[5]

Data Collection and Data Analysis: Using a pre-designed semi-structured study proforma, patient related information was noted. Vitamin D status of the study participants was defined as per the Endocrine Society clinical practice guidelines by Holick on evaluation, treatment, and prevention of Vitamin D deficiency.[6] The serum 25(OH) D concentrations were determined by an electrochemiluminescence immunoassay. It measures the serum 25(OH) D concentrations in the range of 4–100 ng/ml. Serum parathyroid hormone (PTH) concentration was assessed by immunoassay method as well. Other relevant serum biochemistries were obtained. The SPSS 23.0 (SPSS Inc., NY) statistical software package was used for statistical analyses. Results are presented as a mean ± standard deviation or as percentages and numbers for categorical data. Continuous were compared between cases and controlsusing student's t-test. Correlations between 25(OH) D and echocardiographic variables were determined by Spearman's correlation test. Probability of less than 0.05 was considered as statistically significant.

Results

During the study period we included 33 cases of DCM and 35 controls. Baseline information of the participants in the two study groups has been described in Table 1. Mean age, gender distribution and BMI was similar for the two study groups. Obtaining medical history of the patients, distribution of diabetics, hypertensive and smoking habit was also found to be similar in the two study groups. Biochemical profile of the patients is also described in Table 1. Serum calcium levels were found to be significantly lower in the cases as compared to controls (8.1 ± 1.7 vs 9.8 ± 0.9 mg/dl, $p < 0.05$). 25(OH)D3 was also found to be significantly lower among cases as compared to controls (13.8 ± 3.2 vs 32.8 ± 6.4 ng/dl, $p < 0.01$). In addition, level of parathyroid hormones was found to be significantly higher among cases as compared to controls (96.6 ± 14.3 vs 32.8 ± 6.4 pg/ml, $p < 0.001$). Serum albumin and phosphorus levels were found to be similar in the two study groups. Table 2 describes the echocardiographic data of the study participants. We observed that while stroke volume, left ventricular ejection fraction and left ventricular fractional shortening were significantly lower in the cases as compared to controls, left ventricular end-diastolic diameter and left ventricular end-systolic diameter were significantly higher among the cases.Furthermore, we observed that the stroke volume, left ventricular ejection fraction and left

ventricular fractional shortening had a significant positive correlation with serum 25 (OH) D3 levels (Table 3). On the other hand, left ventricular end-diastolic diameter and left ventricular end-systolic diameter had a significant negative correlation with serum 25 (OH) D3 levels.

Table 1: Description of baseline variables and biochemical profile of cases and controls.

Variables	Cases of DCMP (n=33)	Controls (n=35)	p value
Mean age (in years)	47.2 ± 8.43	49.6 ± 7.8	NS
Male:Female	19:14	20:15	NS
Mean BMI (kg/m2)	21.6 ± 2.87	22.5 ± 1.9	NS
Diabetes mellitus (%)	22%	29%	NS
Hypertension (%)	32%	41%	NS
Smoking (%)	35%	40%	NS
Biochemical profile			
Serum calcium (mg/dl)	8.1 ± 1.7	9.8 ± 0.9	< 0.05
25 (OH) D3 (ng/dl)	13.8 ± 3.2	32.8 ± 6.4	< 0.01
Parathyroid hormone (pg/ml)	96.6 ± 14.3	32.8 ± 6.4	< 0.001
Serum albumin (mg/dl)	4 ± 0.7	4.1 ± 0.9	NS
Phosphorus (mg/dl)	3.7 ± 0.5	3.2 ± 0.7	NS

Table 2: Echocardiographic findings of the study participants.

Echocardiographic variables	Cases of DCMP (n=33)	Controls (n=35)	p value
Stroke volume (ml)	46.5 ± 5.11	66.2 ± 12.8	< 0.01
Left ventricular ejection fraction (%)	28.6 ± 4.3	60.4 ± 6.6	< 0.001
Left ventricular fractional shortening (%)	14.6 ± 5.1	29.5 ± 4.7	< 0.05
Left ventricular end-diastolic diameter (mm)	73.4 ± 6.5	47.6 ± 4.7	< 0.01
Left ventricular end-systolic diameter (mm)	66.5 ± 8.9	32.5 ± 6.8	< 0.01

Table 3: Correlation of vitamin D levels with echocardiographic parameters.

Echocardiographic variables	Correlation (r)	p value
Stroke volume (ml)	0.38	< 0.001
Left ventricular ejection fraction (%)	0.49	< 0.01
Left ventricular fractional shortening (%)	0.51	< 0.001
Left ventricular end-diastolic diameter (mm)	– 0.34	< 0.01
Left ventricular end-systolic diameter (mm)	– 0.46	< 0.01

Discussion

Vitamin D deficiency is one of the most underdiagnosed and undertreated nutritional deficiency[7]. Community-based Indian studies done on apparently healthy participants have reported a wide variation in the prevalence of vitamin D deficiency, ranging from 50% to 94%.[8] Similarly, hospital-based studies showed a prevalence of vitamin D deficiency ranging from 37% to 99%.[9] A 2017 school-based study done on over 1200 school children aged 6–18 years in Himachal Pradesh, showed the prevalence vitamin D deficiency to be approximately 80%.[10] Hypocalcemic DCMP has been widely reported not only in the adult population[11], but it has beenattributed as a reversible cause of cardiomyopathy in pediatric population as well[12]. Calcium directly affects the strength of myocardial contraction via excitation–contraction coupling, and this is well established.[13] Low extracellular calcium is believed to shift the activation of the action potential to a lower membrane electro-potential, resulting in increasing excitability. This can impair myocardial contractility and prolong the QT interval, predisposing to ventricular arrhythmias.[14]

Several studies have shown associations of low serum vitamin D levels with fatal and non-fatal cardiovascular events.[15] A study using data from the NHANES III database, vitamin D insufficiency was demonstrated to be associated with heart failure.[16] NT-proBNP is a marker of cardiac dysfunction and failure. It has been shown to have a negative correlation with serum vitamin D levels. Dobnig et. al. found that after correcting for various confounders (cardiovascular risk factors), the risk of death due to heart failure was significantly higher when vitamin D deficient patients with 25(OH) D levels <10 ng/ml were compared against patients with levels >30 ng/ml.[17] These clinical findings were supported by in-vivo studies which reported a link between 1-(OH) ase gene polymorphism and increased risk of heart failure.[18] Vitamin D deficiency also results in secondary hyperparathyroidism. In the present study, DCMP patients had significantly higher serum PTH concentrations compared to controls. Similar observation was made by Laguardia et. al.[19], where serum parathyroid hormone was elevated in patients with congestive heart failure resulting from DCMP.

We did not follow the patients in our study to observe their response to vitamin D supplementation and improvement in DCMP. However, Witte et. al. in the Vitamin D Treating Patients with Chronic Heart Failure trial demonstrated that high-dose vitamin D in addition to optimal medical heart failure therapy increased the LVEF by 8%.[20] Although the underlying mechanism of this clinical improvement is incompletely understood, it is thought that vitamin D by binding to its receptors

in the heart, alters gene transcription, causes renin suppression, and has anti-hypertrophic effects. It is known to improve endothelial function and also have anti-inflammatory and anti-oxidative effects. However, the evidence to support these theories is limited and warrants further investigation.

Conclusion

Vitamin D deficiency is a rare but treatable form of DCMP. In our study, patients with DCMP had lower vitamin D levels than controls, and vitamin D deficiency had a significant correlation with echocardiographic parameters. Based on these findings, we recommend screening patients with DCMP for vitamin D deficiency along with their medical management.

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Conflict of interest: None.

References

1. Miricescu, D, Totan, A, Stanescu, AMA, Stanescu, II, Stefani, C, Greabu, M Vitamin D deficiency and insulin resistance. PracticaMedicala 2019;14,3(67): 227-232.
2. Chen, S, Law, CS, Grigsby, CL, et. al. Cardiomyocyte-specific deletion of the vitamin D receptor gene results in cardiac hypertrophy. Circulation. 2011;124:1838–1847.
3. Elliott P, Andersson B, Arbustini E, Bilinska Z, Cecchi F, Charron P, et. al. Classification of the cardiomyopathies: a position statement from the European Society Of Cardiology Working Group on Myocardial and Pericardial Diseases. Eur Heart J. 2008 Jan;29(2):270–6.
4. Maron BJ, Towbin JA, Thiene G, Antzelevitch C, Corrado D, Arnett D, et. al. Contemporary definitions and classification of the cardiomyopathies: An American Heart Association Scientific Statement from the Council on Clinical Cardiology, Heart Failure and Transplantation Committee; Quality of Care and Outcomes Research and Functional Genomics and Translational Biology Interdisciplinary Working Groups; and Council on Epidemiology and Prevention. Circulation 2006;113:1807–16.
5. Schiller NB, Shah PM, Crawford M, DeMaria A, Devereux R, Feigenbaum H, et. al. Recommendations for quantitation of the left ventricle by two-dimensional echocardiography. American Society of Echocardiography Committee on Standards, Subcommittee on Quantitation of Two-Dimensional Echocardiograms. J Am SocEchocardiogr 1989;2:358–67.
6. Holick MF. Vitamin D deficiency. N Engl J Med 2007;357:266–81.
7. Van Schoor NM, Lips P. Worldwide Vitamin D status. Best Pract Res ClinEndocrinolMetab. 2011;25:671–80.
8. Chowdhury R, Taneja S, Bhandari N, Sinha B, Upadhyay RP, Bhan MK, et. al. Vitamin-D deficiency predicts infections in young North Indian children: A secondary data analysis. PLoS One. 2017;12:e0170509.
9. Sofi NY, Jain M, Kapil U, Seenu V, Ramakrishnan L, Yadav CP, et. al. Status of serum Vitamin D and calcium levels in women of reproductive age in national capital territory of India. Indian J Endocrinol Metab. 2017;21:731–3.
10. Kapil U, Pandey RM, Goswami R, Sharma B, Sharma N, Ramakrishnan L, et. al. Prevalence of Vitamin D deficiency and associated risk factors among children residing at high altitude in Shimla district, Himachal Pradesh, India. Indian J Endocrinol Metab. 2017;21:178–83.
11. Jung YJ, Kim SE, Hong JY, Lee JH, Park DG, Han KR, et. al. Reversible dilated cardiomyopathy caused by idiopathic hypoparathyroidism. Korean J Intern Med 2013;28:605–8.
12. Maiya S, Sullivan I, Allgrove J, Yates R, Malone M, Brain C, et. al. Hypocalcaemia and Vitamin D de ciency: An important, but preventable, cause of life-threatening infant heart failure. Heart 2008;94:581–4.
13. Opie LH. Mechanisms of cardiac contraction and relaxation. In: Braunwald E, editor. Heart disease: a textbook of cardiovascular medicine. Philadelphia: WB Saunders; 2008:509–539.
14. Cheng Z, Yadav SK, Liu X, Yi Q. A reversible hypocalcemic dilated cardiomyopathy caused by primary hypoparathyroidism. Asian Journal of Medical Sciences. 2019 Mar 1;10(2):65-8.
15. Cozzolino M, Ketteler M, Zehnder D. The Vitamin D system: A crosstalk between the heart and kidney. Eur J Heart Fail 2010;12:1031–41.
16. Kim DH, Sabour S, Sagar UN, Adams S, Whellan DJ. Prevalence of hypovitaminosis D in cardiovascular diseases (from the National Health and Nutrition Examination Survey 2001 to 2004). Am J Cardiol 2008;102:1540–4.
17. Dobnig H, Pilz S, Scharnagl H, Renner W, Seelhorst U, Wellni B, et. al. Independent association of low serum 25-hydroxyvitamin d and 1,25-dihydroxyvitamin d levels with all-cause and cardiovascular mortality. Arch Intern Med 2008;168:1340–9.
18. Wilke RA, Simpson RU, Mukesh BN, Bhupathi SV, Dart RA, Ghebranious NR, et. al. Genetic

variation in CYP27B1 is associated with congestive heart failure in patients with hypertension. Pharmacogenomics 2009;10:1789–97.

19. Laguardia SP, Dockery BK, Bhattacharya SK, Nelson MD, Carbone LD, Weber KT. Secondary hyperparathyroidism and hypovitaminosis D in African-Americans with decompensated heart failure. Am J Med Sci 2006;332:112–8.
20. Witte KK, Byrom R, Gierula J, et. al. Effects of Vitamin D on Cardiac Function in Patients With Chronic HF: The VINDICATE Study. J Am CollCardiol 2016;67:2593–603.