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The frequency of vitamin D deficiency in patients with left ventricular systolic dysfunction in Erbil, Iraq

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Objective To assess the frequency of vitamin D deficiency in a group of patients with left ventricular systolic dysfunction.
Methods This cross-sectional study was conducted on 100 patients with left ventricular systolic dysfunction (Group I) and 100 patients with normal left ventricular systolic function as control (Group II). Serum vitamin D levels and other variables were evaluated and compared in both studied groups.
Results Patients with left ventricular systolic dysfunction had a lower mean vitamin D level (8.62 ± 5.44 ng/ml) compared with the control group (18.7 ± 7.5 ng/ml) ($P < 0.001$). The percentage of patients with vitamin D deficiency was higher (84%) in group I compared with group II (70%) ($P < 0.001$).
Conclusion Vitamin D deficiency is common in patients with left ventricular systolic dysfunction.
Keywords vitamin D, vitamin D deficiency, left ventricular systolic dysfunction

Introduction

Chronic heart failure (HF), due to left ventricular systolic dysfunction (LVSD), is an important cause of morbidity and mortality worldwide,[1] affecting 5 million persons in the United States[2] and a similar number in Western Europe.[3] The majority of information on heart failure comes from high-income countries, with much less from middle and low-income countries in Asia and the Middle East.[4] Recent clinical studies showed that low levels of vitamin D are associated with cardiovascular diseases, including coronary artery disease, hypertension, diabetes, and LVH.[5]

According to many previous studies, low vitamin D level is very common in patients with heart failure and it is linked with poor prognosis among these patients.[6,7]

Vitamin D deficiency is a common condition that affects up to one-half of otherwise healthy middle aged to elderly population.[8] Limited cutaneous syntheses due to inadequate sun exposure and inadequate dietary intake are the principle causes of low vitamin D levels. Although vitamin D deficiency involves mainly musculoskeletal system, growing evidence suggests that vitamin D affects the cardiovascular system also.[9] Vitamin D receptors (VDR) are also expressed in multiple tissues within the body that includes vascular smooth muscle, endothelium, and cardiomyocytes.[10]

Role of vitamin D in myocardial contractility was demonstrated in a community study of 870 elderly patients without heart disease during which higher circulating vitamin D levels were found to correlate with better left ventricular (LV) systolic function and smaller LV end-systolic diameter.[11]

Up to our knowledge, there was no previous study done in Erbil city to assess the role of vitamin D deficiency in patients with left ventricular systolic dysfunction. The aim of this study was to assess the frequency of vitamin D deficiency in a group of patients with chronic left ventricular systolic dysfunction in relation to asymptomatic normal LV systolic function.

Patients and Methods

This is a cross-sectional case control study, includes 200 patients of both genders, who had been referred to the Echocardiography unit in Rizgary and Hawler Teaching Hospitals (Erbil, Iraq) for the assessment of left ventricular systolic function due to variable reasons, from September 2017 to September 2018. Those patients were divided into two groups; group I, included patients with LVSD ($n = 100$) and group II, included patients with asymptomatic normal left ventricular systolic function ($n = 100$, as a control). The patients had been referred to the echocardiography unit from Emergency Department, private clinics inside Erbil city and from the surroundings.

The exclusion criteria were any patient with acute illness including those with malignancy, Cushing syndrome, thyroid disease, chronic renal failure, chronic liver disease, primary hyperparathyroidism, malabsorption, inflammatory bowel disease, chronic pancreatitis, gastric or bowel resection, osteomalcia, osteoporosis and patients with deficiency of trace elements. Patients on anticonvulsants, glucocorticoids, vitamin D, calcium supplements, or any other drugs interfering with vitamin D were also excluded.

History of diabetes mellitus (DM), hypertension, ischemic heart disease (IHD), smoking, alcohol consumption, family history (FH) of IHD was recorded for both groups. Body mass index (BMI) was calculated according to a standard definition.[12]

Estimation of serum lipid profile,[13] blood sugar (BS), serum creatinine (S.Cr), serum calcium (S.Ca), hemoglobin level (Hb) and other biochemical parameters were done according to standard methods. 25-Hydroxyvitamin D [25(OH) D] was measured in ng/ml by enzyme-linked immunosorbent assay. Vitamin D deficiency was defined as a 25(OH) D level of <20 ng/ml, vitamin D insufficiency as 21–29 ng/ml and the optimal concentration of 25(OH) D was at least 30 ng/ml.[14]

M mode, two-dimensional and Doppler transthoracic echocardiography using Vivid S 5 GE (USA) was done for all patients. LV systolic function was measured using a previously validated semi-quantitative two-dimensional visual approach incorporating multiple echocardiographic views, according to European Society of Cardiology criteria. Ejection fraction (EF) cut-off point of ≤45% was used to define LV systolic dysfunction.[15]

Ethical considerations

The study protocol was approved by the ethics committee of the College of Medicine of Hawler Medical University. This study was conducted using an informed verbal consent from the patients prior to participation in the study. The purpose of the study was carefully explained to each patient.

Statistical analysis of data

Data were analyzed using the statistical package for social sciences (SPSS, version 19). Differences in variables were tested using Student's *t*-tests (continuous data) or the chi-square test (categorical data). A *P*-value of ≤0.05 was considered as statistically significant.

Results

In this study, 100 consecutive patients with LVSD (55 males, 45 females), mean age: 60.5 ± 10.72 years and 100 control participants (57 males, 43 females), mean age: 53.5 ± 8.57 years were recruited. As shown in Table 1, which represent the baseline, biochemical, and echocardiographic parameters of the studied population, group I patients were older, had a higher BMI, and lower Hb levels than controls.

The mean levels of cholesterol, triglyceride (TG), low density lipoprotein (LDL), BS, parathyroid hormone (PTH) and S.Cr were significantly higher, and the mean levels of high density lipoprotein (HDL), Vit D, S.Ca, and EF were significantly lower in group I patients when compared with group II.

As shown in Fig. 1, group I patients had a significantly higher frequency rate of vitamin D deficiency (84%) compared with control group (70%), $P < 0.001$.

Except for gender and alcohol consumption, all other parameters in Table 2 including hypertension, DM, IHD, hyperlipidemia, smoking and family history of IHD showed statistically significant differences between the two groups. The main finding in this comparison was that the mean value of serum vitamin D was low (8.62 ± 5.44 ng/ml) compared with the control group (18.7 ± 7.5 ng/ml) and it was statistically significant ($P < 0.001$).

Table 3 shows comparison of data in the group I participants according to vitamin D levels (less than or more than 20 ng/ml). The mean values of BMI, LDL, and S.Cr were significantly higher ($P = 0.03$, 0.03, and <0.001, respectively) while the mean value of S.Ca was significant lower ($P < 0.001$) in participants with vitamin D deficiency <20 ng/ml as compared with participants with vitamin D deficiency >20 ng/ml.

Table 1. **Baseline, biochemical, and some echocardiographic parameters of the studied sample**

Variables	Group I (LVSD) ($n = 100$)		Group II (Control) ($n = 100$)		*P*-value
	Mean	SD	Mean	SD	
Age (years)	60.5	10.72	53.5	8.57	0.03
BMI (kg/m^2)	27.23	4.25	24.7	3.77	0.003
Hb (gm/dl)	11.12	1.25	13.2	1.88	0.01
Cholesterol (mg/dl)	201.22	34.21	183.41	20.59	0.034
TG (mg/dl)	173.89	75.71	143.55	19.11	<0.001
LDL (mg/dl)	115.18	28.39	99.52	4.31	0.001
HDL (mg/dl)	35.43	7.82	40.83	1.87	<0.001
Blood sugar (mg/dl)	119.76	3.53	103.51	2.1	0.01
Vitamin D (ng/ml)	8.62	5.44	18.7	7.5	<0.001
PTH (pg/ml)	87.86	21.67	69.71	37.77	<0.001
S.Cr (mg/dl)	0.94	0.2	0.72	0.16	<0.001
S.Ca (mg/dl)	8.94	0.33	9.17	0.26	<0.001
EF (%)	37.5	3.4	58.4	5.6	<0.001

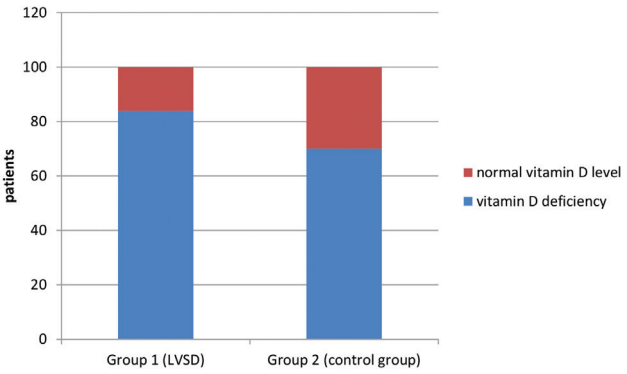

Fig. 1 **Distribution of vitamin D deficiency in the study group.**

Table 2. **Demographics and risk factors of the studied groups**

Variables		Total studied sample (Group I (LVSD $n = 100$	Group II (Control) $n = 100$	*P*-value
		Count	Count	
Gender	Male	55	57	0.55
	Female	45	43	0.47
Hypertension		78	48	<0.001
DM		52	25	<0.001
IHD		70	15	<0.001
Hyperlipidemia		80	65	<0.001
Smoking		45	30	<0.001
Alcohol		7	4	0.07
FH of IHD		33	10	<0.001
Participants with Vit D deficiency		84	70	<0.001

Table 3. **Comparison of baseline and biochemical characteristics in heart failure group (group I) according to serum vitamin D levels**

Variables	LVSD group ($n = 100$)				*P*-value
	Serum vitamin D level < 20 ng/ml ($n = 84$)		Serum vitamin D level > 20 ng/ml ($n = 16$)		
	Mean	SD	Mean	SD	
Age (years)	60.8	13.2	60.3	7.72	0.99
BMI (kg/m^2)	28.5	5.1	25.96	2.92	0.03
Blood sugar (mg/dl)	122.88	32.35	116.64	22.57	0.18
Cholesterol (mg/dl)	204.72	35.4	196.72	33.02	0.07
TG (mg/dl)	179.55	77.12	168.23	74.3	0.14
LDL (mg/dl)	124.26	29.7	106.1	27.08	0.03
HDL (mg/dl)	34.17	6.24	36.26	9.4	0.065
S.Cr (mg/dl)	1	0.15	0.88	0.25	<0.001

Table 4. **Comparison of demographics and some risk factors in group I (heart failure) patients according to vitamin D (Vit D) level**

Variables		(Group I (Patients with LVSD		*P*-value
		Vit D level < 20 ng/ml ($n = 84$)	Vit D level > 20 ng/ml ($n = 16$)	
		Count (%)	Count (%)	
Gender	Male	46 (54.8)	9 (56.2)	0.07
	Female	38 (45.2)	7 (43.8)	0.01
Hypertension		70 (83.3)	8 (50)	<0.001
Diabetes mellitus		45 (53.4)	7 (43.8)	<0.001
IHD		62 (73.8)	8 (50)	<0.001
Hyperlipidemia		73 (86.9)	9 (56.2)	<0.001
Smoking		39 (46.4)	6 (37.5)	<0.001
Alcohol		6 (7.14)	1 (6.25)	0.002
FH of IHD		31 (36.9)	2 (12.5)	<0.001

Table 4 presents comparison of demographics and risk factors in group I (heart failure) participants according to vitamin D levels. Vitamin D deficiency <20 ng/ml was more common in female participants ($P = 0.01$). All risk factors were significantly more common in participants with vitamin D deficiency <20 ng/ml ($P < 0.001$ for all, except alcohol $P = 0.002$).

Discussion

In this study, we tried to report the frequency of vitamin D deficiency in a group of participants with LVSD in Erbil city, Iraq. The prevalence of vitamin D deficiency in patients with chronic HF in this study was 84%. Although this rate was higher than those reported in previous studies, it was within accepted range.[16,17] This study revealed that vitamin D deficiency was frequent in those patients and although vitamin D levels were low in the control group (group II), they were much lower in group I patients.

In parallel with our results, many studies have shown that vitamin D deficiency is a common finding in patients with HF.[18] Some other studies mentioned that vitamin D deficiency might increases the risk of developing HF[14] and might predicts prognosis in patients with severe HF.[19]

Vitamin D deficiency is a common condition that affects up to one-half of otherwise healthy middle aged to elderly population.[8] About 70% of group II participants (control group) in our study had low vitamin D level. This percentage is rather high. Vitamin D deficiency is much more prevalent than previously recognized even in sunny countries.[20] The prevalence of vitamin D deficiency increases in areas away from the equator because of increased atmospheric filtering of Ultraviolet B radiation caused by the oblique angels of the sun's rays at higher latitudes.[21] This is very important if we know that up to 95% of the body's vitamin D requirement comes from the synthesis in the epidermis on sun exposure.[22] Modern human cultures produce less vitamin D cutaneously, in part because of increasingly indoor lifestyles, using sunscreens and by other sun avoidance strategies.[23] Wearing "Hijab" in Islamic societies may be another cause. The question now, is there a possible correlation between vitamin D deficiency and the pathogenesis of LVSD? Many mechanisms may explain this correlation. Vitamin D binds to a specific receptor, the VDR, which is expressed in most body cells, exerting its effects through gene transcription. Vitamin D deficiency predisposes to up-regulation of renin–angiotensin–aldosterone system and hypertrophy of both left ventricle and vascular smooth muscle cell.[9] Human studies indicate that vitamin D inhibits renin synthesis,[24] and suppresses immune and inflammatory responses.[25] All of these processes are important in the development and progression of HF.[26] Serum calcium level was significantly lower in HF group compared with the control group. Vitamin D regulates calcium homeostasis and is also directly involved in calcium-dependent cellular processes, including the influx, re-uptake, and release of calcium from the sarcoplasmic reticulum.[27] This process could also contribute to the impaired contractility of the myocardium in HF patients.[28] Another important finding in our study is that PTH was elevated in patients with HF compared with the control group, and it was also elevated in patients with vitamin D deficiency within the LVSD group. This is compatible with other studies.[29,30] Chronic vitamin D deficiency causes secondary hyperparathyroidism, which in turn may mediate many of the detrimental cardiovascular effects of inadequate vitamin D levels.[31]

In this study, patients with LVSD had significantly higher BMI compared with the control group. This result is concordant with other studies.[19] Individuals with a BMI >30 typically have a low concentration of vitamin D because of its sequestration in subcutaneous fat.[32] Many patients with heart failure tend to be overweight or obese. In addition, as the disease progresses, impaired vitamin D absorption from fluid retention leading to intestinal edema may come into play.[21]

Some studies mentioned that old patients with left ventricular failure had a difficulty in achieving the estimated average nutritional requirements.[33] There is decreased cutaneous photoconversion of vitamin D in patients with heart failure who have difficulty ambulating and obtaining adequate sunlight exposure.[29] Limitation in shopping, food selection, meal preparation, altered appetite, reduced palatability and an edentulous state looks to be another important contributing

factors to vitamin D deficiency and anemia. In our study, patients with LVSD had significantly lower Hb level compared with the control group. Anemia is highly prevalent in patients with heart failure and is of great clinical significance.[34]

Conclusion

Vitamin D deficiency is common in patients with LVSD as well as in the general population. Patients with LVSD may carry multiple risk factors for the development of vitamin D deficiency. We think that it is advisable to evaluate for vitamin D deficiency in high-risk patients with heart failure.

Recommendations

Improvement in clinical outcomes with vitamin D replacement in patients with LVSD is still debate. Accordingly, large prospective studies are needed to determine whether supplementation improves cardiovascular outcomes and retards further progression of heart failure.

Conflicts of Interest

The authors report no conflicts of interest.

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