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Research Article

The Relationship Between the Incidence of the Vitamin D Deficiency and the Heart Failure Stages in Patients with Chronic Heart Failure

Gökhan KESKİN*

Assistant Prof., Amasya University Sabuncuoglu Serefeddin Education and Research Hospital, Department of Cardiology

* **Corresponding Author**: gokhan.keskin@amasya.edu.tr
ORCID: 0000-0002-1695-5624

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Abstract:

Objective: Vitamin D deficiency is known to be associated with increased incidence of hypertension, myocardial infarction (MI), heart failure and stroke. This study aimed to investigate the relationship between vitamin D deficiency and heart failure stages in patients with chronic heart failure.

Materials and Methods: This study included 106 patients who were either treated in clinics or admitted to outpatient cardiology clinics between January and July 2010 in Turkey High Specialized Hospital. The patients were classified between NYHA classes I-IV and physical examination, echocardiography, electrocardiography and routine blood tests were performed on all patients. Blood tests were performed to determine vitamin D and parathormone levels from all patients.

Results and conclusion: The mean age of the patients included in the study was 65.67 ± 10.4 years. At least one risk factor was present in 95% of the patients, and hypertension was found as the most prevalent factor (73.58%). According to the NYHA classification, 41.50% of the vitamin D levels were less than 25 nmol / L and vitamin D levels of patients with NYHA class III and IV heart failure were significantly different ($p < 0.05$). Comparison of the vitamin D levels in the patients with heart failure class C and D were significantly different ($p < 0.05$). Moreover, a statistically positive correlation was found between the heart failure stages and Vitamin D levels ($p < 0.05$; $r = 0.267$). A negative and statistically significant relationship was identified between vitamin D and parathormone levels ($p < 0.05$, $r = -0.417$). Correlation analysis showed that as the class of heart failure increased, the severity of vitamin D deficiency elevated, and this was accompanied with an increased level of parathormone.

Conclusion: In conclusion it was observed that the prevalence of vitamin D deficiency was high in patients with stage C and D heart failure. Reasons for this may include the widespread urban lifestyle and inadequate daylight, disordered vitamin D absorption from intestines due to heart failure, and a decrease in active vitamin D synthesis due to a decrease in renal perfusion. When considering the roles of vitamin D on ventricular contractility, and vitamin D replacement therapy should be considered in heart failure patients and this should be investigated by more comprehensive studies.

1. Introduction

Chronic heart failure is a complex syndrome secondary to hereditary / acquired anatomical or functional cardiac anomalies, affecting approximately 23 million people worldwide and is the leading cause of mortality and morbidity [1-2]. Approximately 10 million patients in Europe are affected by chronic heart failure, and despite significant advances in therapeutic options in recent years, no significant changes in prognosis have been observed in the five-year survival rate of

patients diagnosed with chronic heart failure that is 35-50% [3-4]. There are several mechanisms in the pathogenesis of heart failure that explain the suboptimal effect of existing treatments on the clinical outcome, including hemodynamic abnormalities, neurohormonal activation, enhanced inflammation and micronutrient availability [5]. Vitamin D is an important micronutrient that plays an important role in autocrine and paracrine regulation of cellular functions and in the growth and differentiation of many organs, including the heart. In fact, vitamin D deficiency is known to be associated with increased incidence of hypertension, myocardial infarction (MI), heart failure, and stroke [6]. Although vitamin D was discovered about a century ago, our knowledge about it has altered recently. Over the years, its effects on calcium absorption, roles in bone health, and more recently, effects on neuromuscular function have been proven. In the last 15 years, it has been reported that vitamin D has been metabolized in various cells and tissues such as macrophages and placenta, its receptors are present in almost all body organs and it affects the function of more than 60 genes [7]. Epidemiological studies showed that vitamin D deficiency is associated with increased hypertension, MI, stroke, chronic kidney disease, and type 2 diabetes mellitus [8]. Low vitamin D levels have been found to activate the renin-angiotensin-aldosterone system, cause inflammatory response and endothelial dysfunction. Patients suffering from cardiovascular diseases are often deficient in steroid hormone vitamin D, and vitamin D deficiency has been shown to be associated with the development of chronic heart failure in a number of studies [9]. Around 90% of patients with chronic heart failure, even the ones living in sunny climate, have hypovitaminosis D [10]. Vitamin D has a number of pleiotropic effects that may affect the severity of the disease and adjustment of its doses in chronic heart failure is required [11].Significant observational evidences revealed a link between low vitamin D status and the risk of clinical outcomes in heart failure, including ventricular remodelling and mortality. However, studies evaluating vitamin D supplementation and its impact on clinical outcomes in heart failure have generally been small and inconclusive [12]. The randomized control trial on 400 patients in which the effect of vitamin D supplementation on mortality in heart failure was investigated revealed no change in echocardiographic parameters after 12 months and 36 months, while an increase in the left ventricular diastolic diameter was observed in patients over 50 years of age, however, that increase in the diameter decreased after 36 months [2].

Based on the vascular effects of vitamin D has recently been reported, this study aimed to determine the relationship between low vitamin D incidence and heart failure stages in patients with chronic heart failure.

2. Materials and methods

Type of the Study

This study was a descriptive correlational study.

Location of the Study Conducted

The research was conducted at the Cardiology Clinic in Turkey High Specialization Hospital between January 2010 and July 2010.

Research Population

This study was conducted on the patients either admitted to the cardiology outpatient clinics and the patients treated with the diagnosis of chronic heart failure in Turkey High Specialization Hospital between January 2010 and July 2010.A total of 106 patients (25 from cardiology clinics and 81 from cardiology outpatient clinics) who were diagnosed with chronic heart failure and agreed to participate in the study were included.

Data Collection Tools

Data including physical examination, echocardiography, electrocardiography and routine blood tests of the patients included in the study were examined. Before the study, all patients were informed about the aim of the study and their informed consent forms were obtained. Data were collected by using personal information form and heart failure classifications of the patients were determined according to the New York Heart Association (NYHA) Functional Classification.

Table 1: *NYHA functional classification Criteria [13]*

Class	NYHA functional classification
I	Patients have cardiac disease but without resulting in limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, dyspnea or anginal pain.
II	Patients have cardiac disease resulting in slight limitation of physical activity. Patients are comfortable at rest. Ordinary physical activity results in fatigue, palpitation, dyspnea or anginal pain.
III	Patients have cardiac disease resulting in notable limitation of physical activity. Patients are comfortable at rest. Less than ordinary physical activity results in fatigue, palpitation, dyspnea or anginal pain.
IV	Patients have cardiac disease resulting in inability to carry on any physical activity. Symptoms of cardiac insufficiency or of the anginal syndrome may be present even at rest. Discomfort is increased if any physical activity is undertaken.

The New York Heart Association (NYHA) Functional Classification: NYHA functional classification is a widely used method for classifying the extent of the heart failure in patients with heart failure (Table 1). Its validity was accepted in 1928 and it was revised many times. Its final revised version was published in 1994.

Collection and Evaluation of Data

The data were collected by the researcher between January 2010 and July 2010.In the study, patients who had chronic heart failure were interviewed once, and the information in the informed consent form was read at the interview and their consents were obtained. The treatments of the patients who agreed to participate in the study were planned in accordance with the current treatment guidelines after the admission of the patients to outpatient clinic diagnostic procedures. Their NYHA functional capacity were determined and patients with stage C and D heart insufficiency and with class III and IV and heart failure included in the study and vitamin D deficiency were evaluated. In our study, IMMUCHROM VIT D kits were used, and vitamin D levels were evaluated by using high-performance liquid chromatography (HPLC) method on a SHIMADZU HPLC machine. Then the patients were interviewed, and the interview lasted approximately 30 minutes.

Pathological Q waves, branch blocks, atrial fibrillation, ventricular arrhythmias, ST segment and T wave changes were examined by evaluating the results of 12-lead electrocardiograms of the patients. Heart size and its borders, lung tissue, pulmonary vascular structures, abnormal densities and presence of pleural fluid were examined by echocardiography. Routine blood tests (complete blood count, fasting blood sugar, blood urea nitrogen, creatinine, serum sodium and potassium levels, HDL, LDL, total cholesterol, triglyceride levels, liver and thyroid function tests) were performed. Plasma samples taken from the patients for vitamin D were obtained in the morning while the patients were fasting, and the samples were stored in accordance with the cold chain standards.

The statistical evaluation of the obtained data was conducted by using SPSS for windows computer package program (version 20.0). In the analysis of the data, besides the descriptive statistics (mean, standard deviation, minimum and maximum values and ratio), t-test to test the differences between two groups and chi-square test and Pearson correlation analysis to determine the direction and degree of the relationship between the variables were performed. For determination of the factors affecting mortality, multivariate logistic regression analysis was performed with the variables found important as a result of two-way analysis. A p value lower than 0.05 was considered as statistically significant.

Ethical Aspect of the Research

Approval for this study was obtained from the institutional Educational Planning Board of Turkey High Specialized Hospital. The study was carried out in accordance with the Helsinki Declaration Principles.

Limitations of the Study

Patients receiving renal replacement therapy, having renal insufficiency, received oncological treatment within last one year, diagnosed with primary pulmonary hypertension, having a life expectancy less than six months, having severe pulmonary disorders, having recent surgical history, having history of acute coronary syndrome or having history of pulmonary embolism were excluded from the study although the they were diagnosed with coronary insufficiency.

Results

Table 2 shows personal information of the patients with the percentage and frequency values. Mean age of the participants was 65.67 ± 10.4, and it was found that there was no statistically significant difference between Vitamin D levels and age factor ($p > 0.05$).The educational status of the majority of the patients (74.52%) was middle school and below and the majority of them were male patients (66.99%). Considering the presence of risk factors that may trigger chronic heart failure in patients, it was determined that hypertension was accompanied in the vast majority (73.58%), and it was found that there was a significant difference in comparison with vitamin D levels ($p = 0.002$; $p < 0.05$).In addition, 88.67% of patients stated that they had palpitations.

According to the data obtained as a result of the physical examinations and the test results of the participants, according to the NYHA classification of patients, classes of heart failure were defined. While planning the treatment schedule according to the NYHA classification and other test results, planning was made considering the information from latest the heart failure guidelines (2010) information. A comparison was made between the NYHA classification of patients and routine blood test results. According to the analysis, while there were significant differences between creatine, BUN, uric acid, sodium, LDL, triglyceride, albumin, and haemoglobin levels in patients with NYHA class III and IV heart failure ($p < 0.05$), potassium, HDL, total cholesterol, total protein and WBC levels were not significantly different between two patient groups ($p > 0.05$). In addition,

Table 2: *Comparison of the socio-demographic characteristics of the participants (n = 106)*

	Participants (n=210)		Test Value (Comparison with Vitamin D Levels)	
Socio-demographic Features	**n**	**%**	x^2 / **t***	**p**
Age				
< 45 age	10	9,43	0,222	0,895
46-56 age	12	11,32		
> 57 age	84	79,24		
Average age (mean±SD)	65,67±10,4			
Gender				
Female	35	33,01	1,224	0,269
Male	71	66,99		
Education Status				
Middle school or lower	79	74,52	0,172	0,678
High school and higher	27	25,47		
Presence of a Risk Factor*				
Hypertension	78	73,58	***9,427***	***0,002***
Smoking	46	43,39		
Family History of	56	52,83		
Hyperlipidaemia	44	41,50		
Diabetes	47	44,33		
Presence of Disease-Specific Symptoms *				
Shortness of breath	52	49,05	1,742	0,419
Chest Pain	67	63,20		
Palpitation	94	88,67		

***** Since there was more than one risk factor in the participants, each risk factor has been evaluated according to whole population.

when the vitamin D levels were compared according to NYHA classes, a statistically significant difference between the two groups were observed (Table 3; p = 0,000; p <0.05). In the post hoc analysis (Z test) made according to the result obtained, it was found that the group that constituted the difference was the 50-99.9 nmol / L group of the NYHA class III group.

Table 3: *Comparison of Vitamin D Levels According to NYHA Classification*

		NHYA Groups						Chi-square	
		NHYA III		NHYA IV		Total			
		n	%	n	%	n	%	x^2	p
Vitamin D Level	<25 nmol/L	30	37,97	14	51,85	44	41,50	27.626	0.000
	25-49,9 nmol/L	23	29,12	8	29,63	31	29,25		
	50-99,9 nmol/L	26	32,91	5	18,52	31	29,25		
	Total	79	100,0	27	100,0	106	100,0		

Table 4 shows the analysis results between participants' heart failure stages and vitamin D levels. According to the analysis performed based on the normal distribution of groups of patients with heart failure at stage C and D levels, there was a significant difference between heart failure levels and vitamin D levels (p = 0.000; p <0.05). In the post hoc analysis (Z test) made according to the result obtained, it was found that the <25 nmol / L group of stage D patients that caused the statistical difference in vitamin D level group. According to the correlation analysis between the stages of heart failure and vitamin D levels, there was a positive correlation between the groups (p = 0.006; r = 0.226).In addition, according to the correlation analysis between vitamin D and parathormone levels of patients, there was a negative and significant correlation between two (p = 0.000, r = -0.417).According to these results, it was determined that as the stage of heart failure increased, the level of vitamin D decreased, and this was accompanied by an increase in the level of parathormone.

Table 4: *Comparison of the Heart Failure Stages and Vitamin D Levels*

		Heart Failure Stage Grouping						Chi-square	
		Stage C		Stage D		Total			
		n	%	n	%	n	%	x^2	p
Vitamin D Level	<25 nmol/L	36	39,56	8	53,33	44	41,50	20.218	0,000
	25-49,9 nmol/L	27	29,68	4	26,67	31	29,25		
	50-99,9 nmol/L	28	30,76	3	20,00	31	29,25		
	Total	91	100,0	15	100,0	106	100,0		

Discussion / Conclusion

Vitamin D deficiency is a common and preventable condition. It is estimated to affect more than 1 billion people worldwide. One of the earliest prospective studies to confirm the relationship between vitamin D deficiency and cardiovascular disease was conducted by Wang et al. in 2008 [14]. After providing appropriate treatment for the risk factors in the patients, researchers found a significant association between increased incidence of cardiovascular disease and vitamin D deficiency. It is known that there are various risk factors for cardiovascular diseases not only in Turkey but also in the world. One of these factors is gender [14].Our study was similar to the literature [15], and it was observed that the number of male patients were more than the number female patients, and the mean age (65.67 ± 10.4 years) was similar to the ones with heart failure.

One of the effects of vitamin D on the cardiovascular system is by mediating parathormone levels. It is well known that vitamin

D is included in the calciotropic hormone system together with parathormone [16]. Our research results also showed that there was a negative and significant association between the groups according to the correlation analysis between vitamin D levels and parathormone levels of patients (p = 0,000, r = -0,417).According to these results, it was determined that as the stage of heart failure increases, the level of vitamin D decreases, and this is accompanied by an increase in the level of parathormone. This result is parallel with the literature. Gruson et al. in 2012 stated that the results obtained with the NYHA functional classification were correlated with the results obtained from the studies that they have compared the levels of vitamin D and parathormone levels of patients with chronic heart failure according to the NYHA classification system [17]. A similar result was obtained in our study and it was found that there was a statistically significant correlation between NYHA classification and vitamin D levels. Liu et al. (2011) in their study on the population with stage C heart failure [18], the prevalence of patients in NYHA class III compared to our study were 52% compared to 72%, mean vitamin D levels (<25 nmol / L level) were 14.6ng / mL, whereas in our study the mean vitamin D levels were 36.6 nmol / L in NYHA III. Finally, Gotsman et al. (2012) measured the 25OHD levels by immunoassay in 3009 patients with heart failure and compared it with the levels in the control group [19]. Our study found the prevalence of severe vitamin D deficiency (<10ng / mL or 25 nmol / L) as 34%, similar to that of Gotsman et al. (34%), and confirmed that the lower levels of 25OHD compared to healthy people as it was in patients with heart failure in the study of Gotsman et al. Other data in the literature support this relationship between 25OHD and heart failure. In addition, our results regarding the vitamin D levels according to the stages of heart failure, a similar result was obtained in the NYHA classification. Accordingly, the average vitamin D levels in patients in the stage C group were determined as 36 nmol / L, while the mean vitamin D levels in the stage D group were 28.9 nmol / L and the difference between the groups was found statistically significant (p <0.05). Significant observational evidence has linked low vitamin D status to many problems that may affect the clinical course of heart failure, including cardiac insufficiency, ventricular remodelling and mortality. However, studies evaluating the effect of vitamin D supplementation on markers and clinical outcomes in heart failure have generally been limited and inconclusive. There is insufficient data to recommend routine vitamin D evaluation or vitamin D supplementation for the prevention or treatment of chronic heart failure. Strong and detailed prospective studies are required for clinical outcomes. In conclusion, considering the contribution of vitamin D on ventricular contractility, detection of the vitamin D deficiency and the efficacy of replacement therapy in the heart failure patients with vitamin D deficiency should be investigated by more comprehensive studies.

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