Original Article
DOI: https://doi.org/10.70749/ijbr.v3i2.720

INDUS JOURNAL OF BIOSCIENCE RESEARCH
https://induspublishers.com/IJBR
ISSN: 2960-2793/ 2960-2807

Effect of Vitamin D Level on Severity of Ejection Fraction and Lipid Profile in Myocardial Infarction Patients Presenting to a Tertiary Care Hospital of Mardan

Adeel Ahmed Khalil[1], Chanda Naseem[1], Noor Ul Hadi[2], Abid Ullah Shah[1], Syed Arshad Ullah[3], Jafar Iqbal[3], Azhar Ayub[4]

[1]Faculty of Allied Health Sciences, Superior University, Lahore, Punjab, Pakistan.
[2]Department of Cardiology, Mardan Medical Complex, Mardan, KP, Pakistan.
[3]College of Medical Technology (BKMC), Mardan, KP, Pakistan.
[4]Department of Cardiology, Pakistan Air Force, Hospital, Islamabad, Pakistan.

ARTICLE INFO

Keywords

Vitamin-D, Lipid Profile, Ejection Fraction, Myocardial Infarction.

Corresponding Author: Abid Ullah Shah, Faculty of Allied Health Sciences, Superior University, Lahore, Punjab, Pakistan.
Email: abidullahshah22@gmail.com

Declaration

Authors' Contribution: All authors equally contributed to the study and approved the final manuscript.

Conflict of Interest: No conflict of interest.

Funding: No funding received by the authors.

Article History

Received: 04-01-2025
Revised: 19-02-2025
Accepted: 28-02-2025

ABSTRACT

Background: This study investigates the relationship between serum vitamin D levels and various cardiovascular parameters in patients with myocardial infarction (MI). This research investigates how vitamin D content affects heart functions and lipid measurements in patients with MI. **Methodology:** A total of 100 MI patients participated in this study with median age at 57.5 years and 80% of them being male according to the cross-sectional design. Standard questionnaires together with blood samples and echocardiography served as data collection methods. SPSS version 26 served to analyze the relationship between vitamin D levels and cardiovascular parameters. **Results:** The participants showed a mean heart function at 41.4% (± 9.2%) and presented serum vitamin-D concentrations at 42.9 ng/mL (± 17.1). The study participants showed common dyslipidemic patterns as their mean total cholesterol levels and LDL, HDL, and triglyceride values measured at 214.5 mg/dL (± 54.9), 145.5 mg/dL (± 48.5), 39.7 mg/dL (± 7.1), and 216.3 mg/dL (± 74.3) respectively. The population mainly presented with hypertension combined with diabetes mellitus followed by hyperlipidemia. Study findings demonstrated a positive relationship between vitamin D level and ejection fraction ($R = 0.38$, $p < 0.001$) as well as HDL ($R = 0.39$, $p < 0.001$) and negative correlations between vitamin D and LVEDV ($R = -0.53$, $p < 0.001$) and LVESV ($R = -0.49$, $p < 0.001$). **Conclusion:** The presence of sufficient vitamin-D levels appears to improve both heart function and blood lipid values while reducing left ventricular chamber size which may prevent cardiac remodeling and heart failure progression. Routinely checking levels of vitamin-D combined with appropriate supplementing strategies and certain life-style changes might help MI patients improve their condition. The longitudinal research with longer periods of observation should be pursued to determine cause-and-effect relationships.

INTRODUCTION

Vitamin D (VD) is an essential compound in the human body to execute crucial physiological functions and to maintain Cardiac health, sunlight exposure and consumption of skin-generating foods serves with dietary supplements as alternative ways to produce VD in the human body (1). The two principle forms of VD exist as ergocalciferol (D2) and cholecalciferol (D3) and the source of vitamin D2 originates from mushrooms alongside plant food, from sunshine activation on human skin and animal-based foods containing egg yolks or fish (2). Studies link VD deficiency with cardiovascular diseases like hypertension, coronary artery disease (CAD), myocardial infarction (MI), and heart failure (HF) leading to cardiovascular death (3, 4).

Vitamin D deficiency stands as a public health issue, according to world health organization (WHO), VD shortage impacts above 1 billion people across the world, deficiency occurs because of unhealthy living environments, various health problems, and lifestyle risks work together to reduce VD entry from the skin and food sources (5). Certain CVS conditions such as CAD and LVH and systolic heart failure develop because of widespread vitamin D deficiency in the population (6) The genes responsible for calcium transport through calcium ATPase and sodium-calcium exchangers express under regulatory control from vitamin D, also cardiac rhythm and contractility through calcium and phosphorous homeostasis which vitamin D mediates as

its beneficial action and add in myocardial contractility (7).

Ejection fraction (EF) is an important parameter to measure the heart's pumping ability, study shows that VD affects the working behavior of cardiomyocytes (heart muscle cells) by controlling the interaction with cardiac calcium mechanisms which are essential for heart muscle contractions and relaxations (8). EF operates between 50-70% as its normal operating range and EF below 40% defines HF with reduced ejection fraction (HFrEF) and commonly occurs due to MI (9). The established method of examining LVEF through echocardiography helps to access complications such as HF, arrhythmias and sudden cardiac death (10).

Research confirmed that low VD is a severity parameter for coronary atherosclerosis and a possible risk factor for CAD (11) and a study also highlighted potential benefits for VD supplementation to improve cardiac health (12) and observational study showed a meaningful relationship of HF with reduced VD and also emphasizes the need for additional well-designed studies to clarify the role of VD in heart failure patient outcomes (13). A Study also highlights the administration of VD supplements produced a crucial decrease of LV end-diastolic dimension coupled with its ability to decrease ventricular abnormalities while enhancing heart functioning in patients with HF (14).

The lipid profile stands as an essential diagnostic tool for CVS risk analysis, LDL-C stands as the harmful cholesterol that triggers plaque buildup and HDL-C has a protective function (15). A study demonstrated that VD status directly influences unfavorable lipid profiles and showed a significant relationship between VD deficiency and lipids profile measurement (16) and also confirmed a significant inverse relationship between VD supplements with TG, TC and LDL-C by another study (4). Research also confirms that increased TG as established CVS risk to persons with dyslipidemia disorders (17). Further a multiple regression analysis determined VD deficiency and dyslipidemia as the main factors influencing the severity of CAD (18).

A study shows VD deficiency caused serum TG, LDL, TC elevations and HDL reductions (19) and a negative link between serum VD and TC and LDL while TG also demonstrated this weak relationship (20) and VD therapy led to lowered TG and LDL and TC levels in deficient subjects (21). Moreover, another study utilized mice as experimental subjects shows that insufficient VD leads to heart relaxation dysfunction and abnormal cardiac muscle contractions, leading to heart cell death and heart failure, also effects with decreased EF through caspases activation (22). This research evaluates the contributions of vitamin D to cardiovascular health through determining the effect of Vitamin D Level on severity of EF and lipid profile in myocardial infarction patients.

METHODOLOGY

Research design, setting and duration

This Cross-Sectional Study was conducted in the Cardiology department, Mardan Medical Complex, Khyber Pakhtunkhwa, Mardan, for approximately 6 months after AS&RB or BOS approval.

Sample Size, Sampling Technique and Selection Criteria

The sample size is calculated on the Open-Epi online sample size calculation tool, the total sample size calculated is 100 with an anticipated frequency of myocardial infarction (MI) of 6.65 (23) and confidence interval of 95%.

Applying convenient sampling, patients with characteristics signs and symptoms of MI with ST-T changes in more than two contagious ECG leads and positive cardiac biomarkers (troponins) while patients who do not have history, sign and symptoms and ECG features of MI were excluded.

Ethical Consideration: The study was conducted after successful approval from institutional ethical committee. The confidentiality and privacy of the participant was taken care on priority basis and the participant who did not willing to participate were not forced to participate in the study.

Data Collection Procedure: The data were collected from the patient on a standard questionnaire after taking individual informed consent and institutional ethical board approval. The blood sample was taken from each patient for reporting of lipid profile and vitamin D level and cardiac biomarkers. The ejection fraction of the participants was taken through echocardiography.

Data Analysis: The data analysis was done using SPSS version 26, mean and SD were calculated for numerical variable and analyzed through correlation and regression analysis.

RESULTS

A research sample of 100 participants displayed a median age of 57.5 years with 80% being male among its members. The participants exhibited compromised cardiac function based on their mean ejection fraction measurement of 41.4% (± 9.2%). Serum vitamin D level of 42.9 ng/mL (± 17.1) shows variable results. Lipid tests from the cohort participants displayed dyslipidemia as their main finding. The participants on lipid lower medication were excluded from the analysis. Their mean total cholesterol values came out to 214.5 mg/dL (±54.9) and the mean LDL values amounted to 145.5 mg/dL ± 48.5. The measured high-density lipoprotein levels averaged to 39.7 mg/dL (±7.1) which serve as a protective factor against cardiovascular diseases. The

evaluation of triglyceride levels showed 216.3 mg/dL (±74.3) while elevated levels were detected in these measurements. Among the risk factors hypertension was found in the majority 66.0% and obesity in only 18% (Table 01).

Table 1

Baseline characteristics of study participants (n=100)

Characteristic	Value
Age (years), Mean (± SD)	57.5 (± 11.2)
Male	80 (80.0)
Female	20 (20.0)
Ejection Fraction (%), Mean (± SD)	41.4 (± 9.2)
Vitamin D Level (ng/mL), Mean (± SD)	42.9 (± 17.1)
Total Cholesterol (mg/dL), Mean (± SD)	214.5 (± 54.9)
LDL Level (mg/dL), Mean (± SD)	145.5 (± 48.5)
HDL Level (mg/dL), Mean (± SD)	39.7 (± 7.1)
Triglycerides (mg/dL), Mean (± SD)	216.3 (± 74.3)
Hypertension, Yes n (%)	66 (66.0)
Diabetes Mellitus, Yes n (%)	40 (40.0)
Smoking, Yes n (%)	40 (40.0)
Hyperlipidemia, Yes n (%)	64 (64.0)
Family History of CAD, Yes n (%)	44 (44.0)
Obesity Status, Yes n (%)	18 (18.0)
Physical Activity, sedentary n (%)	54 (54.0)

SD: Standard deviation, LDL: Low density lipoprotein, HDL: High density lipoprotein, CAD: Coronary artery disease

Comparison of Parameters by Gender

The gender-based analysis of different parameters did not reveal any statistically significant differences between the group however, mean value of VD, EF, TC, LDL, LV endiastolic volume were higher in males, while mean HDL, TG and LV end systolic volume were higher in females (Table 02).

Table 2

Comparison of gender by EF, lipid profile and Vit-D levels (n=100)

Variable	Male (Mean ± SD)	Female (Mean ± SD)	P-Value
Vitamin D Level (ng/mL)	43.5 ± 18.3	41.1 ± 11.2	0.5
Ejection Fraction (EF%)	42.0 ± 9.0	39.1 ± 9.8	0.2
Total Cholesterol (mg/dL)	217.5 ± 54.3	202.2 ± 57.2	0.26
LDL (mg/dL)	148.8 ± 48.2	132.2 ± 48.7	0.17
HDL (mg/dL)	38.9 ± 6.5	42.8 ± 8.7	0.07
Triglycerides (mg/dL)	211.8 ± 70.7	234.3 ± 86.8	0.29
LVEDV (ml)	128.9 ± 41.5	128.2 ± 41.5	0.9
LVESV (ml)	75.8 ± 32.2	80.3 ± 34.5	0.59

LVEDV: Left ventricular end diastolic volume, LVESV:Left ventricular end systolic volume

Correlation Analysis Between Variables

Serum vitamin D displayed multiple meaningful relationships with cardiovascular parameters during a correlation test evaluation. Research showed vitamin D displayed a moderate positive relationship with ejection fraction and HDL cholesterol thereby indicating proper vitamin D influences on EF and lipid regulatory processes. No statistical link existed between Vitamin D levels and total cholesterol, LDL cholesterol or triglycerides ($p>0.05$). Further, The research revealed a significant strong negative connection between left ventricular end diastolic volume (LVEDV) and left ventricular end systolic volume (LVESV) with vitamin D ($R=-0.53$, $p<0.001$ and $R=-0.49$, $p<0.001$ respectively). High vitamin D levels appear to decrease dilatation or enlargement of the heart based on study findings as they influence cardiac remodeling mechanisms and improve myocardium health (Table 03).

Table 3

Correlation between Vitamin D Level and other variables (n=100)

Variable	Correlation Coefficient (R)	P-Value
Ejection Fraction (%)	0.38	<0.001
Total Cholesterol (mg/dL)	- 0.16	0.09
LDL (mg/dL)	0.02	0.9
HDL (mg/dL)	0.39	<0.001
Triglycerides (mg/dL)	- 0.02	0.8
Left ventricular end diastolic volume (ml)	- 0.53	<0.001
Left ventricular end systolic volume (ml)	- 0.49	<0.001

Linear Regression Analysis

Linear regression analyses evaluated the distinct relationships between ejection fraction and disease of the heart and between low density lipoprotein (HDL) cholesterol and both left ventricular end diastolic volume (LVEDV) and left ventricular end systolic volume (LVESV) and serum vitamin D levels.

The results demonstrated that ejection fraction had a positive significant link with vitamin D levels ($\beta = 0.21$, 95% CI 0.11 to 0.31, $p < 0.001$). The data indicated that patients with ejection fraction of 10 ml per square meter betterment had about 4 ng/ml stronger vitamin D levels (improved levels) resulting in a 0.14 adjusted R^2 value demonstrating that vitamin D level explained only 14% of ejection fraction changes thus showing better vitamin D levels might lead to enhanced systolic functions and heart output. The research revealed that HDL cholesterol contained a positive association with vitamin D concentrations at 0.16 (95% CI: 0.09 – 0.24, $p < 0.001$) along with an adjusted R^2 value of 0.15. HDL cholesterol variations show that Vitamin D accounts for a 15% change because this vitamin affects positive lipid profiles that benefit cardiovascular wellness (figure 1& 2).

Figure 1

Relationship between vitamin D Levels and ejection fraction

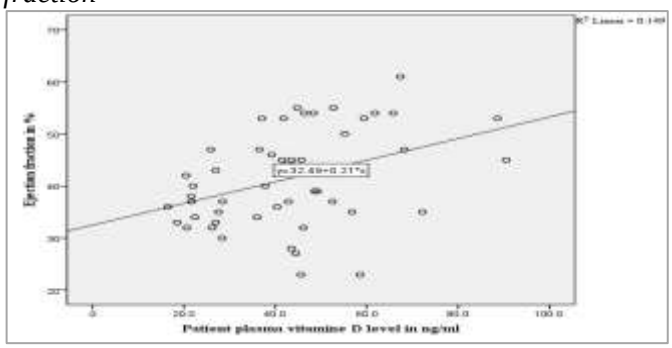
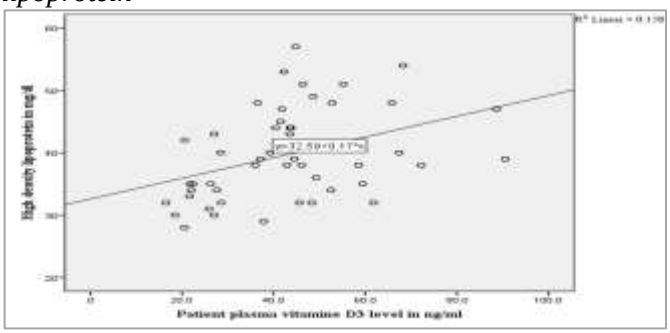


Figure 2

Relationship between vitamin D levels and high-density lipoprotein



The study revealed a negative correlation between vitamin D levels and both LVEDV and LVESV measurements as vitamin D might prevent pathological changes in heart structure. The study found that LVEDV showed an inverse correlation with vitamin D levels through a regression coefficient measurement of -1.29 (95% CI -1.69 to -0.88, p < 0.001) and explaining 28% of LVEDV variation by vitamin D activity levels. Research shows a negative link indicating that increased vitamin D levels tend to decrease the extent of excessive dilation in the left ventricle. Vitamin D levels demonstrated a significant negative relationship to LVESV through the regression coefficient of −0.95 (95% CI: −1.28 to −0.62 P <0.001) when adjusted R^2 reached 0.24. The study results suggest that sufficient vitamin D intake neutralizes ventricular enlargement which serves as a risk factor for heart failure development (Figure 3 & 4).

Figure 3

Relationship between vitamin D Levels and left ventricular end diastolic volume

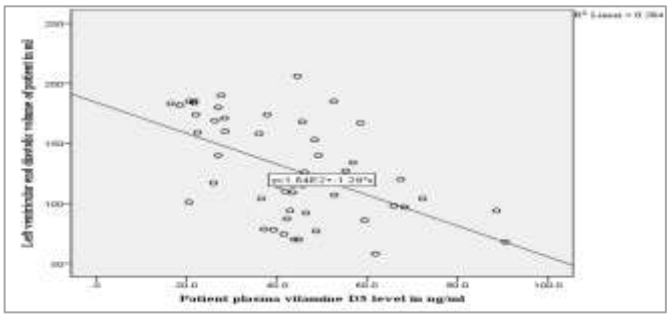
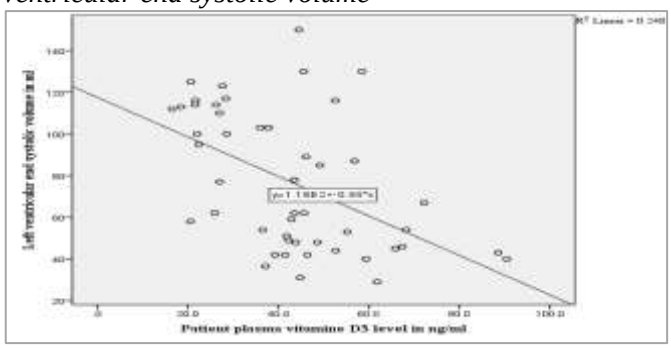


Figure 4

Relationship between vitamin D Levels and left ventricular end systolic volume



The negative relationship between vitamin D amounts and LVEDV and LVESV measures creates potential for vitamin D prevention to stop pathological changes in cardiac structure. The analysis showed that LVEDV could be explained by 0.28% of variation when vitamin D reached 437.2 nmol/L while the regression coefficient was −1.29 (95% CI −1.69 to −0.88 p < 0.001). The inverse correlation between vitamin D levels and left ventricular dilatation indicates that higher amounts of vitamin D could stop excessive dilation of the heart chamber. The analysis between vitamin D level and LVESV revealed an inverse correlation confirmed through a regression coefficient of −0.95 (95% CI: −1.28 to −0.62, p < 0.001) and 0.24 adjusted R square value. Research indicates vitamin D acts as an inhibitor against ventricular dilation that leads to heart failure and related negative cardiac effects (Figure 3 & 4).

Table 4

Results of Linear Regression Analysis (n=100)

Dependent Variable	Independent Variable	β (95% CI)	*P*-Value	Adjusted R^2
Ejection Fraction (%)	Vitamin D Level	0.21 (0.11 to 0.31)	<0.001	0.14
HDL (mg/dL)	Vitamin D Level	0.166 (0.09 to 0.24)	<0.001	0.15
Left ventricular end diastolic volume (ml)	Vitamin D Level	-1.29 (-1.69 to -0.88)	<0.001	0.28
Left ventricular end systolic volume (ml)	Vitamin D Level	-0.95 (-1.28 to - 0.62)	<0.001	0.24

DISCUSSION

The study group consisted mostly of males (80%) in the 57.5-year-old average population. The examination by Rasouli et al (24) revealed 86.9% male participants in their study. The mean age is consistent with another study (25) and also with the average age of 58.6 years with male participants comprising 82.2% of the group according to Masudi S, et al (26). Results show minimal differences between male and female distribution of cardiovascular risk elements because the gender-based characteristics appear small enough to avoid skewing the research findings and demonstrated that hyperlipidemia together with history of MI and patient age strongly

affected the VD levels (all p <0.0) (11). Another analysis showed an inverse relationship between vitamin D results and patient age with a negative correlation value of r = −0.290 and a statistical significance level of p = 0.003 (18).

The mean measured VD amount in our study participants was 42.9 ng/ml. A study shows VD serum average levels as 33.62 ng/ml but 52.85 percent or 73 of patients demonstrated insufficient or deficient status (26) while 58 of patients displayed 15.85 ng/mL 25(OH)D compared to 13.31 ± 12.8 ng/mL (24). The mean serum vitamin D readings reached 13.35 ± 7.49 ng ml according to the study (55). Research studies have shown that vitamin D levels averaged 13.35 ± 7.49 ng/ml but this value was significantly lower than reports in the US and EU. Sun exposure as well as dietary habits and supplements consumption in the studied region could explain the observed variance in results. Opposed to other findings, participants with vitamin D deficiency experienced increased cardiac mortality during subsequent follow-up periods according to study results (26).

In our study group hypertension and diabetes mellitus affected 66% and 40% of our patients which exceeds the rates reported by Mahkameh Rasouli, et.al Research shows that insufficient vitamin D levels create an extremely strong link toward diabetic foot complications development. People possessing diabetic infections along with diabetic ulcers often have severe vitamin D deficit (24). Multiple research investigations have utilized vitamin D receptor knockout mice to show that vitamin D helps regulate BP while potentially functioning as an antihypertensive agent. Research shows that 37.3% of hypertensive and 26.8% of diabetic women had normal serum 25(OH)D levels (27), At the same time there exists a strong correlation (p = 0.0001) between serum 25(OH)D levels and coronary atherosclerosis severity (11).

Vitamin D deficiency exists in directly opposite correlation to the number of arteries involved in the disease process (multi vessel disease 83.3%, triple vessel disease 80%, double vessel disease 28.6%, single vessel disease 21.7%) with statistical significance and a negative association between vitamin D level and syntax score was found (-0.339) while 44% of CAD patients come from families with CAD history and multiple linear regression determined diabetes and VD deficiency as risk factors for severe CAD with a p value of <0.05 (28).

Along with standard CVS risk elements studies show that VD deficiency provides its own independent indication of severe CAD development including stenosis stages and vessel numbers as well as coronary artery mineralization (18). Studies demonstrating a prospective analysis showed persons with elevated serum VD concentrations showed a 16 percent reduction in risk development for hypertension and also 25 nmol/L rise in serum vitamin D concentration produces a 5% reduction in risk for developing hypertension (29).

People in the high SYNTAX scores group had a roughly 2 times greater severe coronary artery stenosis incidence rate compared to the group with the highest 25(OH)D category levels (30). The absorption of vitamin D3 delivered through oral supplements does not lead to any substantial improvements in BP levels among those with VD deficiency and it is also observed BP reductions affected the systolic measurements in individuals who were obese and VD deficient along with persons who were above fifty years of age (31). Short-term mortality statistics for ACS did not show a meaningful relationship between VD shortage among subjects with STEMI, Nevertheless, these patients group had more VD insufficiency conditions (32). Variations in study subjects and initial disease seriousness and research methodologies might account for varied findings regarding vitamin D deficiency effects on outcomes across different studies. Our research group consisting mainly of hypertension, hyperlipidemia and diabetes which fits the category of advanced cardiovascular disease risk patients.

Patients demonstrated elevated mean total cholesterol levels at 214.5 ± 54.9 mg/dL and LDL cholesterol at 145.5 ± 48.5 mg/dL as well as increased mean triglyceride levels at 216.3 ± 74.3 mg/dL while mean HDL cholesterol stood at 39.7 ± 7.1 mg/dL. HDL cholesterol shared a strong positive link with vitamin D concentrations while the relationship between vitamin D levels and total cholesterol, LDL cholesterol and triglycerides remained non-existent. Vitamin D demonstrates a selective impact on the levels of HDL cholesterol by explaining 15% of HDL cholesterol variability thus playing a role in preventing unhealthy lipid profiles and cardiac disease development. The study produced incredible lipid results with total cholesterol measuring 4.4 mmol/l and LDL at 3.08 mmol/l and triglycerides at 1.58 mmol/l above the 3.7 mmol/l, 2.6 mmol/l and 1.05 mmol/l reported by Rasouli et al (24).

The mean ejection fraction value was 41.4 $\pm$ 9.2 and the mean end diastolic volume was 28.9 $\pm$ 41.5 and the mean end systolic volume was 78.05 $\pm$ 33.35. The research finds that Vitamin D shows a positive significant association with LVEF. When patients received high dose vitamin D3 for one year they experienced enhanced heart function and decreased endopathies and endoeqlastolly of the LV by 6.07+2.32 mm and 4.75+2.32 mm respectively, p 0.001 (33). Subgroup analysis established that patients using vitamin D showed less LVEDD compared to the control group when examining both adults and adolescents and the intervention involving high-dose vitamin D intake

above 4000 IU/day along with low dose vitamin D consumption below 4000 IU/day showed decreased LVEDD (14). Over two months the subjects receiving high vitamin D dose demonstrated statistically significant improvements in ejection fraction together with reduced end diastolic volume levels and heart failure in the intervention, and also albumin and VD in the serum was higher than in the placebo group (34). Among one subset of hypertensive patients with normal LVEF there was left ventricular mass and myocardial performance index impairment in the presence of the low VD (<20 ng/mL) (35) also clinical studies have shown inverse association between serum VD levels and the degree of vascular calcifications (36). Study by Algowhary M et al enrolled 188 consecutive CAD patients with a median age of 55(50–62) and 151 (80.3%) were male brought to diagnosis by cardiac catheterization; and these patients vs 131 normal controls were compared, the research showed that CAD patients displayed significantly diminished VD levels of 14.65 ng/mL (9.25–21.45) as compared to the control group who had 42 ng/mL (32.0–53.0) at $p < 0.001$ (37).

Study indicates that vitamin D supplements successfully enhance left ventricular ejection fraction and functional ability among patients who are vitamin D deficient (34). Evidence also shows that patients with 25 hydroxyvitamin D deficiency encounter higher death risks from heart failure with left ventricular systolic dysfunction (38) Patients with heart failure with preserved ejection fraction (HFpEF) exhibited significantly lower 25(OH)D levels as compared to healthy controls (11.4±0.6 ng/mL vs. 19.1±2.1 ng/mL, P=0.001), and more than 90% showed vitamin D insufficiency (<20 ng/mL) and 30% deficiency (<10 ng/mL) respwctively (38). Among HFpEF patients, but not in healthy controls, 25(OH)D levels were positively associated with exercise capacity measures, including peak VO_2 (r=0.26, P=0.007), and 6-minute walk distance (r=0.34, P <0.001) (24) and a study also showed VD3 supplementation was associated with a significant increase in LV ejection fraction (39).

CONCLUSION

Research findings show that sufficient vitamin D levels in the blood create positive effects on heart performance together with lipid concentrations and oppose larger left ventricular chamber measurements. Both improved ejection fraction and elevated HDL cholesterol levels and smaller values of LVEDV and LVESV which support cardiac remodeling prevention and heart failure risk reduction are linked to adequate vitamin D levels.

Recommendations

Checking vitamin D status and offering supplemental vitamin D should become standard care practice for heart attack patients because it leads to better heart function and lipid measurement results. Physical activity combined with a vitamin D-rich balanced diet enables people to maintain the health of their cardiovascular system together with optimal vitamin D levels. Research with long-term follow-up should investigate both causal effects and lasting health benefits that vitamin D provides for cardiac health.

Limitations

The study utilized a small number of participants that reduces the ability to generalize its results. This research design as a cross-section fails to show whether vitamin D levels cause any changes to cardiovascular parameters or whether they are unrelated. Selection bias appears because of convenient sampling methods that affect the generalization capability of the study. The research restrictions to broader populations because it was performed solely in one medical facility.

REFERENCE

1. Haider, F., Ghafoor, H., Hassan, O. F., Farooqui, K., Bel Khair, A. O., & Shoaib, F. (2023). Vitamin D and cardiovascular diseases: An update. *Cureus*. https://doi.org/10.7759/cureus.49734
2. Guo, J., Lovegrove, J. A., & Givens, D. I. (2017). 25(OH)D 3 -enriched or fortified foods are more efficient at tackling inadequate vitamin D status than vitamin D 3. *Proceedings of the Nutrition Society*, *77*(3), 282-291. https://doi.org/10.1017/s0029665117004062
3. Wang, C. (2013). Role of vitamin D in Cardiometabolic diseases. *Journal of Diabetes Research*, *2013*, 1-10. https://doi.org/10.1155/2013/243934
4. Surdu, A. M., Pînzariu, O., Ciobanu, D., Negru, A., Căinap, S., Lazea, C., Iacob, D., Săraci, G., Tirinescu, D., Borda, I. M., & Cismaru, G. (2021). Vitamin D and its role in the lipid metabolism and the development of atherosclerosis. *Biomedicines*, *9*(2), 172. https://doi.org/10.3390/biomedicines9020172
5. Chen, X., Zhao, W., Zhao, Y., Ma, J., Bu, H., & Zhao, Y. (2023). Vitamin D on cardiac function in heart failure: A systematic review and meta-analysis of 10 RCTs. *Reviews in Cardiovascular Medicine*, *24*(11). https://doi.org/10.31083/j.rcm2411325
6. Pandit, A., Mookadam, F., Boddu, S., Aryal Pandit, A., Tandar, A., Chaliki, H., Cha, S., &

Lee, H. R. (2014). Vitamin D levels and left ventricular diastolic function. *Open Heart*, *1*(1), e000011. https://doi.org/10.1136/openhrt-2013-000011

7. Achinger, S. G., & Ayus, J. C. (2005). The role of vitamin D in left ventricular hypertrophy and cardiac function. *Kidney International*, *67*, S37-S42. https://doi.org/10.1111/j.1523-1755.2005.09506.x
8. Norman, P., & Powell, J. (2014). Vitamin D and cardiovascular disease. *Circulation Research*, *114*(2), 379-393. https://doi.org/10.1161/circresaha.113.301241
9. Lang, R. M., Badano, L. P., Mor-Avi, V., Afilalo, J., Armstrong, A., Ernande, L., Flachskampf, F. A., Foster, E., Goldstein, S. A., Kuznetsova, T., Lancellotti, P., Muraru, D., Picard, M. H., Rietzschel, E. R., Rudski, L., Spencer, K. T., Tsang, W., & Voigt, J. (2015). Recommendations for cardiac chamber quantification by echocardiography in adults: An update from the American Society of echocardiography and the European Association of cardiovascular imaging. *Journal of the American Society of Echocardiography*, *28*(1), 1-39.e14. https://doi.org/10.1016/j.echo.2014.10.003
10. Solomon, S. D., Zile, M., Pieske, B., Voors, A., Shah, A., Kraigher-Krainer, E., Shi, V., Bransford, T., Takeuchi, M., Gong, J., Lefkowitz, M., Packer, M., & McMurray, J. J. (2012). The angiotensin receptor neprilysin inhibitor LCZ696 in heart failure with preserved ejection fraction: A phase 2 double-blind randomised controlled trial. *The Lancet*, *380*(9851), 1387-1395. https://doi.org/10.1016/s0140-6736(12)61227-6
11. Dziedzic, E. A., Smyk, W., Sowińska, I., Dąbrowski, M., & Jankowski, P. (2021). Serum level of vitamin D is associated with severity of coronary atherosclerosis in postmenopausal women. *Biology*, *10*(11), 1139. https://doi.org/10.3390/biology10111139
12. Batsi, C., Gkika, E., Astrakas, L., Papadopoulos, A., Iakovou, I., Dogoritis, A., Fotopoulos, A., & Sioka, C. (2021). Vitamin D deficiency as a risk factor for myocardial ischemia. *Medicina*, *57*(8), 774. https://doi.org/10.3390/medicina57080774
13. Hagău, A. C., Pușcaș, A., Togănel, R., & Muntean, I. (2023). Is Hypovitaminosis D a risk factor for heart failure? *Life*, *13*(2), 372. https://doi.org/10.3390/life13020372
14. Zhao, J., Jia, J., Dong, P., Zhao, D., Yang, X., Li, D., & Zhang, H. (2018). Effect of vitamin D on ventricular remodelling in heart failure: A meta-analysis of randomised controlled trials. *BMJ Open*, *8*(8), e020545. https://doi.org/10.1136/bmjopen-2017-020545
15. Grundy, S. M., Stone, N. J., Bailey, A. L., Beam, C., Birtcher, K. K., Blumenthal, R. S., Braun, L. T., de Ferranti, S., Faiella-Tommasino, J., Forman, D. E., Goldberg, R., Heidenreich, P. A., Hlatky, M. A., Jones, D. W., Lloyd-Jones, D., Lopez-Pajares, N., Ndumele, C. E., Orringer, C. E., Peralta, C. A., & Saseen, J. J. (2019). 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol. *Circulation*, *139*(25), 1082–1143. https://doi.org/10.1161/cir.0000000000000625
16. Lupton, J. R., Faridi, K. F., Martin, S. S., Sharma, S., Kulkarni, K., Jones, S. R., & Michos, E. D. (2016). Deficient serum 25-hydroxyvitamin D is associated with an atherogenic lipid profile: The very large database of lipids (VLDL-3) study. *Journal of Clinical Lipidology*, *10*(1), 72-81.e1. https://doi.org/10.1016/j.jacl.2015.09.006
17. Ginsberg, H. N., Packard, C. J., Chapman, M. J., Borén, J., Aguilar-Salinas, C. A., Averna, M., Ference, B. A., Gaudet, D., Hegele, R. A., Kersten, S., Lewis, G. F., Lichtenstein, A. H., Moulin, P., Nordestgaard, B. G., Remaley, A. T., Staels, B., Stroes, E. S., Taskinen, M., Tokgözoğlu, L. S., … Catapano, A. L. (2021). Triglyceride-rich lipoproteins and their remnants: Metabolic insights, role in atherosclerotic cardiovascular disease, and emerging therapeutic strategies—a consensus statement from the European atherosclerosis society. *European Heart Journal*, *42*(47), 4791-4806. https://doi.org/10.1093/eurheartj/ehab551
18. El Mokadem, M., Boshra, H., Abd el Hady, Y., & Abd el Hameed, A. S. (2021). Relationship of serum vitamin D deficiency with coronary artery disease severity using multislice CT coronary angiography. *Clínica e Investigación en Arteriosclerosis*, *33*(6), 282-288. https://doi.org/10.1016/j.arteri.2021.02.008
19. Ahmad Bashir, N. (2019). Effect of vitamin D deficiency on lipid profile. *American Journal of Laboratory Medicine*, *4*(1), 11. https://doi.org/10.11648/j.ajlm.20190401.12

20. Kostecka, D., Schneider-Matyka, D., Barczak, K., Starczewska, M., Szkup, M., Ustianowski, P., Brodowski, J., & Grochans, E. (2022). The effect of vitamin D levels on lipid, glucose profiles and depression in perimenopausal women. *PubMed*, *26*(10), 3493–3505. https://doi.org/10.26355/eurrev_202205_28844
21. Dibaba, D. T. (2019). Effect of vitamin D supplementation on serum lipid profiles: A systematic review and meta-analysis. *Nutrition Reviews*, *77*(12), 890-902. https://doi.org/10.1093/nutrit/nuz037
22. Bae, S., Singh, S. S., Yu, H., Lee, J. Y., Cho, B. R., & Kang, P. M. (2013). Vitamin D signaling pathway plays an important role in the development of heart failure after myocardial infarction. *Journal of Applied Physiology*, *114*(8), 979-987. https://doi.org/10.1152/japplphysiol.01506.2012
23. Robbers, L. F., Eerenberg, E. S., Teunissen, P. F., Jansen, M. F., Hollander, M. R., Horrevoets, A. J., Knaapen, P., Nijveldt, R., Heymans, M. W., Levi, M. M., Van Rossum, A. C., Niessen, H. W., Marcu, C. B., Beek, A. M., & Van Royen, N. (2013). Magnetic resonance imaging-defined areas of microvascular obstruction after acute myocardial infarction represent microvascular destruction and haemorrhage. *European Heart Journal*, *34*(30), 2346-2353. https://doi.org/10.1093/eurheartj/eht100
24. Rasouli, M., Shahverdi, E., Kamali, S., Khojastepour, F., Manouchehri, R., Hajabdo, M., & Karami, P. (2023). Is there an association between vitamin D status and left ventricular ejection fraction. *Journal of Clinical Cardiology and Cardiology Research*, *2*(1), 1-6. https://doi.org/10.59657/2837-4673.brs.23.003
25. Shah, A. U., Bahrul Amin, Muhammad Shahzeb, Muhammad Tayyeb, Asad Khan, Naqash Ahmad, Muhammad Imran, Shehryar Ahmad, & Ashfaq Ahmad. (2023). Recent pattern of coronary artery disease and its risk factors: Comparision in gender and age groups. *Journal of Khyber College of Dentistry*, *13*(04), 40-45. https://doi.org/10.33279/jkcd.v13i04.30
26. Seyed-mohammadzad, M., Lamei, H., Masudi, S., Ashena, S., Kahourian, O., & Toobaey, Y. (2024). Vitamin D deficiency and its impact on outcomes in myocardial infarction patients: A prospective observational study. *Cardiovascular Biomedicine Journal*. https://doi.org/10.18502/cbj.v4i1.16228
27. Yammine, K., Hayek, F., & Assi, C. (2019). Is there an association between vitamin D and diabetic foot disease? A meta-analysis. *Wound Repair and Regeneration*, *28*(1), 90-96. https://doi.org/10.1111/wrr.12762
28. Mehta, A., Chokka, D., N., S., Seshu, A., R., P., & M., M. P. (2022). Correlation of vitamin D level and severity of coronary artery disease. *Biomedicine*, *42*(5), 943-948. https://doi.org/10.51248/.v42i5.1911
29. Mokhtari, E., Hajhashemy, Z., & Saneei, P. (2022). Serum vitamin D levels in relation to hypertension and pre-hypertension in adults: A systematic review and dose–response meta-analysis of epidemiologic studies. *Frontiers in Nutrition*, *9*. https://doi.org/10.3389/fnut.2022.829307
30. Chen, W. R., Qian, Y. A., Chen, Y. D., Shi, Y., Yin, D. W., Wang, H., Zhu, P., Liu, H. W., & Sha, Y. (2014). The effects of low vitamin D on coronary artery disease. *Heart, Lung and Circulation*, *23*(4), 314-319. https://doi.org/10.1016/j.hlc.2013.08.012
31. He, S., & Hao, X. (2019). The effect of vitamin D3 on blood pressure in people with vitamin D deficiency. *Medicine*, *98*(19), e15284. https://doi.org/10.1097/md.0000000000015284
32. Ikramullah, S., Khokhar, A., Ali, M. U., Mustafa, B., Raza, S. A., & Ahmad, I. (2022). Frequency of Vitamid deficiency in patients with acute ST elevation MI. *Pakistan Journal of Medical and Health Sciences*, *16*(5), 1102-1104. https://doi.org/10.53350/pjmhs221651102
33. Witte, K. K., Byrom, R., Gierula, J., Paton, M. F., Jamil, H. A., Lowry, J. E., Gillott, R. G., Barnes, S. A., Chumun, H., Kearney, L. C., Greenwood, J. P., Plein, S., Law, G. R., Pavitt, S., Barth, J. H., Cubbon, R. M., & Kearney, M. T. (2016). Effects of vitamin D on cardiac function in patients with chronic HF. *Journal of the American College of Cardiology*, *67*(22), 2593-2603. https://doi.org/10.1016/j.jacc.2016.03.508
34. Hassanzadeh-Makoui, R., Jamei, M., Hassanzadeh-Makoui, M., & Khederlou, H. (2020). Effects of vitamin D on left ventricular ejection fraction in patients with systolic heart failure: A double-blind randomized clinical trial. *International Journal of Endocrinology and Metabolism*, *18*(3). https://doi.org/10.5812/ijem

.103528
35. Seker, T., Gur, M., Ucar, H., Turkoglu, C., Baykan, A. O., Özaltun, B., Harbalioglu, H., Yuksel Kalkan, G., Kaypakli, O., Kuloglu, O., Sen, O., Koc, M., & Cayli, M. (2015). Lower serum 25-hydroxyvitamin D level is associated with impaired myocardial performance and left ventricle hypertrophy in newly diagnosed hypertensive patients. *The Anatolian Journal of Cardiology*, *15*(9), 744-750. https://doi.org/10.5152/akd.2014.5637
36. Barreto, D. V., Barreto, F. C., Liabeuf, S., Temmar, M., Boitte, F., Choukroun, G., Fournier, A., & Massy, Z. A. (2009). Vitamin D affects survival independently of vascular calcification in chronic kidney disease. *Clinical Journal of the American Society of Nephrology*, *4*(6), 1128-1135. https://doi.org/10.2215/cjn.00260109
37. Algowhary, M., Farouk, A., El-Deek, H. E., Hosny, G., Ahmed, A., Abdelzaher, L. A., & Saleem, T. H. (2023). Relationship between vitamin D and coronary artery disease in Egyptian patients. *The Egyptian Heart Journal*, *75*(1). https://doi.org/10.1186/s43044-023-00419-5
38. Cubbon, R. M., Lowry, J. E., Drozd, M., Hall, M., Gierula, J., Paton, M. F., Byrom, R., Kearney, L. C., Barth, J. H., Kearney, M. T., & Witte, K. K. (2018). Vitamin D deficiency is an independent predictor of mortality in patients with chronic heart failure. *European Journal of Nutrition*, *58*(6), 2535-2543. https://doi.org/10.1007/s00394-018-1806-y
39. Witte, K. K., Byrom, R., Gierula, J., Paton, M. F., Jamil, H. A., Lowry, J. E., Gillott, R. G., Barnes, S. A., Chumun, H., Kearney, L. C., Greenwood, J. P., Plein, S., Law, G. R., Pavitt, S., Barth, J. H., Cubbon, R. M., & Kearney, M. T. (2016). Effects of vitamin D on cardiac function in patients with chronic HF. *Journal of the American College of Cardiology*, *67*(22), 2593-2603. https://doi.org/10.1016/j.jacc.2016.03.508