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ORIGINAL ARTICLE

Cholecalciferol, serum calcium and left ventricular hypertrophy in essential hypertension.

Khalil Ahmed Memon[1], Iram Jehan Balouch[2], Safia Bano[3]

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ABSTRACT… Objective: To assess the correlation of vitamin cholecalciferol and serum calcium with left ventricular hypertrophy (LVH) in essential hypertension patients presenting at a tertiary care hospital. **Study Design:** Cross Sectional Comparative study. **Setting:** Department of Cardiology and Medicine, Liaquat University of Medical and Health Sciences, Jamshoro, Sindh. **Period:** July 2019 to January 2021. **Material & Methods:** 100 diagnosed LVH+ Essential Hypertenison cases and 100 diagnosed essential hypertension (controls) were selected through non- probability purposive sampling. Echocardiography, serum cholecalciferol, calcium, phosphate, parathyroid hormone (PTH), alkaline phosphatase (ALP), urea and creatinine were measured form sera. Devereux's formula measured the LV thickness LVH. SPSS ver. 21.0 analyzed the descriptive statistics and compared the variables at 95% Confidence interval ($P \leq 0.05$). **Results:** Serum calcium, phosphate and parathyroid hormone were found elevated in LVH cases compared to control ($P=0.0001$). Cholecalciferol in LVH cases was low noted as 27.3 ± 7.84 ng/dl compared to 39.5 ± 0.43 ng/dl in controls ($P=0.0001$). Cholecalciferol in mild, moderate and severe LVH cases was descending order as 30.67 ± 7.84, 24.76 ± 7.72 and 14.96 ± 6.12 mm respectively (P-0.0001). Serum cholecalciferol proves inverse association ($r= -0.180$) with LVH ($p=0.003$). **Conclusion:** The present study reports vitamin cholecalciferol deficiency increases the chances of left ventricular hypertrophy through increased secretion of parathyroid hormone that induces de – novo protein synthesis of ventricular myocardium.

Key words: Cholecalciferol, Essential Hypertension, Left Ventricular Hypertrophy.

INTRODUCTION

Systemic hypertension is a common health problem. It is also known as the essential hypertension and is a clinical entity that increases the stress on left ventricle (LV) and causes left ventricular hypertrophy (LVH) in long standing uncontrolled cases. In Essential hypertension, the after load of left ventricle is increased depending on the degree of inclining of blood pressure and its duration. With passage of time, the end result of essential hypertenison causes a compensatory remodeling of LV, eventually culminating in hypertrophy and consequent failure.[1] LV contractility on the serum calcium levels that is dependent on the parathyroid hormone (PTH) and circulating levels of Cholecalciferol. There is cross tie among calcium, PTH, Cholecalciferol and LV contractility.[2] PTH and Cholecalciferol are essential for maintaining normal homeostasis and serum calcium levels.[2,3] LVH is an established risk factor of cardiac morbidities and mortality in essential hypertension.[4] The LVH is considered a compensatory physiological response of LV to increased stress induced by elevated essential hypertension that eventually becomes pathological and results in left ventricular failure (LVF). Prevalence of LVH is proportionate to degree of severity of essential hypertension. Essential hypertension has a vague pathophysiology often described as of ambiguous unknown etiology where exact cause is a mystery. Essential hypertension is multifactorial perplexed by dietary habits, life style, environmental factors, personality, etc.[1,4] In Pakistan, a large number of populations are victim of essential hypertension.[5] As the essential hypertension increases, the

1. MBBS, DCP, M.Phil, Lecturer Pathology, Liaquat University of Medical and Health Sciences (LUMHS), Jamshoro, Sindh, Pakistan.
2. MBBS, Dip. Card, FCPS, Assistant Professor Cardiology, NICVD, Satellite Center, LUMHS, Hyderabad, Sindh, Pakistan.
3. MBBS, FCPS, Senior Registrar Medicine, Bilawal Medical College, LUMHS, Jamshoro, Sindh, Pakistan.

Correspondence Address:
Dr. Khalil Ahmed Memon
Department of Pathology
Liaquat University of Medical and Health Sciences, Jamshoro, Sindh, Pakistan.
giggly786@gmail.com

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chances of LVH increase proportionately with consequent problem of cardiac failure and associated cardiac health issues.[3,4] Recently, much interest has arisen in the deficiency of vitamin cholecalciferol and LVH in essential hypertension. A cross talk of serum calcium, PTH and cholecalciferol has gained attention in medical research since decades back. Concurrently, the vitamin cholecalciferol deficiency is becoming a major health problem even in normal healthy persons in Pakistan.[5] Its deficiency in essential hypertension, has been linked with vitamin cholecalciferol deficiency, increased PTH activity and serum calcium levels.[5,6] A search of medical literature of Pakistan shows a few studies are published that lag behind the rising burden of essential hypertenison, LVH and vitamin cholecalciferol deficiency. The present study was planned to determine the vitamin cholecalciferol, serum calcium and parathyroid hormone and associated factors in diagnosed left ventricular hypertrophy (LVH) in essential hypertension patients presenting at our tertiary care hospital.

MATERIAL & METHODS

A cross sectional study was conducted at the Department of Cardiology and Medicine, Liaquat University of Medical and Health Sciences, Jamshoro, Sindh during the period July 2019 to January 2021 after approval from ethics committee (LUMHS/019/2019/001). One hundred diagnosed LVH with Essential Hypertenison (cases) and 100 diagnosed essential hypertension (controls) were selected through non- probability purposive sampling. Echocardiography, serum cholecalciferol, calcium, phosphate, parathyroid hormone (PTH), alkaline phosphatase (ALP), urea and creatinine were measured form sera. Devereux's formula measured the LV thickness LVH. Inclusion criteria of cases were diagnosed cases of Essential hypertension (>10 years) according to the JNC – VIII criteria, LVH (Devereux's formula), age 40 – 60 years, volunteers and either gender. Patients suffering from secondary hypertension, renal failure, diabetic hypertensive patients, liver disease, heart failure, ischemic heart disease and coronary syndrome were excluded from study protocol.

Subjects were approached according to the ethics criteria of "Declaration of Helsinki". Each patient underwent an interview to meet inclusion and exclusion criteria, and purpose of study for volunteer participation. Consultant cardiologist and physician examined the patients and findings were noted in a pre – structured proforma. Blood pressure was measured by Palpatory and Auscultatory methods after five minutes. Consultant cardiologist performed the Echocardiography [(2.5 MHz – 3D cardiac probe) (Model – SSA 270; Toshiba company Japan)]. Devereux's formula was employed for estimation of LV thickness (LVH).[7] Blood samples were centrifuged to get sera for the estimation of serum cholecalciferol, calcium, phosphate, alkaline phosphatase (ALP), urea and serum creatinine. Laboratory investigations were performed at the State of the Art Laboratory – Diagnostic and Research LUMHS – Jamshoro. Biochemical parameters were investigated by ELISA and standard laboratory methods. SPSS ver. 21.0 analyzed the descriptive statistics and compared the variables by Student`s Independent samples t – test at 95% Confidence interval ($P \leq 0.05$).

RESULTS

Descriptive statistics of study variables are shown in Table-I. Serum calcium, serum phosphate and serum parathyroid hormone were found elevated in LVH cases compared to control ($P<0.05$). Cholecalciferol in LVH cases was low noted as 27.3 ± 7.84 ng/dl compared to 39.5 ± 0.43 ng/dl in controls ($P=0.0001$). Table-II show the Cholecalciferol in mild, moderate and severe LVH cases as 30.67 ± 7.84, 24.76 ± 7.72 and 14.96 ± 6.12 mm respectively (P-0.0001) (Figure-1).

DISCUSSION

We are the first reporting on the findings of determining analyzing vitamin cholecalciferol, serum calcium, parathyroid hormone and associated factors in the diagnosed cases of left ventricular hypertrophy in essential hypertension cases from out tertiary care hospital. The present is the first study proves the evidence of serum cholecalciferol deficiency in LVH cases associated with raised serum calcium and

parathyroid hormone (PTH). In present study, the serum calcium, serum phosphate and serum parathyroid hormone were found elevated in LVH cases compared to control (P<0.05). Cholecalciferol in LVH cases was low noted as 27.3±7.84 ng/dl compared to 39.5±0.43 ng/dl in controls (P=0.0001). Cholecalciferol in mild, moderate and severe LVH cases was noted as 30.67±7.84, 24.76±7.72 and 14.96±6.12 mm respectively (P-0.0001).

	Control	Cases	P-Value
Age (years)	50.4±7.8	51.3±11.8	0.078
Male	43 (43%)	57 (57%)	0.065
Female	56 (56%)	44 (44%)	
Systolic BP (mmHg)	120.58±5.6	158.3±11.3	0.0001
Diastolic BP (mmHg)	74.7±9.6	91.5±8.1	0.0001
Serum calcium (mg/dl)	9.7±0.63	10.2±0.14	0.0001
Serum phosphate (mg/dl)	4.3±0.63	3.7±0.4	0.0001
Cholecalciferol (ng/dl)	39.5±0.43	27.3±7.84	0.0001
Serum PTH (pg/ml)	49.5±15.8	55.3±9.3	0.02
Alkaline phosphatase (ng/dl)	148.5±38.0	157.7±25.6	0.046
Urea (mg/dl)	31.4±10.8	29.2±10.7	0.15
S. Creatinine (mg/dl)	0.98±0.21	0.99±0.11	0.81
LVH (mm)	13.12±1.57	16.97±2.65	0.0001

Table-I. Findings of control and cases

	Mean± SD	P-Value
Mild (11-13 mm)	30.67±7.84	0.0001
Moderate (14-16 mm)	24.76±7.72	
Severe (≥17 mm)	14.96±6.12	

Table-II. Cholecalciferol (ng/dl) in LVH (mm) cases

	Correlation co-efficient (r-value)	P-Value
Serum calcium (mg/dl)	0.312	0.0001
Serum phosphate (mg/dl)	0.257	0.0001
Cholecalciferol (ng/dl)	-0.180	0.003
Serum PTH	0.370	0.0001

Table-III. Correlation of left ventricular hypertrophy in cases

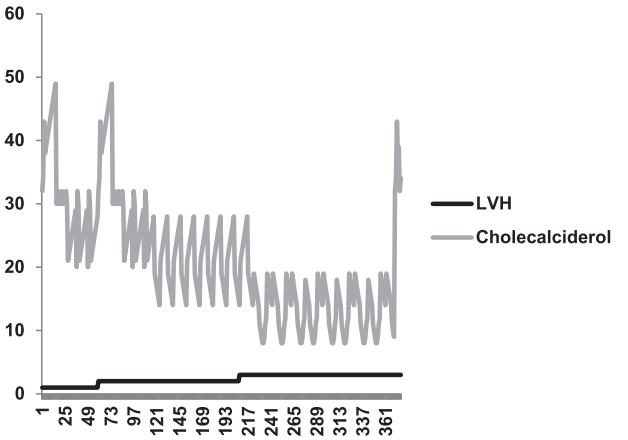

Figure-1. Cholecalciferol distibition in LVH cases

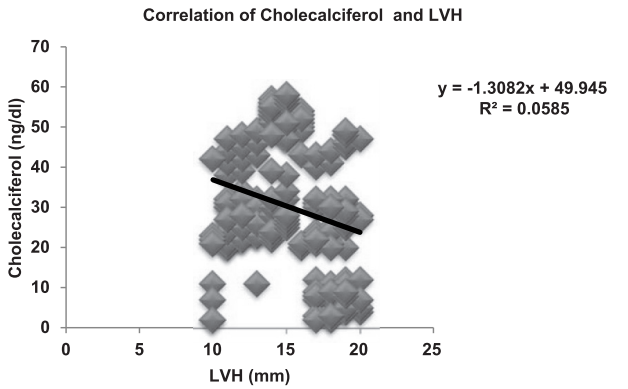

Figure-2. Cholecalciferol distibition in LVH cases

The findigns are supported by previous studies.[8,9] Low serum cholecalciferol is consistent finding with previous studies. There is much debate in current medical literature regarding the association of cholecalciferol deficiency and LVH in essential hypertension from various countries.[10-12] The finding of low serum cholecalciferol shows highly negative correlation that was in descending order as shown in Table-II, the finding is in agreement with a recent study from Pakistan.[8] The serum PTH and serum calcium were found elevated in LVH cases, this is being highly consistent with previous studies.[10-12] It has been debated that the elevated PTH is responsible for remodeling of LV causing it hypertrophy. However, the exact role of how does it cause LVH is exactly not known and needs more studies to be conducted with large sample size. Serum calcium (r=0.312, p=0.0001), phosphate (r= 0.257, p=0.0001) and PTH (r= 0.370, p=0.0001) show positive

correlation with LVH while serum cholecalciferol proves inverse association (r= -0.180) with LVH the finding is of grave consideration as it was significant (p=0.003). Our findings are highly consistent with recent reports.[8-14] We found elevated serum PTH in circulation of LVH patients the finding is consistent with previous studies.[15,16] Few previous studies[17,18] suggested raised vitamin cholecalciferol levels in essential hypertension that is in disagreement with present study. The reason of such discrepancy may be different study population belonging to different geographical areas with different dietary habits and prosperity. In present study, the PTH was raised but the active vitamin cholecalciferol was found low in those with severe LVH this is in disagreement with previous study[16] that reported PTH is essential for the of vitamin cholecalciferol through activation of renal 1- 25-hydroxylase enzyme that is under control of PTH.[12] The finding of high PTH and low cholecalciferol in LVH is supported by other previous studies.[16,19] In our opinion, the controversial findings may be due to different study designs, different study populations of developing and developed countries that are matchless.

Previous studies reported the low cholecalciferol with concomitant high PTH in essential hypertension could be a compensatory response to calcium loss in uring.[20,21] The finding is matchless with present with present study as we could not measure urinary calcium loss, however, the finding of low cholecalciferol and high PTH are consistent findigns. Positive association of PTH and LVH of present study is in agreement with a previous study.[15,21] We suggest the serum cholecalciferol with associated risk factors need to be researched on large scale in indigenous population as the prevalence and incidence of essential hypertension is increasing in country. This will help for better understanding of pathogenesis of LVH in essential hypertension, and for making proper strategies for halting the development of LVH and related cardiac morbidities. One of major limitation of present study that the findings cannot be generalized is the limited sample size, hospital based study, and study subjects belonged to particular ethnicity hence it may not be true for other geographical areas in particular the developed countries. However, the major strength present study is the prospective design and findigns were matched with normal healthy age and gender matched controls.

CONCLUSION

We found vitamin cholecalciferol deficiency in left ventricular hypertrophy of essential hypertension. Serum calcium and parathyroid hormones were found elevated. Parathyroid hormone might be involved in remodeling, cardiac de-novo protein synthesis leading to left ventricular hypertrophy. However, the exact cause at molecular level needs to be researched. We recommend vitamin cholecalciferol screening and supplementations in this particular group of population.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Khalil Ahmed Memon	Reserach designing, feasibility, data collection.	
2	Iram Jehan Balouch	Patient examination, sample calculation, Research designing, feasibility, data collection, echocardiography.	
3	Safia Bano	Performa sample collection, Research designing, literature review, feasibility, data collection, echocardiography.	