Journal of Cardiovascular Disease Research
ISSN: 0975-3583, 0976-2833 VOL15, ISSUE 10, 2024

ASSESSMENT OF VITAMIN D LEVEL IN HEART FAILURE PATIENTS – A CROSS SECTIONAL STUDY

[1]Dr. Alok Sharma, [2]Dr. Hardeep Jogi

[1]Assistant Professor, Department of Cardiology, MLB Medical College, Jhansi, Uttar Pradesh, India
[2]Assistant Professor, Department of Medicine, Government Institute of Medical Science, Greater Noida, Uttar Pradesh, India

Corresponding Author:
Dr. Alok Sharma
Email: dr.alok.s@gmail.com

Received: 15/09/2024 Accepted: 20/10/2024 Published: 26/10/2024

ABSTRACT
Background: Vitamin D, as a steroid hormone, has multiple effects on human body and its deficiency has been associated with an increased risk of heart failure (HF) and unfavourable outcomes.
Objectives: The present study investigated the prevalence of vitamin D deficiency and its relationship with cardio metabolic parameters in heart failure (HF) patients
Methods: This was a cross-sectional study, enrolled ≥40 years age group HF patients. Vitamin D status was assessed by measuring serum 25-hydroxyvitamin D (25OHD), considering deficiency when level <20 ng/ml. Socio-demographic data, history, physical examination and relevant investigation was done in all recruited patients.
Results: Patients with HF had a higher prevalence (29.2%) of Vitamin d deficiency. Majority of the patients (35.8%) were 51-60 years age group with mean age was 55.63 years, slightly female predominance. Vitamin d deficiency were significantly associated with female sex and diabetes mellitus (p=0.01). There were no differences between the groups with and without Vitamin d deficiency regarding NYHA-FC, classification of LVEF, body mass index, history of smoking and alcohol ingestion (p>0.05). eGFR was significantly lower whereas PTH was significantly higher in vitamin d deficiency patients (p<0.05).
Conclusion: Vitamin D deficiency (25(OH) D and 1, 25(OH) 2D) was significantly associated with heart failure in cross-sectional analyses and predict future deaths due to heart failure.

Keywords: Vitamin d deficiency, heart failure, vitamin d, 25 hydroxyvitamin d, 1, 25(OH) D.

INTRODUCTION

Heart failure (HF) is a complex clinical syndrome, which often occurs in ventricular filling or impaired blood ejection due to cardiac dysfunction [1]. Heart failure harasses about 64.3 million people globally, and its prevalence is rising [2]. Vitamin D is a nutrient obtained from sunlight, dietary and supplemental intake. Vitamin D supplementation improves hypertension [3] and reduces the risk of myocardial infarction, whereas vitamin D deficiency appears to increase the risk of HF [4]. Vitamin D has a pleiotropic role in heart failure pathology [5]. Recent evidence suggests that sub-optimal levels of vitamin D adversely affect the cardiovascular system and associated with activation of several pathways contributing to adverse cardiac remodelling, inflammation and worsening heart failure. Low vitamin D levels activate the renin–angiotensin–aldosterone system, induce inflammatory response and cause endothelial dysfunction [6]. Therefore, CHF is closely associated with vitamin D levels. In addition, clinical trials have demonstrated that vitamin D deficiency is prevalent and associated with poor prognosis in patients with CHF [7]. Vitamin D deficiency is highly prevalent in the United States and worldwide. Low levels of 25-hydroxyvitamin D (25-OH D), the principal circulating storage form of vitamin D, are present in as many as one third to one half of otherwise healthy middle-aged to elderly adults [8]. Limited cutaneous synthesis due to inadequate sun exposure or pigmented skin and inadequate dietary intake are the principal causes of low 25-OH D levels. There are two major forms of vitamin D. A First form of vitamin D, cholecalciferol (or Vitamin D3) is also found naturally in fatty fish, fish oils, and egg yolks and is also industrially manufactured. A second form of vitamin D, ergocalciferol (or vitamin D2) is produced by irradiation of ergosterol, a membrane sterol found in the ergot fungus. Whether derived from the diet or synthesized cutaneously, vitamins D2 and D3 are biologically inert and require activation by successive hydroxylation steps. Several studies have shown that vitamin D acts as a negative regulator of the rennin angiotensin– aldosterone system (RAAS) [9] and modulates myocardial extracellular matrix turnover. Consistently, vitamin D receptor (VDR) knockout mice show increased RAAS activity, which leads to

hypertension, cardiac hypertrophy, increased water intake and sodium retention [10], and VDR knockout mice show increased metallo-protease activity, which promotes the destruction of myocardial tissue, leading to ventricular remodelling [11] Therefore, lack of vitamin D could result in deterioration of heart function and accelerate myocardial remodelling. At present, different studies have reported controversial conclusions regarding the influence of vitamin D on ventricular remodelling in patients with HF.

Aims & objectives: Present study evaluates the vitamin d levels in heart failure patients and their association.

MATERIALS AND METHODS

This was a cross-sectional observational hospital based study, conducted in the department of cardiology in a Indian tertiary care centre. Patients diagnosed as HF, hospitalized during the data collection period were enrolled in this study.

Inclusion criteria:

- Men and women aged 30 to 70 years
- Patients diagnosed as HF by clinical, laboratory and echocardiography parameters
- Patients who provided written informed consent for the study

Exclusion criteria:

- Individuals with a diagnosis of genetic diseases of bone metabolism or lipodystrophies
- Patients using vitamin D supplementation and chronic use of glucocorticoid
- Patients with history of alcoholism or currently smoking
- Patients with severe liver or kidney diseases, thyroid dysfunctions and malignancy
- Patients who not provided consent for the study

Patient's socio-demographic profile, history of smoking, history of alcohol consumption and chronic statin use, and clinical examination was done. The quantitative variables evaluated were age, body mass index (BMI), hemoglobin A1c (HbA1c), estimated glomerular filtration rate (eGFR, according to the Chronic Kidney Disease Epidemiology Collaboration formula),13) sérum PTH, total cholesterol, high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, triglycerides, and LVEF. serum vitamin d level, fasting blood analysis, Electrocardiogram (ECG) and echocardiogram (2D ECHO) were recorded.

Classification of HF [12]:
HF with preserved ejection fraction when LVEF ≥50%,
HF with mildly reduced ejection fraction when LVEF 41–49%
HF with reduced ejection fraction when LVEF ≤40%
We considered Vit. D deficiency, if serum 25OHD <20 ng/mL (<50 nmol/L), insufficiency between 20–30 ng/mL (50–75 nmol/L) and sufficiency if 25OHD ≥30 ng/mL (≥75 nmol/L) [13].

Statistical analysis: Statistical analysis was performed using the Statistical Package for Social Sciences® version 21 software (IBM Corp., Armonk, NY, USA). Qualitative variables were presented using frequencies and proportions and compared using Pearson's chi-square test. A P value <0.05 considered as statistically significant.

RESULTS

A total of 120 patients of HF were enrolled and analysed in this study. Majority of the patients (35.8%) were 51-60 years age group with mean age was 55.63 years, slightly female predominance. Most of them resided in urban area (58.3%) and belong to middle socio-economic class (39.2%). Maximum no of patients was overweight (38.2%).

Table 1: General characteristics of the study patients

Sociodemographic variables		**Frequency**	**Percentage**
Age Group (in years)	30-40	14	11.7%
	41-50	28	23.3%
	51-60	43	35.8%
	>60	35	29.2%
Mean ±SD = 55.63±4.3 years			
Gender	Male	56	46.7%
	Female	64	53.3%

Residential Status	Urban	70	58.3%
	Rural	50	41.7%
Socio economic status	Lower	31	25.8%
	Middle	47	39.2%
	Upper	42	35%
Body mass index	Normal	33	27.5%
	Overweight	46	38.3%
	Obesity	41	34.2%

Prevalence of vitamin d deficiency was 29.2% cases, insufficiency in 35% cases and sufficiency in 35.8% heart failure cases.

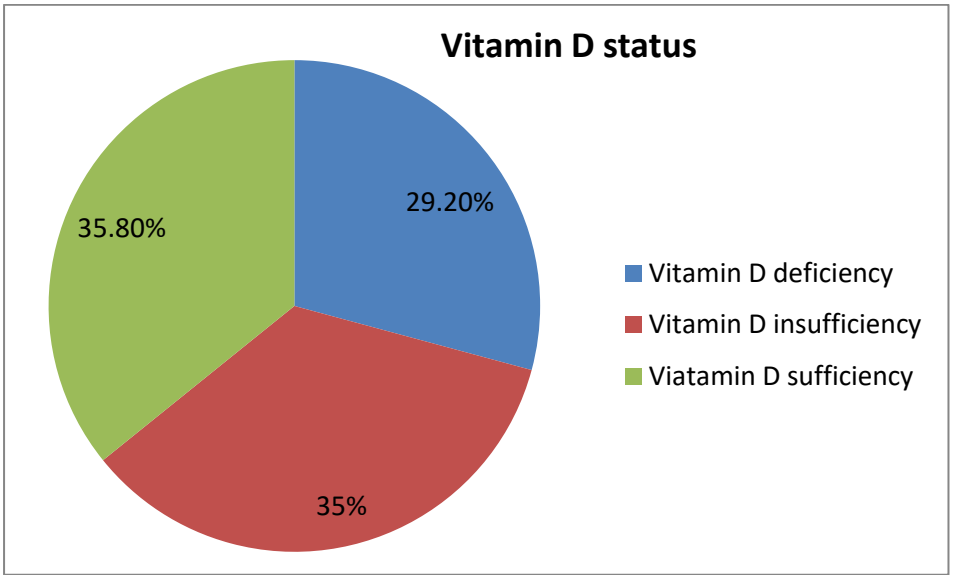

Figure 1: Estimation of serum vitamin D level in heart failure patients

Vitamin d deficiency were significantly associated with female sex (68.6% vs. 47.1%; p=0.031) and diabetes mellitus (65.7% vs. 40%, p=0.01). There were no differences between the groups with and without Vitamin d deficiency regarding NYHA-FC, classification of LVEF or presence of hypertension (p>0.05). Likewise, there were no associations between Vitamin d deficiency with body mass index, history of smoking and alcohol ingestion (p>0.05). eGFR was significantly lower and PTH was significantly higher in vitamin d deficiency patients (p<0.05). Details were shown in Tables 2.

Table 2: Characteristics of heart failure patients with or without vitamin D deficiency

Characteristics		**Vitamin D deficiency**		**P value**
		Yes (n=35)	**No (n=85)**	
Gender	Male	11 (31.4%)	45 (52.9%)	**0.031**
	Female	24 (68.6%)	40 (47.1%)	
Diabetes mellitus	Yes	23 (65.7%)	34 (40%)	**0.010**
	No	12 (34.3%)	51 (60%)	
Hypertension	Yes	19 (54.3%)	41 (48%)	0.546
	No	16 (45.7%)	44 (52%)	
History of smoking	Yes	14 (40%)	38 (44.7%)	0.636
	No	21(60%)	47 (55.3%)	
Alcohol ingestion	Yes	16 (45.7%)	47 (55.3%)	0.339
	No	19 (54.3%)	38 (44.7%)	
NYHA-FC	I-II	13 (37.1%)	38 (44.7%)	0.446
	III-IV	22 (62.9%)	47 (55.3%)	
LVEF classification	Reduced	14 (40%)	29 (34.1%)	0.825
	Mildly Reduced	5 (14.3%)	14 (16.5%)	
	Preserved	16 (45.7%)	42 (49.4%)	
Body mass index	Normal	10 (28.6%)	34 (40%)	0.496

	Overweight	13 (37.1%)	26 (30.6%)	
	Obesity	12 (34.3%)	25 (29.4%)	
eGFR (mL/ min/1.73m^2)		64.6±17.5	75.2±20.6	< **0.001**
PTH (pg/mL)		44.8±7.5	24.5±3.3	< **0.001**

Table 3: Vitamin d supplementation and outcome of HF patients

Outcome		**Frequency**	**Percentage**
Vitamin D supplementation	**Yes**	16	(13.3%)
	No	104	(86.7%)
outcome	Died due to HF	7	(5.8%)
	Survives	113	(94.2%)

DISCUSSION

There is a relationship between vitamin D and heart failure (HF) prognosis. Due to excess ionized calcium (Ca^{2+}) in myocardial cells, HF affects the contraction and relaxation of the heart. On the other hand, vitamin D deficiency may affect the activities of Ca^{2+} in cardiac cells, leading to fibrosis, intra-organizational inflammation, and cardiomyocyte hypertrophy In addition, low vitamin D levels can cause inflammation, the renin-angiotensin system is activated and endothelial dysfunction [14].

In this study most of the patients were 51-60 years age group predominantly females with mean age was 55.63±4.3 years, consistent finding shown by Zhao J-D, et al [15] and Paramjit S, et al [16].
The prevalence of vitamin d deficiency among heart failure was higher (29.2%) in the present study, our results comparable with the Lucian, et al [17], reported vitamin d deficiency was 27.2% in their study. One of the possible explanations for the lower levels of vitamin D in patients with HF is the lower sun exposure in outdoor activities.

Our study found that vitamin d deficiency was significantly higher among female patients as compared to male ($p<0.05$), in agreement with the Moretti et al [18].

The present data also highlight a potential interaction between vitamin D deficiency and hypertension. Hypertension plays a key role in the development of left ventricular hypertrophy and vascular remodelling, concordance with the Wang et al [19].

We have found an association between Vitamin d deficiency and higher levels of PTH and lower eGFR, like-wise, a study done by Xing et al [20].

Current study found no significant associations between vitamin d deficiency and BMI or abdominal obesity, as demonstrated in study carried out by Mansouri M, et al [21].

Significant relationships was observed between vitamin d deficiency and presence of DM or worse glycemic control in this study, constant results seen by Zhao H, et al [22].

Vitamin d deficiency was significantly associated with the heart failure in the present study, similar to many other studies like: Ting Wang, et al [23], Cosentino, N, et al [24] and Hazique M, et al [25].

In our study mortality was higher among HF patients with vitamin d deficiency as compared to without vitamin d deficiency, our finding correlates with the Busa V, et al [26]. Vitamin D was found to be an independent factor in predicting survival rates in HF patients. Another long-term research looked at the causes of higher hospitalization and mortality rates in HF patients with vitamin D deficiency [27].

CONCLUSION

Vitamin D has a weak and ambiguous impact on ventricular remodelling and cardiac function in patients with CHF. CHF patients with sufficient vitamin D have a decreased risk of all-cause death, even after considering potential confounding variables. We also found that deficiency of vitamin D is associated with increased risk of hospitalizations, mortality, and poor clinical outcomes among heart failure patients.

REFERENCES

1. Tsao CW, Aday AW, Almarzooq ZI, Alonso A, Beaton AZ, Bittencourt MS, et al. Heart disease and stroke statistics-2022 update: a report from the American Heart Association. Circulation. (2022) 145:e153–639.

2. Gao N, Li X, Kong M, Ni M, Wei D, Zhu X, Wang Y, Hong Z and Dong A (2022) Associations Between Vitamin D Levels and Risk of Heart Failure: A Bidirectional Mendelian Randomization Study. Front. Nutr. 9:910949
3. Ziaeian B, Fonarow GC. Epidemiology and etiology of heart failure. Nat Rev Cardiol. (2016) 13:368–78. Doi: 10.1038/nrcardio.2016.25.
4. JonesNR, Roalfe AK, Adoki I, Hobbs FDR, Taylor CJ. Survival of patients with chronic heart failure in the community: a systematic review and meta-analysis. Eur J Heart Fail. (2019) 21:1306–25. doi: 10.1002/ejhf.1594.
5. Mirhosseini N, Vatanparast H, Kimball SM. The association between Serum 25(OH) D Status and blood pressure in participants of a community based program taking Vitamin D supplements. Nutrients. (2017) 9:E1244. doi: 10.3390/nu9111244.
6. Acharya P, Dalia T, Ranka S, Sethi P, Oni OA, Safarova MS, et al. The effects of Vitamin D supplementation and 25-Hydroxyvitamin D levels on the risk of myocardial infarction and mortality. J Endocr Soc. (2021) 5:bvab124. doi: 10.1210/jendso/bvab124.
7. de la Guía-Galipienso F, Martínez-Ferran M, Vallecillo N, Lavie CJ, Sanchis-Gomar F, Pareja-Galeano H. Vitamin D and cardiovascular health. Clin Nutr. (2021) 40:2946–57. doi: 10.1016/j.clnu.2020.12.025.
8. Gardner DG, Chen S, Glenn DJ. Vitamin D and the heart. Am J Physiol Regul Integr Comp Physiol. (2013) 305:R969–977. doi: 10.1152/ajpregu.00322.2013.
9. Gruson D, Buglioni A, Burnett JC Jr, PTH: Potential role in management of heart failure. Clin Chim Acta. 2014; 433:290–296. 10.
10. Pourdjabbar A, Dwivedi G, Haddad H. The role of vitamin D in chronic heart failure. Curr Opin Cardiol. 2013; 28:216 222.
11. Agarwal M, Phan A, Willix Jr R, et al. Is vitamin D deficiency associated with heart failure? A review of current evidence. J Cardiovasc Pharmacol Ther 2011; 16: 354:e63.
12. Heidenreich PA, Bozkurt B, Aguilar D, et al. 2022 AHA/ACC/HFSA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on clinical practice guidelines. Circulation 2022; 145:e895-1032.
13. Holick MF, Binkley NC, Bischoff-Ferrari HA, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2011; 96:1911-30.
14. Jessup, M.; Brozena, S. Heart failure. N. Engl. J. Med. 2003, 348, 2007–2018.
15. Zhao J-D, Jia J-J, Dong P-S, et al. Effect of vitamin D on ventricular remodelling in heart failure: a meta-analysis of randomised controlled trials. BMJ Open 2018; 8:e020545. doi:10.1136/ bmjopen-2017-020545
16. Paramjit S.Tappia,*,Rhea Lopez, Shirley Fitzpatrick-Wong, Bram Ramjiawan, Understanding the Role of Vitamin D in Heart Failure, Rev. Cardiovasc. Med. 2023;24(4): 111
17. Lucian Batista de Oliveira, Mariana Andrade de Figueiredo Martins Siqueira , Rafael Buarque de Macedo Gadêlha , Jessica Garcia , and Francisco Bandeira , Vitamin D Deficiency in Patients Hospitalized for Heart Failure Living in the Tropics, Int J Heart Fail. 2024 Apr;6(2):84-90
18. Heidi D. Moretti* , Vincent J. Colucci and Bradley D. Berry, Vitamin D3 repletion versus placebo as adjunctive treatment of heart failure patient quality of life and hormonal indices: a randomized, double-blind, placebo controlled trial, BMC Cardiovascular Disorders (2017) 17:274
19. Thomas J. Wang, Michael J. Pencina, Sarah L. Booth, Paul F. Jacques, Erik Ingelsson, Katherine Lanier, Emelia J. Benjamin, Ralph B. D'Agostino, Myles Wolf,*; Ramachandran S. Vasan, Vitamin D Deficiency and Risk of Cardiovascular Disease, Circulation January 29, 2008
20. Xing W, Lv X, Gao W, et al. Bone mineral density in patients with chronic heart failure: a meta-analysis. Clin Interv Aging 2018;13:343-53
21. Mansouri M, Miri A, Varmaghani M, et al. Vitamin D deficiency in relation to general and abdominal obesity among high educated adults. Eat Weight Disord 2019; 24:83-90.
22. Zhao H, Zhen Y, Wang Z, et al. The relationship between vitamin D deficiency and glycated hemoglobin levels in patients with type 2 diabetes mellitus. Diabetes Metab Syndr Obes 2020;13:3899-907
23. Ting Wang, Zhenguo Liu, Jianli Fu & Zhiqian Min (2019) Meta-analysis of vitamin D supplementation in the treatment of chronic heart failure, Scandinavian Cardiovascular Journal, 53:3, 110-116, DOI: 10.1080/14017431.2019.1612084
24. Cosentino, N.; Campodonico, J.; Milazzo, V.; De Metrio, M.; Brambilla, M.; Camera, M.; Marenzi, G. Vitamin D and Cardiovascular Disease: Current Evidence and Future Perspectives. Nutrients 2021, 13, 3603. https:// doi.org/10.3390/nu13103603
25. Hazique M, Khan K, Ramesh P, et al. (September 06, 2022) A Study of Vitamin D and Its Correlation With Severity and Complication of Congestive Heart Failure: A Systematic Review. Cureus 14(9): e28873. DOI 10.7759/cureus.28873

26. Busa V, Dardeir A, Marudhai S, et al. (October 07, 2020) Role of Vitamin D Supplementation in Heart Failure Patients with Vitamin D Deficiency and Its Effects on Clinical Outcomes: A Literature Review. Cureus 12(10): e10840. DOI 10.7759/cureus.10840
27. Cubbon RM, Lowry JE, Drozd M, et al.: Vitamin D deficiency is an independent predictor of mortality in patients with chronic heart failure. Eur J Nutr. 2019, 58:2535-43. 10.1007/s00394-018-1806-y