ORIGINAL ARTICLE

ASSOCIATION OF PLASMA LEPTIN AND OMENTIN-1 WITH ORAL VITAMIN D INTAKE IN PATIENTS WITH CORONARY ARTERY DISEASES

Shazia Nazar[1], Syeda Hina Abbas[2], Syeda Sana Abbas[3]

Author's Affiliation
[1] Department of Physiology, Dow University of Health Sciences Karachi
[2] Department of Pathology, Dow University of Health Sciences Karachi
[3] Department of Medicine, Abbasi Shaheed Hospital Karachi

Corresponding Author
Shazia Nazar
Department of Physiology, Dow University of Health Sciences Karachi
Email: adrshazia@gmail.com

ABSTRACT

Objective: To evaluate the association of oral vitamin D intake on leptin & omentin-1 circulating levels in patients diagnosed with coronary artery disease.

Material & Methods: The study was conducted at the Cardiology unit of Civil Hospital Karachi. A total count of 200 diagnosed patients of coronary artery disease with insufficient vitamin D and were prescribed oral vitamin D by their doctors, were selected for the study. Patients were assigned to the daily dose of 2000IU vitamin D for 8 weeks. Anthropometric measurements and circulating vitamin D, omentin-1 & leptin levels were assessed at the beginning and post-treatment.

Results: A notable decrease in leptin (3776 ± 0.422 vs. 3187 ± 0.144, $p < 0.001$), omentin-1 (245 ± 26.1 vs. 296.5 ± 28.11, $p < 0.001$), and high-density lipoprotein levels (36.80 ± 13.46 vs. 45.2 ± 14.31, $p < 0.001$) were found after oral vitamin D intake.

Conclusion: Vitamin D supplements over an 8-week period substantially reduced serum levels of leptin, whereas they raised omentin-1 and high-density lipoprotein levels in coronary artery disease patients.

Key Words: Biomarkers, Cardiac disease, Leptin, Omentin-1, Vitamin D.

This article may be cited as: Nazar S, Abbas SH, Abbas SS. Association of plasma leptin and omentin-1 with oral vitamin D intake in patients with coronary artery diseases. Ann Allied Health Sci. 2024;10(2):34-38.

INTRODUCTION

Coronary Artery Disease (CAD) is a major cause of morbidity and mortality.[1] Atherosclerosis of principal coronary arteries, is the major cause of CAD.[2] Approximately 17.7 million deaths globally each year are attributed to CAD, accounting for 31% of all deaths.[3] Atherosclerosis, or the hardening of the arteries, is the primary cause of CAD. This inescapable process can begin in adolescence or even early childhood.[4] Atherosclerosis is associated with wide range of independent predisposing factors, including aging, smoking, diabetes mellitus, hypertension, abnormal cholesterol levels, stress, and lifestyle.[5]

Emerging data from studies on humans revealed that insufficient vitamin-D levels might be a significant contributing factor in the pathogenesis of CAD.[6] vitamin-D is a pleotropic vitamin, acquired from food, supplements, or sun exposure, and is involved in a variety of biological activities, exists in a couple of primary forms: ergocalciferol and cholecalciferol. 7-dehydrocholesterol is metabolized into vitamin-D within the skin, upon exposure to ultraviolet light.[7] Long-term deficiency of vitamin-D is associated with an increased risk of infections., cognitive and neurological disease, autoimmune disorders, cardiovascular disease, and various carcinomas, including colon, breast, and prostate tumors.[8]

Although the exact mechanism of pathophysiology caused by insufficient vitamin-D is still unknown, however, vitamin-D has been

linked to an increase in nitric oxide (NO) expression in vascular endothelial cells, combined with endothelial progenitor cells' increased angiogenic capabilities.[9] Secondly, by modulating the synthesis of pro-inflammatory and anti-inflammatory cytokines, vitamin-D has a tendency to regulate immune cells, contributing to protect blood vessels.[10] Furthermore, a lack of vitamin D may activate the renin gene, which raises angiotensin II levels and may cause hypertension and ventricular hypertrophy Furthermore, a lack of vitamin-D may activate the renin gene, which raises angiotensin II levels and may cause hypertension and ventricular hypertrophy.[11] Vitamin-D inhibits the inflammatory signaling pathways of NF-κB and MAPK, thereby reducing inflammation.[12] Visceral adipose tissues (VAT) have high expression of the anti-inflammatory adipocytokine omentin-1, which is supposed to reduce inflammation by suppressing COX2/ NFKB and deactivating the JUN pathway.[13] Owing to the close proximity of epicardial adipose tissue to the myocardium and vascular endothelium, Omentin-1 directly influences the development of CAD.[14] Reduced circulating levels of omentin-1 have been found in CAD patients.[15] Leptin is expressed in white adipose tissues (WAT).[16] Research has demonstrated that leptin-mediated signal pathways impact numerous target genes' transcription, which plays a role in innate/adaptive immunity and inflammation.[17] Leptin is believed to be correlated with endothelial oxidative stress and thickening of the intimal and medial layers of coronary arteries, which contributes to development of atherosclerosis. [18] The objective of the current research was to assess oral vitamin D intake affects omentin-1 and leptin levels in individuals with coronary artery disease.

MATERIAL AND METHODS

This interventional study was carried out at the cardiology units of Civil Hospital Karachi (CHK), Pakistan, from August 2022 to July 2023. The research study included 200 patients diagnosed with CAD with insufficient or deficient levels of vitamin-D, and were prescribed vitamin-D tablets by their doctors. The institutional review committee of Dr. A. Q. Khan Institute of Genetics and Biotechnology approved the study under reference number: KIBGE/ICE/345.

According to endocrine society, individuals with ≤ 20 ng/mL were declared as deficient, 21-29 ng/mL considered as inadequate, ≥ 30 ng/mL considered as optimal levels of vitamin-D. All subjects were provided with a detailed explanation of the research study's objectives, and their informed consents were signed and recorded. Individuals who were identified to have CAD based on angiographic results that showed ≤50% Constriction in major coronary arteries, were included in the study. Sociodemographic information, such as age, sex, food preferences, lifestyle factors, family history of CAD, and past infections, was collected utilizing a standardized questionnaire. Furthermore, participants underwent anthropometric measurements and medical examinations. The circumference of the abdomen slightly above the belly button, was measured to determine the waist circumference (WC), whereas, hip circumference (HC) was measured with a measuring tape around the hips' widest point. Body mass index (BMI), was expressed in kilogram per square of meters. Using an enzyme linked immunosorbent test (ELISA), the circulating levels of omentin-1, leptin, and vitamin-D were measured. Cal-Biotech, catalog #VD200B, was the ELISA kit used to measure the vitamin-D levels in plasma, and it had a sensitivity of 2.5 ng/ml. The ELISA kit, catalog #RD191100200R, from Bio-vender, Czech Republic, was utilized to measure omentin-1, whereas, DRG Instruments GmbH, Germany's ELISA-2395 kit was used to determine leptin levels. Participants received a regular dosage of 2000 IU of oral vitamin-D for a period of eight weeks. Anthropometric measures, lipid profiles, levels of circulating vitamin D, omentin-1, & leptin, were evaluated both before and after the supplementation. A quantitative analysis of the collected data was conducted using SPSS, version 22 (Chicago, IL, USA).

Descriptive statistics were used to summarize continuous variables such as vitamin D, omentin-1, leptin, and anthropometric measurements. Paired t-tests were used to assess within-group changes in each parameter from baseline to post-intervention. To determine the differences between the pre- and post-treatment measures,

paired t-tests were applied. An independent t-test was utilized to assess the impact of vitamin D on omentin-1, leptin, and lipid profiles in CAD patients. A *p*-value less than 0.05 was considered significant.

RESULTS

A total of 200 patients with CAD (120 males and 80 females, with average age of (51.05±11.55) participated in the study. Only a small percentage of individuals were unable to follow-up due to personal issues, pregnancy, or overseas relocation. Anthropometric measurements, including body weight, BMI, WC, and blood pressure of participants were assessed before and after oral intake of vitamin D. Decreases in weight (86.98 ± 7.01 vs. 85.67 ± 6.06, p = .78), BMI (32.47 ± 4.05 vs. 30.06 ± 4.06, p = .34), WC (118 ± 10.56 vs. 114.3 ± 11.06, p = .29) were noted. There was an increase in SBP (130.23± 10.71 vs. 133.58±9.01, p= .77) from baseline to the conclusion. However, these changes did not reach statistical significance. **(Table 1)**

The findings indicate significant reduction in leptin concentration (3776 ± 0.422 vs. 3187 ± 0.144, $p < 0.001$). In addition, circulating omentin-1 levels (245.09 ± 267.1 vs. 296.5 ± 280.11, $p < 0.001$) and HDL-c levels (36.80 ± 13.46 vs. 45.2 ± 14.31, $p < 0.001$) were detected as substantially higher. **(Table 2)**

Significant improvements were observed in both males and females from the start point to the endpoint of the study across two groups: deficient and insufficient. Males in the deficient group improved from 9.0 ± 3.7 to 18.9 ± 1.0, and females from 7.8 ± 1.6 to 16.0 ± 2.1, both with a p =0.001. In the insufficient group, males increased from 17.09 ± 5.8 to 32 ± 7.8, and females from 14.9 ± 3.8 to 26 ± 8.9, p = 0.001. These findings show that all groups have improved statistically significantly. **(Table 3)**

Table 1: Anthropometric measurements and blood pressure before and after the oral vitamin D

	Baseline	End of study	Change	P-value
Weight (kg)	86.98 ± 7.01	85.67 ± 6.06	1.31 ± 0.95	0.78
BMI (kg/m^2)	32.47 ± 4.05	30.06 ± 4.06	2.41 ± 0.97	0.34
WC (cm)	118 ± 10.56	114.3 ± 11.06	4.66 ± 1.19	0.29
SBP (mm of Hg)	130.23± 10.71	133.58±9.01	3.35± 1.7	0.77
DBP (mm of Hg)	90.98±5.89	90.33±7.87	0.35± 2.02	0.89

Table 2: Impact of oral vitamin D on plasma vitamin D, omentin-1, leptin, and lipid profile

	Baseline	End of study	Change	P-value
Omentin-1 (mg/dL)	245.09 ± 26.1	296.5 ± 28.11	51.49 ± 2.01	0.001
leptin (ng/mL)	3776 ± 0.422	3187 ± 0.144	−589 ± 0.278	0.001
FBS (mg/dL)	100.70 ± 9.86	96.96 ± 10.84	−3.7 ± 0.98	0.070
TG (mg/dL)	172.36 ± 94.33	135.06 ± 64.5	−37.3 ± 29.83	0.001
HDL-c (mg/dL)	36.80 ± 13.46	45.2 ± 14.31	9.2 ± 0.85	0.001
LDL-c (mg/dL)	139.50 ± 74.60	130.20 ± 54.48	−9.3 ± 20.12	0.451
TC (mg/dL)	205.13 ± 77.93	190.03 ± 73.21	−15.10 ± 4.72	0.065

Table 3: Gender-wise distribution of vitamin D levels at the onset and end of the study

		Baseline	End of study	P-value
Deficient				
	Male	16±3.7	28.9±1.0	0.001
	Female	10± 1.6	25.0±2.1	0.001
Insufficient				
	Male	25.09±5.8	38±7.8	0.001
	Female	23.9±3.8	34± 8.9	0.001

DISCUSSION

Vitamin D is a lipid-soluble, pleotropic vitamin that is essential for various biological processes.[19] Literature has revealed the correlation of inadequate vitamin D levels with CAD.[20] Bjelakovic *et al*.'s meta-analysis, which included almost two million Americans, discovered that daily vitamin- D consumption reduced the risk of cardiovascular diseases.[21] These results support the idea that vitamin D plays an important role in the proper functioning of the circulatory system.

The current investigation discovered that following vitamin-D intervention, there were higher levels of omentin-1 (245.09 ± 26.1 vs. 296.5 ± 28.11, $p = 0.001$). However, following a regular dosage of 2,000 IU of vitamin-D for three months, the Cheshmazar *et al*., observed no change in omentin-1 blood levels.[22] However, Jafari *et al.*, discovered that omentin-1 levels were raised after four months of consistent 2,000 IU vitamin-D intake.[23]

The current analysis identified a substantial decrease in leptin levels from (3776 ± 0.4 ng/mL to 2576 ± 0.1 ng/mL, $p = 0.001$) after the eight weeks. Manoy *et al*., discovered that there were not significant variations in the levels of leptin in osteoarthritis patients at a dose of 4000 IU weekly for the period of six months.[24] Whereas, According to Mousa *et al*., vitamin-D supplements at a dose of 4000 IU daily for sixteen weeks caused significant differences in the serum concentrations of leptin in obese individuals with vitamin-D levels ≤ 50 nmol/L.[25] Anthropometric indices such as height, body weight, BMI, and WC did not change in the current study compared to a previous study that found that levels of these indices significantly decreased after an eight-week intervention.[22] The results of this investigation concluded that oral vitamin-D intake also significantly raised the concentration of HDL-c in the serum. According to Lorvand Amiri *et al*., vitamin-D treatment in patients with fatty liver disease (NAFLD) raised HDL-c concentrations in the intervention group and significantly decreased triglyceride levels, which is consistent with our findings.[26] The observed significant improvements in both deficient and insufficient groups align the study by Forno *et al*. demonstrated that vitamin D supplementation significantly improved serum vitamin-D levels in both deficient and insufficient patients of asthma.[27]

CONCLUSION

The current study concluded that oral vitamin-D in CAD patients resulted in a marked decrease in serum leptin levels, along with elevated omentin-1 and HDL-c levels.

REFERENCES

1. Bergström G, Persson M, Adiels M, Björnson E, Bonander C, Ahlström H, Alfredsson J, Angerås O, Berglund G, Blomberg A, Brandberg J. Prevalence of subclinical coronary artery atherosclerosis in the general population. Circulation. 2021 Sep 21;144(12):916-29.
2. Frąk W, Wojtasińska A, Lisińska W, Młynarska E, Franczyk B, Rysz J. Pathophysiology of cardiovascular diseases: new insights into molecular mechanisms of atherosclerosis, arterial hypertension, and coronary artery disease. Biomedicines. 2022 Aug 10;10(8):1938.
3. Khan MA, Hashim MJ, Mustafa H, Baniyas MY, Al Suwaidi SK, AlKatheeri R, Alblooshi FM, Almatrooshi ME, Alzaabi ME, Al Darmaki RS, Lootah SN. Global epidemiology of ischemic heart disease: results from the global burden of disease study. Cureus. 2020 Jul;12(7).
4. Silvis MJ, Demkes EJ, Fiolet AT, Dekker M, Bosch L, van Hout GP, Timmers L, de Kleijn DP. Immunomodulation of the NLRP3 inflammasome in atherosclerosis, coronary artery disease, and acute myocardial infarction. Journal of Cardiovascular Translational Research. 2021 Feb;14:23-34.
5. Teo KK, Rafiq T. Cardiovascular risk factors and prevention: a perspective from developing countries. Canadian Journal of Cardiology. 2021 May 1;37(5):733-43.
6. Verdoia M, Gioscia R, Nardin M, Rognoni A, De Luca G. Low levels of vitamin D and coronary artery disease: Is it time for therapy?. Kardiologia Polska (Polish Heart Journal). 2022;80(4):409-16.
7. Han JH, Ginde AA, Brown SM, Baughman A, Collar EM, Ely EW, Gong MN, Hope AA, Hou PC, Hough CL, Iwashyna TJ. Effect of early high-dose vitamin D3 repletion on cognitive outcomes in critically ill adults. Chest. 2021 Sep 1;160(3):909-18.
8. Szymczak-Pajor I, Drzewoski J, Śliwińska A. The molecular mechanisms by which vitamin D prevents insulin resistance and associated disorders. International journal of molecular sciences. 2020 Sep 11;21(18):6644.
9. Pál É, Ungvári Z, Benyó Z, Várbíró S. Role of vitamin D deficiency in the pathogenesis of cardiovascular and cerebrovascular diseases. Nutrients. 2023 Jan 9;15(2):334.
10. Krajewska M, Witkowska-Sędek E, Rumińska M, Stelmaszczyk-Emmel A, Sobol M, Majcher A, Pyrżak B. Vitamin d effects on selected anti-inflammatory and pro-

inflammatory markers of obesity-related chronic inflammation. Frontiers in Endocrinology. 2022 Jun 13;13:920340.
11. Latic N, Erben RG. Interaction of vitamin D with peptide hormones with emphasis on parathyroid hormone, FGF23, and the renin-angiotensin-aldosterone system. Nutrients. 2022 Dec 6;14(23):5186.
12. Cimmino G, Morello A, Conte S, et al. Vitamin D inhibits Tissue Factor and CAMs expression in oxidized low-density lipoproteins-treated human endothelial cells by modulating NF-κB pathway. European Journal of Pharmacology. 2020 Oct 15;885:173422.
13. Wang J, Gao Y, Lin F, Han K, Wang X. Omentin-1 attenuates lipopolysaccharide (LPS)-induced U937 macrophages activation by inhibiting the TLR4/MyD88/NF-κB signaling. Archives of biochemistry and biophysics. 2020 Jan 15;679:108187.
14. Miroshnikova VV, Polyakova EA, Pobozheva IA, Panteleeva AA, Razgildina ND, Kolodina DA, Belyaeva OD, Berkovich OA, Pchelina SN, Baranova EI. FABP4 and omentin-1 gene expression in epicardial adipose tissue from coronary artery disease patients. Genetics and molecular biology. 2021 Sep 29;44:e20200441.
15. Askin L, Duman H, Ozyıldız A, Tanriverdi O, Turkmen S. Association between omentin-1 and coronary artery disease: Pathogenesis and clinical research. Current cardiology reviews. 2020 Aug 1;16(3):198-201.
16. Mazuecos L, Pintado C, Rubio B, Guisantes-Batán E, Andrés A, Gallardo N. Leptin, acting at central level, increases FGF21 expression in white adipose tissue via PPARβ/δ. International Journal of Molecular Sciences. 2021 Apr 28;22(9):4624.
17. Dessie G, Ayelign B, Akalu Y, Shibabaw T, Molla MD. Effect of leptin on chronic inflammatory disorders: insights to therapeutic target to prevent further cardiovascular complication. Diabetes, Metabolic Syndrome and Obesity. 2021 Jul 17:3307-22.
18. Puchałowicz K, Kłoda K, Dziedziejko V, et al. Association of adiponectin, leptin and resistin plasma concentrations with echocardiographic parameters in patients with coronary artery disease. Diagnostics. 2021 Sep 26;11(10):1774.
19. Verdoia M, Nardin M, Rolla R, Negro F, Gioscia R, Afifeh AM, Viglione F, Suryapranata H, Marcolongo M, De Luca G, Novara Atherosclerosis Study Group. Prognostic impact of Vitamin D deficiency in patients with coronary artery disease undergoing percutaneous coronary intervention. European journal of internal medicine. 2021 Jan 1;83:62-7.
20. Surdu AM, Pînzariu O, Ciobanu DM, Negru AG, Căinap SS, Lazea C, Iacob D, Săraci G, Tirinescu D, Borda IM, Cismaru G. Vitamin D and its role in the lipid metabolism and the development of atherosclerosis. Biomedicines. 2021 Feb 9;9(2):172-180.
21. Bjelakovic G, Gluud LL, Nikolova D, et al. Vitamin D supplementation for prevention of mortality in adults. Cochrane database of systematic reviews. 2014 Feb 1(1): 132-145.
22. Cheshmazar E, Hosseini AF, Yazdani B, Razmpoosh E, Zarrati M. Effects of vitamin D supplementation on omentin-1 and spexin levels, inflammatory parameters, lipid profile, and anthropometric indices in obese and overweight adults with vitamin D deficiency under low-calorie diet: a randomized placebo controlled trial. Evidence-based Complementary and Alternative Medicine. 2020 Oct;2020.
23. Jafari-Sfidvajani S., Ahangari R., Hozoori M., Mozaffari-Khosravi H., Fallahzadeh H., Nadjarzadeh A. The effect of vitamin D supplementation in combination with low-calorie diet on anthropometric indices and androgen hormones in women with polycystic ovary syndrome: a double-blind, randomized, placebo-controlled trial. Journal of Endocrinological Investigation. 2018;41(5):597–607.
24. Manoy P, Yuktanandana P, Tanavalee A, Anomasiri W, Ngarmukos S, Tanpowpong T, Honsawek S. Vitamin D supplementation improves quality of life and physical performance in osteoarthritis patients. Nutrients. 2017;9(8):1–13.
25. Mousa A, Naderpoor N, Wilson K, Plebanski M, de Courten MPJ, Scragg R, de Courten B. Vitamin D supplementation increases adipokine concentrations in overweight or obese adults. European Journal Nutrition. 2020; 59(1):195–204.
26. Lorvand Amiri H., Agah S., Mousavi S. N., Hosseini A. F., Shidfar F. Regression of non-alcoholic fatty liver by vitamin D supplement: a double-blind randomized controlled clinical trial. Archives of Iranian Medicine. 2016;19(9):631–638.
27. Forno E, Bacharier LB, Phipatanakul W, Guilbert TW, et al. Effect of vitamin D3 supplementation on severe asthma exacerbations in children with asthma and low vitamin D levels: the VDKA randomized clinical trial. Jama. 2020;324(8):752-60.