*Original Article*

# Effects of Vitamin D Supplementation on Omentin-1, Leptin, and Lipid Profile in Patients with Coronary Artery Disease

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## ABSTRACT

**Background:** Vitamin D has drawn impressive interest because of its significance in various extra-skeletal illnesses, including multiple sclerosis, malignancies, diabetes mellitus, and cardiovascular disease. Vitamin D exhibits anti-inflammatory properties, too, yet the role of vitamin D supplementation in decreasing inflammatory biomarkers remains generally obscure. This study aimed to evaluate the effects of oral vitamin-D intake on lipid profile, anthropometric indices and plasma levels of adipokines, including leptin and omentin-1, in patients with coronary artery disease (CAD).

**Methods:** This study was conducted at the Cardiac Units Civil Hospital in Karachi, Pakistan from January to December 2023. A total of 200 diagnosed patients with coronary artery disease who had already been prescribed oral vitamin D due to insufficient vitamins were included in the study. Their health care consultants prescribed patients a daily dose of 2000IU vitamin D for 8 weeks. Lipid profile, anthropometric measurements and serum levels of vitamin D, omentin-1 and leptin were assessed at the beginning and end of the study.

**Results:** Vitamin-D supplementation led to a notable decrease in leptin concentration (3776±0.422 vs. 3187±0.144, p<0.001). Moreover, circulating omentin-1 levels (245±26.1 vs. 296.5±28.11, p<0.001) and HDL-cholesterol levels (36.80±13.46 vs. 45.2±14.31, p< 0.001) were found significantly higher at the end of study.

**Conclusion:** This study demonstrated that an 8 week vitamin D supplementation in CAD patients significantly reduced leptin levels while increasing omentin-1 and HDL-c levels, suggesting their potential cardioprotective effects.

**Keywords:** Adipokines, Biomarkers, Coronary artery disease, Vitamin D, Lipid metabolism.

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## INTRODUCTION

Coronary Artery Disease (CAD) is a leading cause of illness and death worldwide, characterized by the narrowing or blockage of coronary arteries, resulting in chest pain, shortness of breath, and potentially myocardial infarction[1].

Atherosclerotic plaque accumulation in coronary artery walls is the primary cause, involving buildup of cholesterol, fatty deposits, calcium, and inflammatory cells[2]. CAD accounts for approximately 17.7 million deaths globally each year, representing 31% of all deaths[3]. Atherosclerosis can begin in adolescence or childhood, with arterial changes progressing silently before plaques grow or rupture, triggering potentially life-threatening events[4]. Several risk factors contribute to atherosclerosis development, including age, smoking, diabetes, hypertension, abnormal cholesterol levels (high LDL, low HDL), stress, and sedentary lifestyle. Managing these factors through lifestyle modifications and medical interventions is essential for reducing atherosclerosis burden[5].

Evidence suggests that low vitamin D levels may constitute a significant risk factor for CAD pathogenesis. Vitamin D, a pleiotropic nutrient obtainable through diet, supplements, or sunlight exposure, exists primarily as ergocalciferol (D2) from plant sources and cholecalciferol (D3) from sunlight or animal foods[6]. Both forms convert to 25-hydroxyvitamin-D in the liver and subsequently to 1,25-dihydroxyvitamin-D (calcitriol) in the kidneys. Vitamin D regulates calcium and phosphate metabolism, supports bone health, modulates immune function, and potentially protects against cardiovascular diseases, diabetes, and certain cancers[7]. Deficiency is associated with infections, neurological disorders, autoimmune diseases, cardiovascular disease, and various carcinomas[8].

While precise mechanisms linking vitamin D deficiency to CAD remain unclear, evidence highlights its importance in vascular health. Vitamin D enhances nitric oxide expression in vascular endothelial cells, maintaining vasodilation, reducing oxidative stress, and preventing endothelial dysfunction. It also improves angiogenic capabilities of endothelial progenitor cells essential for vascular repair[9]. Additionally, vitamin D regulates immune cells by altering pro-inflammatory and anti-inflammatory cytokine expression, protecting blood vessels[10].

Vitamin D deficiency may activate the renin gene, increasing angiotensin II levels and potentially causing hypertension and ventricular hypertrophy[11]. Vitamin D exerts anti-inflammatory effects by inhibiting nuclear factor kappa B (NF-κB) activation and interfering with the mitogen-activated protein kinase (MAPK) pathway, thereby reducing pro-inflammatory cytokine production[12].

Visceral adipose tissue secretes omentin-1, an anti-inflammatory adipocytokine that inhibits inflammatory pathways like COX-2/NF-κB and deactivates the JUN pathway, helping control inflammation associated with obesity and metabolic disorders[13]. Due to epicardial adipose tissue's proximity to cardiac muscles and vascular endothelium, omentin-1 directly impacts CAD development[14]. CAD patients show reduced omentin-1 levels[15].

Leptin, a 16 kDa pro-inflammatory adipocytokine expressed in white adipose tissue[16], regulates signaling pathways affecting genes involved in immune responses and inflammation. By influencing immune cells like macrophages and T-cells, leptin alters pro-inflammatory cytokine production, contributing to inflammatory conditions including obesity, autoimmune diseases, and metabolic disorders[17]. Leptin is believed to correlate with the renin-angiotensin-aldosterone system, endothelial oxidative stress, and arterial wall thickening, contributing to atherosclerosis[18].

This study aimed to investigate how oral vitamin D supplementation affects omentin-1 and leptin levels in CAD patients, potentially providing insights into CAD progression and management through these adipokines' roles in inflammation, immune response, and metabolic regulation.

## METHODOLOGY

### *Study Design*

This observational study was conducted at the Cardiac Units of Civil Hospital Karachi, Pakistan, from January 2023 to December 2023.

### *Sample Size and Sampling Technique*

Two hundred diagnosed patients with CAD who had vitamin D insufficiency and were prescribed oral vitamin D supplementation were included.

According to the Endocrine Society, individuals with vitamin D levels of ≤20 ng/mL are classified as vitamin D deficient, while those with levels ranging from 21 to 29 ng/mL are considered to have insufficient vitamin D. Levels of ≥30 ng/mL are regarded as optimal for maintaining proper physiological functions and health.

### *Recruitment of Participants*

Individuals who were identified to have CAD based on angiographic results that showed more than 50% stenosis in main coronary arteries, such as the right coronary artery, left circumflex or anterior descending branch of the

left coronary artery, were included in the study. Participants were provided with complete explanations of the study's objectives, and their written informed consents were obtained.

***Data Collection Procedure***

Sociodemographic information, such as age, sex, family history of CAD, and past infections, was collected utilizing a standardized questionnaire. Potential confounding variables were noted but not controlled, including dietary intake, physical activity, and concurrent use of medications such as lipid-lowering agents, anti-diabetic drugs, and anti-hypertensives.

Participants underwent anthropometric measurements and medical examinations. Measurements were made to the nearest 0.1 cm for waist circumference (WC), hip circumference (HC), height, and weight. The circumference of the abdomen between the lower costal border and the iliac crest, slightly above the belly button, was measured to determine the WC. In contrast, HC was measured with tape around the hips' widest point. Body mass index (BMI) was expressed in $kg/m^2$.

Using an enzyme-linked immunosorbent test (ELISA), the plasma levels of omentin-1, leptin, and vitamin D were measured. Cal-Biotech, catalogue #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, catalogue #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 daily dosage of 2000 IU of oral vitamin D for eight weeks. Anthropometric measures, lipid profiles, levels of circulating vitamin D, omentin-1, and leptin were evaluated before and after the supplementation.

Participants' compliance was monitored through follow-up visits, where they were questioned about their adherence. Serum vitamin D levels were measured at baseline and at the end of the study to confirm supplementation intake, along with the concentrations of omentin-1 and leptin, which were measured at baseline and at regular intervals to assess changes over time.

***Statistical Analysis***

A quantitative analysis of the collected data was conducted using a statistical package for social sciences (SPSS, version 22, Chicago, IL, USA). To evaluate the differences between the pre- and post-treatment measures, paired t-tests were conducted. This allowed for comparing the same patients' biomarkers, such as omentin-1, leptin, and lipid profiles, before and after vitamin D supplementation. Additionally, an independent t-test was used to assess the overall impact of vitamin D on these biomarkers in CAD patients, comparing results between groups with different baseline vitamin D levels. A p-value of less than 0.05 was considered statistically significant.

***Ethical Considerations***

This study was conducted according to the ethical principles of the Declaration of Helsinki. Before collecting data, ethical approval was obtained from the Institutional Review Board of Civil Hospital Karachi. Participants were informed about the purpose, procedures, potential risks, and benefits of the study and asked to provide written informed consent before enrolling. Participants were informed that their data would be confidential and anonymous, and that they could withdraw from the study at any time without impact on their medical care. All biological samples were treated with biosecurity procedures, and data was stored to minimize access to authorized personnel only.

## RESULTS

A total of 200 patients with CAD (120 males and 80 females, with a mean age of (51.05±11.55) participated in the study. Only a small percentage of individuals could not follow up due to personal issues, pregnancy, or overseas relocation.

**Table-1 Anthropometric measurements and blood pressure of participants before and after the oral intake of vitamin-D**

| Variables | Baseline | After 8-weeks | 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±4.95 | 30.06±4.01 | 2.41±0.94 | 0.94 |
| **WC (cm)** | 118±10.56 | 114.3±11.06 | 4.66±1.19 | 0.29 |
| **W/H** | 0.95±3.43 | 0.94±0.12 | 0.01±3.31 | 0.93 |
| **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 |

### Anthropometric Measurements

The anthropometric measurements, including body weight, BMI, WC, and blood pressure, of participants both before and after oral intake of vitamin D. Decreases in weight (86.98±7.01 vs 85.67±6.06, p=0.78), BMI (32.47±4.95 vs 30.06 ± 4.01, p=0.94), WC (118 ± 10.56 vs 114.3 ± 11.06, p=0.29) were noted. However, values are statistically non-significant. There was an increase in SBP (130.23±10.71 vs. 133.58±9.01, p=0.77) from baseline to the conclusion. However, these changes did not reach statistical significance (Table-1).

### Metabolic Markers and Lipid Profile

The impact of oral vitamin D on circulating levels of omentin-1, leptin, vitamin D and lipid profile. The findings indicate a significant reduction in leptin concentration (3776±0.422 vs. 3187±0.144, p<0.001), TG (172.36±94.33 vs 135.06±64.5, p<0.001). LDL-c levels were also reduced but statistically found insignificant. 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 found to be significantly higher (Table-2).

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

| Variables | Baseline | After 8-weeks | 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 | 0.134 |
| **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 | 0.945 |
| **TC (mg/dL)** | 205.13±77.93 | 190.03±73.21 | −15.10±4.72 | 0.161 |

### Gender Differences

Table-3 shows significant improvements in both males and females from the starting position to the end 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. Gender distribution of plasma vitamin-D levels at the beginning and end of the study**

| | Baseline | After 8-weeks | 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

Several recent studies have explored the effects of vitamin D supplementation on cardiovascular health, yielding mixed results. While our study demonstrated a significant increase in omentin-1 and HDL-c levels and decreased leptin concentrations, other research has reported inconsistent findings. A meta-analysis by Ford et al. (2020) found that while vitamin D supplementation was associated with improved endothelial function, its impact on lipid metabolism remained inconclusive. Similarly, the VITAL trial, a large-scale study by Manson et al. (2019), reported no significant reduction in major cardiovascular events with vitamin D supplementation alone[20]. These discrepancies may arise due to variations in study design, sample size, supplementation dose, duration, and baseline vitamin D status of participants.

One potential explanation for the differing results is the population characteristics. Our study specifically included patients with diagnosed vitamin D insufficiency, whereas some studies included participants with sufficient vitamin D levels at baseline, potentially reducing the observable impact of supplementation. Additionally, genetic factors and differences in vitamin D receptor (VDR) polymorphisms may influence individual responses to supplementation. Another key factor is adherence to supplementation; in our study, compliance was assessed through follow-up visits and serum vitamin D measurements, ensuring that participants maintained adequate levels. Furthermore, lifestyle factors such as diet, physical activity, and concurrent medication use may confound the effects of vitamin D on cardiovascular health. Some trials failed to control for these variables, leading to heterogeneity in results. It is also possible that vitamin D exerts its cardiovascular benefits through indirect pathways, such as reducing systemic inflammation or improving insulin sensitivity[21], which may require longer durations to manifest in clinical outcomes. Given these variations, further well-controlled, long-term studies with larger sample sizes are needed to clarify the role of vitamin D supplementation in cardiovascular disease prevention and treatment.

The current investigation found that after vitamin D supplementation, there was a significant increase in the levels of omentin-1, with measurements rising from $245.09 \pm 26.1$ to $296.5 \pm 28.11$ ($p=0.001$). In contrast, a study by Cheshmazar et al. observed no change in omentin-1 blood levels following a daily dose of 2,000 IU of vitamin D for three months. These contrasting results highlight the variability in response to vitamin D supplementation and suggest that further research is needed to understand better the factors influencing omentin-1 regulation in different populations[22]. However, Jafari et al. found that omentin-1 levels increased after four months of consistent 2,000 IU vitamin D intake. This supports the notion that prolonged vitamin D supplementation may positively affect omentin-1 levels, further suggesting that the duration and consistency of supplementation could be key factors in determining its impact on adipokine regulation. This finding contrasts with the results of Cheshmazar et al., where no change in omentin-1 levels was observed, highlighting the potential variability in response to vitamin-D supplementation across different studies[23].

The current analysis revealed a significant decrease in leptin levels, from $3776 \pm 0.4$ ng/ml to $2576 \pm 0.1$ ng/ml ($p=0.001$) after eight weeks of vitamin-D supplementation. In contrast, Manoy et al.[24] found no significant changes in leptin levels in osteoarthritis patients who received 4000 IU of vitamin D weekly for six months. These differences may reflect variations in the duration, dosage, and patient populations, suggesting that the effects of vitamin D on leptin levels could be influenced by factors such as underlying health conditions, supplementation duration, and dosage.

According to Mousa et al., vitamin D supplementation at a dose of 4000 IU daily for 16 weeks led to significant changes in serum leptin concentrations in obese individuals with baseline vitamin D levels ≤50 nmol/L. This study suggests that vitamin D supplementation may notably impact leptin levels, particularly in individuals with low vitamin D status, further highlighting the potential benefits of addressing vitamin D deficiency in managing obesity-related metabolic disturbances[25]. In the current study, anthropometric indices such as height, body weight, BMI, and waist circumference (WC) did not show significant changes following the intervention. This contrasts with a previous study

that observed a significant reduction in these indices after an eight-week intervention. The discrepancies between the studies could be attributed to variations in the study design, sample size, participant characteristics, or the type of intervention used, suggesting that the impact of vitamin D supplementation on anthropometric measures may vary depending on these factors[22].

This investigation demonstrated that vitamin D supplementation significantly increased the serum's HDL-c concentration. This aligns with findings by Mousa et al., who reported that vitamin-D treatment led to elevated HDL-c levels and a significant reduction in triglyceride concentrations in the intervention group. These results are consistent with our findings, suggesting that vitamin D may be beneficial in improving lipid profiles, particularly HDL-c and triglycerides[26].

The observed significant improvements in the current study's deficient and insufficient groups align with the findings of Forno et al., who demonstrated that vitamin D supplementation significantly improved serum vitamin D levels in both deficient and insufficient asthma patients. This supports the notion that vitamin D supplementation can effectively correct deficiency and insufficiency, regardless of baseline levels, and may offer therapeutic benefits across various conditions, including those with underlying inflammatory components such as asthma and coronary artery disease[27].

## CONCLUSION

The study highlights the potential role of vitamin D in modulating adipokines and improving lipid metabolism in coronary artery disease patients. The reduction in leptin and increase in omentin-1 and HDL-c suggest possible anti-inflammatory and cardioprotective effects. These findings emphasize the need for larger, long-term studies to validate the results and assess sustained benefits. Future research should explore optimal dosing, duration, and mechanisms of action. Understanding these factors could help establish vitamin D as a supportive therapy in cardiovascular disease management.

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**Author Contributions**
**Shazia Nazar** supervised the study and reviewed the final draft. **Hina Abbas** collected data and wrote the initial draft. **Sana Abbas** analyzed data and revised the manuscript. All authors approved the final version.

**Ethical Approval**
This study received approval from the Institutional Ethical Review Committee (Ref No: KIBGE/ICE/345) of Dr. A. Q. Khan Institute of Genetics and Biotechnology.

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None.

**Conflict of Interests**
None.

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