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Vitamin d3 levels in patients of left ventricular hypertrophy in essential hypertension; a case control study

Samia Siddiqui[1], Sana Roshan[2], Mazahir Buriro[3], Arsalan Ahmed Uqaili[4], Kumayl Abbas Meghji[5]

[1]Associate Professor, Department of Physiology, Isra University, Hyderabad
[2]Associate Professor, Department of Anatomy, Suleman Roshan Medical College Tando Adam
[3]Medical Officer, Resident, Department of medicine, LUMHS, Jamshoro
[4,5]Assistant Professor, Department of Physiology, Isra University, Hyderabad

Author`s Contribution

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Address of Correspondent
Dr. Arsalan Ahmed Uqaili
Department of Physiology,
Isra University, Hyderabad
drarsalan311@gmail.com

ABSTRACT

Objective: Analysis of serum cholecalciferol in essential hypertension and its correlation with left ventricular hypertrophy (LVH).

Methodology: This cross sectional study was conducted at Department of Medicine, Isra University, Hyderabad from September 2017 to March 2018. Hundred controls and Hundred diagnosed cases of essential hypertension with left ventricular hypertrophy were selected. LVH was estimated by echocardiography. Blood samples were centrifuged at 4000 rpm (10 minutes) to separate sera for biochemical estimation of serum cholecalciferol, serum calcium, serum phosphate and alkaline phosphatase. Statistical analysis was performed on statistical software (SPSS 22.0) and Microsoft excel. Continuous variables were presented as mean ± S.D as analysed by Student`s t-test. Statistical significance was taken at 95% confidence interval (P-value ≤0.05).

Results: Serum cholecalciferol was low in cases 22.84±5.10 ng/dl compared to controls 47.09±7.65 ng/dl (p=0.0001). Mean ± SD interventricular septum and posterior wall thickness was noted as 12.39±1.82 mm in cases. Serum cholecalciferol revealed negative correlation with LVH (r= - 0.774, p=0.0001).

Conclusion: Low serum cholecalciferol was found in the essential hypertension with left ventricular hypertrophy.

Key words: Left ventricular hypertrophy, Essential Hypertension, Cholecalciferol.

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Introduction

Cholecalciferol is a fat soluble vitamin that belongs to the secosteroid family. Hydroxylation of cholecalciferol at position 25 and 1 produces the active 1, 25- dihydroxy cholecalciferol that is the physiologically active hormone.[1] The 1, 25- dihydroxy cholecalciferol binds with vitamin D receptors in the target organs and is primarily involved in the calcium and phosphate homeostasis and bone mineralization. Low serum cholecalciferol is prevalent in the developing countries. Previous studies shows 90% prevalence of cholecalciferol deficiency in Pakistani population.[2,3] It is reported that the low serum cholecalciferol adversely affects the cardiovascular functioning. Previous studies reported that the serum cholecalciferol deficiency has negative impact on the myocardial contraction and remodeling.[4] Serum cholecalciferol deficiency has been implicated in the pathogenesis of cardiac diseases.[5] Association of cholecalciferol deficiency has been reported as risk factor for the left ventricular hypertrophy (LVH) in essential hypertension. LVH is a patho-physiological response to raised after load of essential hypertension. LVH is the result of persistent chronic rise in systemic arterial pressure. LVH predisposes to heart failure, systolic and diastolic dysfunction and sudden cardiac death (SCD).

LVH is a predictor of future cardiac disease,[6] such as the cardiac failure, coronary artery disease, cerebrovascular stroke, etc.[7] Emerging evidence of cholecalciferol deficiency and LVH shows the correlation is realistic. A previous study reported that cholecalciferol and calcium supplements improved cardiovascular survival in hemodialysis patients.[8] The previous studies reported that the cholecalciferol supplementation rectifies the pro inflammatory cytokines in cardiac failure patients.[9,10] Cholecalciferol deficiency in essential hypertension adversely affects the cardiac functioning with a tendency to left ventricular hypertrophy. Cholecalciferol deficiency in essential hypertension increases the chances of left ventricular hypertrophy.[11,12] Cause effect association of cholecalciferol deficiency and ventricular functioning is not established. As the cholecalciferol deficiency is prevalent in the Pakistan, including the essential hypertension, but the association has not been researched in the local population. Essential hypertension is on rise in the local population because of dietary habits, sedentary life style, immobility, intake of excessive calories, and a genetic tendency. Hence, it is worth to analyze and associate the serum cholecalciferol in essential hypertension, particularly its correlation with left ventricular hypertrophy. The present study hypothesized that there is no correlation of serum cholecalciferol with left ventricular hypertrophy in essential hypertension. The present study aimed to determine serum cholecalciferol and its association with left ventricular hypertrophy in essential hypertension.

Methodology

The present cross sectional study was conducted Department of Medicine, Department of Medicine, Isra University, Hyderabad from September 2017 to March 2018. A sample of 100 age and gender matched control subjects and 100 diagnosed cases of essential hypertension with left ventricular hypertrophy were selected through non- probability convenient sampling. Patients were selected according to inclusion and exclusion criteria. Inclusion criteria were; diagnosed cases of essential hypertension with left ventricular hypertrophy, age > 40 years and male gender. Subjects suffering from congestive cardiac failure, secondary hypertension, valvular disease and renal disease were excluded. Diagnosed cases of essential hypertension with left ventricular hypertrophy were selected for an interview about the purpose of research study. To gain patient confidence, the subjects were informed about the benefit and loss to them. They were informed that their biodata and other information will be confidential and they can withdraw from study at any time if feeling any problem without telling to the researcher. Volunteers who gave written consent were examined; diagnosis was confirmed by echocardiography, biodata was noted and blood samples were taken from antecubital vein. Signing of written informed consent was mandatory for participation by volunteers. For the diagnosis of LVH, an opinion of consultant cardiologist was necessary. 12 lead ECG was recorded by and interpretation was made with a consultant cardiologist. Echocardiography was performed by a senior cardiologist registrar. LVH (interventricular septum and posterior wall thickness) was defined as mild, moderate and severe according to criteria as cited.[13] Blood samples were centrifuged at 4000 rpm (10 minutes) to separate sera for biochemical analysis. In case of delay in performing the analysis, the sera were stored at -80ºC. Serum cholecalciferol was estimated on ARCHITECT I 1000 DiaSys Merck system. Serum calcium, phosphate and alkaline phosphatase were analyzed on Roche Chemistry Analyzer. Data was entered on Microsoft excel sheet and was copied on the SPSS 22.0 statistical software.

Results

Age of controls and cases was noted as 50.45±7.98 and 55.34±5.7 years respectively (P=0.914). Body weight, systolic and diastolic blood pressure, serum creatinine, calcium and phosphate levels are shown in table 1. Serum Ca^{++}, PO_4 and Alkaline phosphatase were noted as 9.49±0.61 and 9.06±0.43 mg/dl (0.031), 3.01±0.57 and 2.84±0.47 mg/dl (0.0001) & 121.5±18.5 and 125±19.7 U/L (0.761) respectively. Serum cholecalciferol showed significant reduction in cases 22.84±5.10 ng/dl compared to controls 47.09±7.65 ng/dl (p=0.0001). Cases showed LVH (interventricular septum and posterior wall thickness) of 12.39±1.82 mm compared to 9.40±0.55 mm in controls (p=0.0001) as shown in table 1. Pearson's analysis revealed negative correlation of serum cholecalciferol with LVH (r= - 0.774, p=0.0001) and positive correlation with serum Ca++ (r=0.382, p=0.0001). Serum cholecalciferol revealed non-significant association with Serum PO_4 (r=0.110, p=0.981). Figure 1 and 2 shows the correlation of cholecalciferol and LVH in control and diagnosed cases

Table I: Characteristics and biochemical findings of study subjects

	Controls (n=100)	Cases (n=100)	P-value
Age (years)	50.45±7.98	55.34±5.7	0.914
Body weight (kg)	70.35±5.42	71.65±8.07	0.718
Systolic BP (mmHg)	121.5±10.5	143.90±33.5	0.0001
Diastolic BP(mmHg)	70.0±8.5	89.5±17.5	0.0001
S. Creatinine (mg/dl)	0.83±0.31	0.82±0.29	0.67
Serum Ca++ (mg/dl)	9.49±0.61	9.06±0.43	0.031
Serum PO4 (mg/dl)	3.01±0.57	2.84±0.47	0.00001
Alkaline Phosphatase (mg/dl)	121.5±18.5	125±19.7	0.761
Cholecalciferol (ng/dl)	47.09±7.65	22.84±5.10	0.00001
LVH (mm)	9.40±0.55	12.39±1.82	0.0001

Table II: Pearson`s correlation of Cholecalciferol

	LVH (mm)	Serum Ca++ (mg/dl)	Serum PO_4 (mg/dl)
r-value	- 0.774**	0.382**	0.110**
P-value	0.0001	0.0001	0.981

***. Correlation is significant at the 0.01 level (2-tailed).*

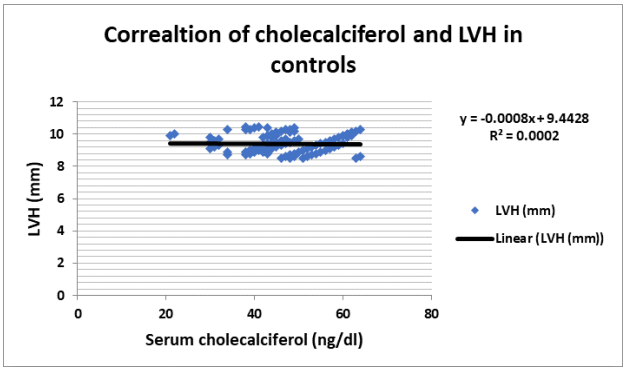

Figure 1. Correlation of serum cholecalciferol and LVH in controls

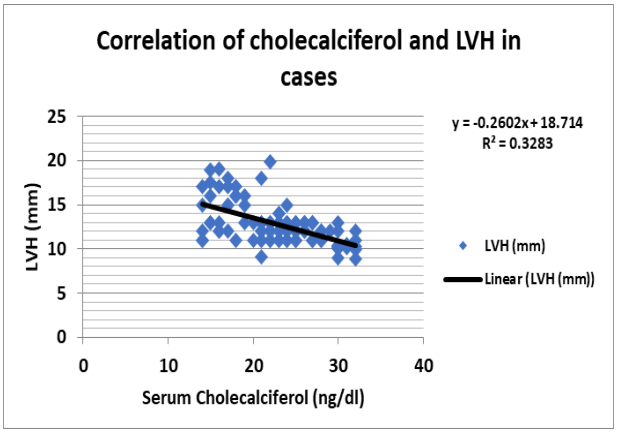

Figure 2. Correlation of serum cholecalciferol and LVH in cases

Discussion

The present study found low serum cholecalciferol in essential hypertension with left ventricular hypertrophy. Serum cholecalciferol showed negative correlation with LVH. The null hypothesis (H_0) was rejected because negative correlation of serum cholecalciferol with LVH was proved. Serum cholecalciferol was significantly low in cases 22.84±5.10 ng/dl compared to controls 47.09±7.65 ng/dl (p=0.0001). The findings of low serum cholecalciferol and its negative correlation with LVH of present study are supported by previous studies.[14,15] Our findings are also in keeping with other previous studies.[16,17] These studies reported that the cholecalciferol deficiency stimulates the parathyroid hormone (PTH) that in turn induces myocardial hypertrophy and heart rate.[16,17] However, the underlying mechanism was not elucidated. A previous study[16] concluded that the essential hypertension causes hypernatremia and calciuresis. Hypocalcemia releases the PTH that causes myocardial hypertrophy through protein synthesis, and ultimately the LVH.[15] In present study the serum cholecalciferol showed negative correlation with LVH (r= - 0.774, p=0.0001), positive correlation with serum Ca++ (r=0.382, p=0.0001) and non-significant association with Serum PO_4 (r=0.110, p=0.981). Negative correlation of serum cholecalciferol and LVH are in accordance to Ambarwati et al[17] This previous study significant negative correlation between serum cholecalciferol and left ventricular ejection fraction (LVEF). Findings of the present study are supported by previous study.[18] The previous studies reported the underlying rise in PTH is responsible for the LVH.[19,20] A previous study[21] reported regression of left atrial hypertrophy by cholecalciferol supplements. Still another study[22] reported that the cholecalciferol supplements in cardiac failure patients resulted in PTH reduction significantly. The findings of above studies indirectly support that the low cholecalciferol affects the myocardium adversely through PTH secretion. Low serum cholecalciferol with negative correlation with LVH of present study is consistent with reported study by Helvaci et al.[23] They reported low serum cholecalciferol was found with high PTH, increased urinary calcium excretion and increased LV mass.[23] In present study, serum calcium level was found low (table 1), this is consistent to Hevlaci et al.[23] The Nitta et al[24] reported low serum calcium in LVH subjects compared to normal controls and LVH supplemented with cholecalciferol. Low serum calcium of present study is consistent with

above study.[24] In present study, the serum Ca^{++}, PO_4 and Alkaline phosphatase were found low in cases compared to control, the findings are in full agreement with previous studies.[14-17] In light of evidence based findings of present study, supported by previous studies, it is clear that the serum cholecalciferol has adverse effects on the left ventricular mass, which needs further studies with large sample size. The present study suggests the cholecalciferol may be an independent modifiable risk factor that may be corrected to prevent from the left ventricular hypertrophy, and related morbidity and mortality.

Limitation: The present study has a few limitations such as a small sample size, serum PTH and urinary calcium were not detected and we studied a particular ethnic group of subjects, hence the findings cannot be generalized to other geographical areas. The findings of present study needs further research to elucidate the underlying mechanisms.

Conclusion

Serum cholecalciferol was found decreased in patients of essential hypertension with left ventricular hypertrophy. Serum cholecalciferol showed negative correlation with left ventricular hypertrophy. Hence the present study concludes the cholecalciferol may be an independent modifiable risk factor for left ventricular hypertrophy. Cholecalciferol supplements may help improve the left ventricular function.

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