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The Association of Serum Vitamin D With Anthropometric Indices, Lipid Profile, ICAM-1, and IL-17 in Patients Undergoing Coronary Artery Bypass Graft Surgery

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ABSTRACT

This study aimed to assess the relationship between serum levels of vitamin D with anthropometric indices, lipid profile and vascular inflammatory factors, in patients who candidate for coronary artery bypass grafting (CABG). This analytical cross-sectional study was conducted in patients who were candidate for CABG. Demographic information, medical records, anthropometric indicators, blood samples, and physical activity of 150 patients were collected. 146 participants with mean ± standard deviation of age: 61.8 ± 10.0 years and body mass index: 26.9 ± 3.7 kg/m^2 completed the study. Based on serum levels of vitamin D, patients were divided into 2 groups; groups with sufficient (≥ 30 ng/mL) and insufficient amount of vitamin D (< 30 ng/mL). The 30.14% of the patients had serum vitamin D deficiency. Ejection fraction (EF) % between the 2 groups had significant difference. Unexpectedly the EF% increased 7% in patients with insufficient level of vitamin D (odds ratio [OR], 1.07; 95% confidence interval [CI], 1.03–1.11; p = 0.001). Vitamin D status had a significant inverse association with body weight. The odds of vitamin D deficiency significantly increased by 4% with increasing one kg in weight (OR, 1.04; 95% CI, 1–1.08; p = 0.044). There were no significant association between serum vitamin D level and intra cellular adhesion molecule-1, interleukin-17, fasting blood glucose, and lipid profile (p > 0.05). Considering the inverse association observed between serum vitamin D with EF% and body weight, vitamin D may play a role in modulating of these indices.

Keywords: Coronary artery bypass; Interleukin-17; Intercellular adhesion molecule-1 (ICAM-1); Vitamin D; Cross-sectional studies

Conflict of Interest

The authors declare that they have no competing interests.

Author Contributions

Conceptualization: Tafteh N, Abdollahzad H, Sabzi F, Rezaeian S; Data curation: Tafteh N, Abdollahzad H, Sabzi F; Formal analysis: Rezaeian S; Investigation: Tafteh N, Abdollahzad H, Sabzi F, Rezaeian S; Writing - original draft: Tafteh N, Abdollahzad H, Sabzi F; Writing - review & editing: Abdollahzad H.

INTRODUCTION

Coronary artery bypass grafting (CABG) is the most frequent therapeutic approach in management of coronary artery occlusion. It still remains an ideal way to relieve angina pectoris, improve heart muscle contraction, and restore normal heart function, so that extends life expectancy and survival in patients with congenital heart disease (CHD) [1]. CABG also can elicit an inflammatory response by activating the immune system and exacerbate the chronic systemic inflammation associated with atherosclerosis plaques in the inner lining of the coronary artery which can lead to increase the risk of heart attacks and strokes [2]. Interleukin (IL)-17 is a pro-inflammatory cytokine that have a role in induction of many immune signaling molecules. It induces the production of many other cytokines such as IL-6, IL-8, and tumor necrosis factor-α [3]. IL-8 may promote neutrophil–endothelial cell adhesion by increasing the expression of endothelial cell adhesion molecules (CAMs). The induction of monocyte pro-coagulant activity with either IL-6 or IL-8 has been proposed as a possible link between the inflammation and thrombosis in patients with coronary artery disease [4]. Serum concentrations of CAM might be higher in patients with atherosclerosis, and an age-dependent increase of the expression of CAM on the surface of vascular endothelium cells might has a role in development of atherosclerotic lesions [5]. Therefore, inflammatory responses must be managed in patients who underwent CABG surgery.

The role of antioxidant compounds in ameliorating inflammatory and degenerative processes especially in the cardiovascular system has been reported in several studies. In a previous study we showed that dietary total antioxidant capacity was associated with increased serum levels of total antioxidant capacity and decreased CAMs in patients who candidate for CABG surgery [6]. Vitamin D is known as the sunshine vitamin with antioxidant and anti-inflammatory properties. Its active form, i.e., 1,25-dihydroxy vitamin D (1,25$[OH]_2$D), has a high tendency to bind to vitamin D receptor (VDR). Following binding to VDR, changes in gene expression occur. These genes usually involve in the growth and differentiation of heart muscle, vascular endothelium, and immune cells, especially lymphocytes and macrophages [7]. Therefore, vitamin D in the cardiovascular system has a critical role in controlling inflammatory pathways and immune responses [8].

The minimum level of serum vitamin D for optimal biological functions has been proposed to be 30 ng/mL. It has also been reported that heart attack risks at levels below 30 ng/mL can be elevated. The deficiency of this vitamin is so common that it occurs in almost 30%–50% of the population [7]. According to a previous study in Iran, 72.1% of men and 75.1% of women suffer from varying degrees of vitamin D deficiency [8]. In recent years, vitamin D deficiency has been shown to be associated with many risk factors for cardiovascular diseases, i.e., high blood pressure, dyslipidemia, insulin resistance, metabolic syndrome, diabetes mellitus, obesity, overweight, and a noticeable increase in waist circumference [7,9]. However, data on the association between vitamin D deficiency and cardiovascular diseases such as acute myocardial infarction, stroke, heart failure, ischemic heart disease, acute coronary syndrome, peripheral vascular disease and cardiac arrhythmias are very challenging [9,10]. Due to its antioxidant properties, vitamin D reduces the production of free radicals, the causing factors of inflammation and arrhythmias [11]. Vitamin D has also been shown to play an important role in preventing vascular stiffness and endothelial dysfunction, so its deficiency leads to increased levels of vascular calcification and the progression of atherosclerosis [12]. Moreover, according to the studies, the mortality rate is significantly higher after CABG surgery or catheterization in patients with vitamin D deficiency [13]. Therefore, the current

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study aimed to evaluate the relationship between serum vitamin D with anthropometric indicators (body mass index [BMI], waist and hip circumferences), lipid profile, fasting blood glucose (FBG), ejection fraction (EF%), and vascular inflammatory factors (IL-17 and intra cellular adhesion molecule [ICAM]-1) in patients who were candidates for CABG surgery.

MATERIALS AND METHODS

This cross-sectional study was performed among patients who were candidate for CABG surgery. Recruitment of patients occurred from October 2017 to February 2018. The study was a part of MSc dissertation which consisted of consecutive outpatients who referred to the cardiovascular clinic of Imam Ali Hospital in Kermanshah, Iran. Patients who candidate for CABG were recruited the study through the convenience sampling method. Finally, 150 eligible cases were included in the analysis. The study protocol was approved by the Ethics Committee of Kermanshah University of Medical Sciences (ethics code: IR.KUMS.REC.1397.130). According to the Helsinki Declaration, after explanation the objectives of study, an informed written consent was obtained from each participant.

The inclusion criteria were patients between 30 and 80 years with clogged arteries who needed the CABG surgery based on the physician's diagnosis and angiography results. Also, the calorie intakes of eligible participants were between 2,000 and 3,000 kcal per day. Patients with liver disorders (i.e., hepatitis, cirrhosis, and gallstones), kidney stones, pulmonary infection, diabetes, cancer, malabsorption, thyroid disorders, heart attacks and strokes or surgical history in previous 6 months were excluded. Also, candidates consuming drugs (i.e., aspirin, warfarin, clopidogrel, and immunosuppressive drugs, corticosteroids) and dietary supplements (i.e., antioxidants) in a month before the study were excluded. Other exclusion criteria were unwillingness to continue or failure to have the surgery for any reason.

For all participants a questionnaire containing demographic and socioeconomic information, medical and medication records was completed. Also, the time of exposure to sunlight was asked and entered as minutes per day in the relevant questionnaire. Dietary information was collected using a food frequency questionnaire including 125 food items by face-to-face interview. Participants responded questions about the frequency and amount of food consumed. To assess the level of physical activity, a short questionnaire of the International Physical Activity Questionnaire-Short Form was used [6]. The physical activity time (hours or minutes per day) of each person was asked and recorded. The data were extracted and used based on metabolic equivalents per hour per week and categorized as low, moderate, and severe activity.

Height was measured by a stadiometer with an accuracy of 0.1 cm, and weight using a digital scale; both measurements were done in the fasting state with minimal cloths and without shoes. BMI was calculated by dividing weight (kg) to height (m^2). The waist and hip circumferences were measured using an inelastic tape and the waist-to-hip ratio (WHR) was calculated.

On the first day of hospitalization, 10 mL of blood was collected from each patient after fasting for more than 10 hours. Samples were immediately centrifuged for 30 minutes at the hospital laboratory and then separated serum samples were stored at −40°C until laboratory analysis. FBG and serum lipid levels including total cholesterol (TC), low-density lipoprotein-

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cholesterol (LDL-C), high-density lipoprotein-cholesterol (HDL-C), and triglyceride (TG) were measured enzymatically using Pars Azmoon kits (Iran). The serum levels of inflammatory markers, including IL-17 and ICAM-1 were measured using the Eastbiofarm kits (China). In addition, serum levels of 25-hydroxyvitamin D (25[OH]D) were measured using the Monobind kit (Monobind Inc., Lake Forest, CA, USA). Based on the serum levels of 25(OH)D, patients were divided into 2 groups; vitamin D deficient patients (serum vitamin D < 30 ng/mL) and vitamin D sufficient patients (serum vitamin D ≥ 30 ng/mL). EF% was assessed using the echocardiography.

Statistical analysis

The normality was assessed by the Kolmogorov-Smirnov test. We expressed continuous variables as mean ± standard deviation and median (interquartile range) for normally and not normally distributed data, respectively; and the categorical and nominal variables as frequencies. The χ^2 test or Fisher's exact test was applied to compare the qualitative variables. On the other hand, independent-samples t-test and Mann-Whitney U test were applied to compare the variables with normal and non-normal distribution between the 2 groups (vitamin D-sufficient group vs. vitamin D-deficient group), respectively. Variables with significant differences between the 2 groups, such as gender, smoking, BMI, waist and hip circumference, and EF%, were considered as confounding variables. Then, these significant variables entered into the linear regression model for estimating the propensity scores (the continuous dependent variable was serum levels of 25-hydroxy vitamin D). The accuracy of the propensity score model was done using the C-statistic (the C-statistic of 0.80 showed a good discrimination of model). Among the 3 methods to use the predicted propensity score, the stratification method was used. In the stratification method, the predicted propensity score would be divided into 5 strata. Finally, to determine the relationship between vitamin D-deficient and biochemical measures, the strata of the propensity score was also added to the logistic regression model. The adjusted odds ratio (OR) with 95% confidence interval was reported. All analyses were performed using STATA 14.2 software (Stata Corp., College Station, TX, USA). A 2-side p value of less than 0.05 was considered as statistically significant.

RESULTS

One hundred fifty eligible patients were enrolled in the current study. Among them, 4 patients were excluded from the study (unwillingness to participate [n = 1], the cancellation of surgery [n = 2], and withdrawal from the surgery [n = 1]). A total of 146 individuals, 40 women and 106 men, completed the study process and were included in the analyses. The participants' mean of age was 61.78 ± 10.04 years; weight was 73.03 ± 11.02 kg (46.3–103.3); BMI was 26.89 ± 3.67 kg/m^2 (18.63–39.69); and duration of exposure to sunlight was 118.65 ± 108.93 minutes per week (2–480).

The comparison of demographic and anthropometric characteristics between the 2 groups according to vitamin D levels are shown in **Table 1**. We found that a total of 44 patients (30.14%) had a vitamin D deficiency (< 30 ng/mL) at the time of hospitalization for surgery. There was no significant difference in demographic variables such as age, marital status, and alcohol consumption between the 2 groups; vitamin D-deficient group vs. vitamin D-sufficient group. The odds of vitamin D deficiency in women were twice as high as that of men, which was statistically significant (OR, 2.16; p = 0.048). Smokers are 60% less likely to lack vitamin D than non-smokers, indicating statistical significance (OR, 0.42; p = 0.028). The average EF%

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Table 1. Demographic, anthropometric, and some other characteristics among patients based on serum vitamin D status

Variables	Serum vitamin D		p value	Adjusted model	p value
	< 30 ng/mL (n = 44)	≥ 30 ng/mL (n = 102)		OR (95% CI)*	
Age (yr)	59.88 ± 8.26	62.64 ± 10.73	0.130	-	-
Gender			0.046		
Men	27 (61.4)	79 (77.5)		-	-
Women	17 (38.6)	23 (22.5)		-	-
Marital status			0.495		
Married	37 (84.1)	90 (88.2)		1.00	-
Widowed	7 (15.9)	12 (11.8)		1.10 (0.331–3.42)	0.917
Smoking			0.026		
No	32 (72.7)	54 (52.9)		1.00	-
Yes	12 (27.3)	48 (47.1)		0.40 (0.179–0.88)	0.023
Alcohol consumption			0.724†		
No	42 (95.5)	95 (93.1)		1.00	-
Yes	2 (4.5)	7 (6.9)		0.56 (0.099–3.12)	0.506
Weight (kg)	75.66 ± 11.75	71.89 ± 10.55	0.058	1.04 (1–1.08)	0.044
BMI (kg/m^2)	28.14 ± 4.00	26.36 ± 3.39	0.007	1.10 (0.99–1.23)	0.076
Waist circumference (cm)	105.93 ± 8.09	102.42 ± 9.04	0.028	1.00 (0.991–1.08)	0.126
Hip circumference (cm)	97.79 ± 7.20	93.97 ± 8.86	0.013	1.00 (0.994–1.1)	0.080
WHR	1.08 ± 0.06	1.09 ± 0.11	0.527	0.34 (0.006–18.4)	0.597
SBP (mmHg)	124.04 ± 12.96	128.47 ± 18.99	0.161	0.99 (0.96–1.01)	0.208
DBP (mmHg)	80.79 ± 9.83	80.05 ± 10.70	0.696	1.00 (0.96–1.04)	0.960
Heart rate (beats/min)	74.90 ± 13.54	72.81 ± 11.95	0.352	1.01 (0.97–1.04)	0.686
Ejection fraction %	47.38 ± 9.79	40.44 ± 11.14	0.001	1.07 (1.03–1.11)	0.001
Myocardial Infarction			1.000†		
No	42 (95.5)	96 (94.1)		1.00	-
Yes	2 (4.5)	6 (5.9)		1.02 (0.19–5.55)	0.979
Heart arrhythmia			0.704		
No	32 (72.7)	71 (69.6)		1.00	-
Yes	12 (27.3)	31 (30.4)		1.50 (0.58–3.65)	0.417
Sunlight exposure (min/day)	60 (30–120)	120 (30–180)	0.093‡	1.00 (0.99–1)	0.153
Physical activity (MET-min/week)			0.394		
Low: < 600	30 (68.2)	59 (57.8)		1.00	-
Moderate: 600–1,500	13 (29.5)	35 (34.3)		0.73 (0.32–1.66)	0.457
High: > 1,500	1 (2.3)	8 (7.9)		0.33 (0.04–2.87)	0.315

Data are presented as mean ± standard deviation, median (interquartile range), or frequencies.
OR, odds ratio; CI, confidence interval; BMI, body mass index; WHR, waist-to-hip ratio; SBP, systolic blood pressure; DBP, diastolic blood pressure; MET, metabolic equivalents.
*Adjusted for BMI, age and sex using logistic regression.
The p values were calculated by χ^2 test for qualitative variables and independent-sample t-test for quantitative variables, unless otherwise indicated: †The p value was obtained from Fisher's exact test; ‡The p value was obtained from Mann-Whitney U test.

was significantly higher of the vitamin D-deficient group than that of the vitamin D-sufficient group (47.38 ± 9.79 vs. 40.44 ± 11.14; p = 0.001). Additionally, the analysis was conducted to compare the groups based on BMI (obese vs. normal) and there was no correlation between the level of vitamin D and CHD related risk factors. After adjusting for BMI, age and sex, the odds of vitamin D deficiency were positively related to the EF% (OR, 1.07; p = 0.001). We found that the mean of BMI, waist and hip circumference were significantly higher in vitamin D-deficient patients than those in vitamin D-sufficient patients. Although there was no significant difference in WHR between the 2 groups, body weight showed a difference toward significance between the 2 groups (75.66 ± 11.75 vs. 71.89 ± 10.55; p = 0.058). Adjusted logistic regression model showed a significant relationship for weight only. In other word, the odds of vitamin D deficiency significantly increased by 4% with increasing one kg in weight (OR, 1.04; p = 0.044).

Between-groups difference in biochemical factors is shown in **Table 2**. Serum metabolic factors, including lipid profiles and FBG, did not differ significantly between vitamin

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Table 2. Biochemical measures among patients based on serum vitamin D status

Variables	Serum vitamin D		p value	Adjusted model	p value
	< 30 ng/mL (n = 44)	≥ 30 ng/mL (n = 102)		OR (95% CI)*	
FBG (mg/dL)	109.75 ± 20.91	109.68 ± 20.87	0.987	1.000 (0.983–1.018)	0.982
TG (mg/dL)	139.54 ± 53.49	127.42 ± 49.24	0.186	1.000 (0.997–1.01)	0.159
HDL-C (mg/dL)	38.86 ± 8.87	36.81 ± 8.96	0.206	1.020 (0.985–1.07)	0.216
LDL-C (mg/dL)	82.15 ± 20.38	84.62 ± 25.42	0.570	0.993 (0.977–1.01)	0.359
Total cholesterol (mg/dL)	151.04 ± 29.19	148.33 ± 35.85	0.659	1.000 (0.993–1.01)	0.487
ICAM-1 (ng/mL)	212.60 (175.47–254.32)	218.91 (182.85–420.82)	0.080	0.998 (0.996–1)	0.063
Interleukin-17 (pg/mL)	24.35 (17.97–50.10)	25.20 (18.95–46.15)	0.971	1.000 (0.992–1.01)	0.914

Data are presented as mean ± standard deviation or median (interquartile range).
OR, odds ratio; CI, confidence interval; FBG, fasting blood glucose; TG, triglyceride; HDL-C, high density lipoprotein-cholesterol; LDL-C, low density lipoprotein-cholesterol; ICAM-1, intra cellular adhesion molecule-1.
*Propensity score adjusted for gender, smoking, body mass index, waist and hip circumferences, and ejection fraction.

D-deficient and vitamin D-sufficient patients. Although there was no significant difference in IL-17 levels, a difference toward significance was seen in ICAM-1 levels between the 2 groups (212.6 vs. 218.91 ng/mL; p = 0.08). The results of the propensity score adjusted model were still not significant.

DISCUSSION

In the current study, serum levels of 25-hydroxy vitamin D less than 30 ng/mL were considered as deficiency. According to this definition, 44 individuals (30.14%) of the study participants had vitamin D deficiency, including 42.5% of women and 25.4% of men. The mean serum levels of 25(OH)D in vitamin D deficient and sufficient individuals were 11.61 and 52.22 ng/mL, respectively.

Many studies have examined the prevalence of vitamin D deficiency in the Iranian population. Separham et al. [14] reported vitamin D deficiency (< 20 ng/mL) in 26.3% of men and 32.6% of women who have coronary artery obstruction. Also, Mahdavi et al. [9] observed that about 72% of patients with the acute coronary syndrome in Ahvaz city suffered from vitamin D deficiency (< 20 ng/mL). The reason for the lower prevalence of vitamin D deficiency in the present study compared to the previous studies could be due to the smaller sample size of the study and unequal sex distribution (106 men vs. 40 women). Meanwhile, although the study season was similar in Mahdavi et al.'s study [9] and our study (autumn and winter), it seems that in Ahvaz city, due to the hot weather, people are less inclined to face direct sunlight. The results of the present study showed that the direct exposure time to sunlight in individuals with an optimum level of vitamin D was significantly higher than that in the patients with vitamin D deficiency, which is quite expected and justifiable. Since the main way to produce this vitamin in the skin is through the exposure of sunlight and the conversion of 7-dehydrocholesterol to pro-vitamin D [9], it has been claimed that 95% of people's vitamin D needs are met by direct exposure to sunlight [7].

In the current study, despite the inequality in sex distribution, vitamin D deficiency was more common in women than men. In line with our results, some studies have reported an increase in vitamin D deficiency in women. Moradzadeh et al. [8] reported a higher prevalence of severe vitamin D deficiency (< 20 ng/mL) in women in Tehran, Tabriz, Bushehr, and Shiraz provinces. Bonakdaran et al. [15] reported a higher prevalence of vitamin D deficiency in diabetic women. Also, in the study of Ziaee et al. [16] performed on diabetic people aged 30–70 years, deficiency of vitamin D was more common in women. In all of

these studies, the cause of the higher prevalence of vitamin D deficiency in women has been attributed to a sedentary lifestyle, women's clothing, and sometimes low milk consumption. In a study in Saudi Arabia, severe vitamin deficiency was clearly more common in women (despite the hot, sunny weather in Saudi Arabia), which itself could be a reason for the importance of women's lifestyle over geographical conditions [17].

In the present study, blood pressure and heart rate did not differ significantly between the 2 groups; however, unexpectedly the EF% was higher in individuals with vitamin D deficiency. Vitamin D deficiency leads to high blood pressure through stimulating the renin-angiotensin and aldosterone system [7], so it expected that blood pressure in people with vitamin D deficiency would be higher. This discrepancy could be the result of the use of antihypertensive drugs in the candidates of this study, which were a part of the fixed medications in all patients. In this regard, Yarjanli et al. [18] reported higher mean blood pressure for people with vitamin D deficiency (< 20 ng/mL). However, the participants in Yarjanli et al.'s study [18] had no history of cardiovascular disease and medication at the time of entry into the study. In contrast, in the study of Mahdavi et al. [9] which participants had acute coronary syndrome, similar to those in our study, there was no relationship between vitamin D deficiency and the prevalence of hypertension. In another study, that was conducted on participants without previous myocardial infarctions, heart failure, or prevalent valvular disease, higher 25(OH)D was positively associated EF [19]. According to the effect of calcium on cardiac contractions and the close association of calcium with vitamin D, if there is a sufficient level of the vitamin, sufficient calcium ions are provided to regulate heart rate and heart contractions. So, individuals with vitamin D deficiency were expected to have a higher average heart rate and reduced EF. The controversial results observed in this study can be justified from 2 perspectives. First, the subjects were treated with antiarrhythmic agents. Secondly, in vitamin D deficiency condition, parathyroid hormone regulates the blood level of calcium by increasing its intestinal absorption, moving bone calcium sources, and increasing calcium reabsorption in the kidneys; it provides the level needed to modulate heart contractions and EF. Therefore, it can be assumed that people with vitamin D deficiency enter the compensatory phase to provide enough calcium in the blood, but this increase in calcium levels can lead to atherosclerosis and even calcification of the heart valves [7]. This also may be the case for our observation that odds of vitamin D deficiency in smokers is significantly 60% lower than non-smokers. The effect of smoking on circulating level of vitamin D has been reported in several studies. Although in a study by Stürmer et al. [20] no statistically significant effect on circulating vitamin D levels was observed, there is growing body of evidence indicating the negative effects of smoking on 25(OH)D and calcium metabolism [21]. Apart from the effect of compensatory phase, this discrepancy may be due to the small number of our study patients in both smoking and non-smoking group, which makes it the difficult to discern a definitive conclusion.

In the present study, mean of weight, waist circumference, and BMI were higher in people with vitamin D deficiency and there was an inverse association between vitamin D deficiency and body weight. The results of many studies are in line with the present study. Yarjanli et al. [18] reported that people with vitamin D levels less than 20 ng/mL had a higher BMI. In Ziaee et al.'s study [16], there was an inverse relationship between vitamin D status and mean of waist circumference. Also, in the study of Heidari et al. [12], people with lower levels of vitamin D had higher waist circumference. In an investigation by Gepner et al. [22] postmenopausal women with vitamin D deficiency had a higher average weight. In confirmation of the above, other studies have shown that obesity is one of the risk factors for vitamin D deficiency [7]. It is believed that overweight and obese people have a sedentary

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lifestyle and are less exposed to sunlight. On the other hand, it is hypothesized that due to the steroidal nature of vitamin D, this vitamin can be stored in adipose tissue [9]. Therefore, in obese people with increased waist circumference, a significant amount of the vitamin is stored in adipose tissue. It was also explained that in the absence of vitamin D, the level of parathyroid hormone increases, which leads to an increase in lipogenesis and a decrease in lipolysis in adipose tissue [23]. Therefore, people with higher BMI are expected to have lower vitamin D levels. In connection with the effect of vitamin D status on lipid profile and fasting blood sugar (FBS) levels, the results of studies are very challenging. Yarjanli et al. [18] observed that people with vitamin D levels less than 20 ng/mL had higher TC and TG levels. Heidari et al. [12] concluded that vitamin D levels are inversely related to FBS levels, TG and LDL, and directly to HDL levels in diabetics. Gepner et al. [22] studied non-diabetic postmenopausal women and found that people with lower levels of vitamin D had higher FBG. Moreover, Alhamad et al. [17], in a study on the elderly with an average of 75 years old, reported that vitamin D levels less than 30 ng/mL could cause higher FBS levels and lower HDL. Several studies suggest that people with vitamin D deficiency have higher levels of blood sugar and lipids. To address this issue, it has been suggested that vitamin D deficiency reduces insulin sensitivity, decreases insulin production, disrupts lipids metabolisms, create a pre-diabetic and diabetic situation, and eventually increases levels of FBS, hemoglobin A1c, and 2-hour postprandial glucose [12]. Additionally, a number of studies believe that cholesterol absorption increases in people with vitamin D deficiency, but the exact mechanism is not mentioned [24]. Vitamin D actually acts as a nuclear transcription factor affecting gene function and protein transcription [7]. So far, more than 200 genes have been identified in this regard, one of which is the gene encoding the lipoprotein lipase enzyme. Since this enzyme clears circulating lipoproteins in muscle and fat tissue and ultimately modifies the lipid profile, the prevalence of dyslipidemia was expected to be higher in people with vitamin D deficiency [25]. Though, in a number of studies in which the sample size and clinical conditions of individuals were similar to ours, no association was observed between vitamin D deficiency and the prevalence of hyperlipidemia or increased FBS levels [9,15]. In explaining this issue, it can be noted that the participants in our study were treated with lipid-lowering drugs and did not include people with diabetes. Therefore, the observed results might be related to the characteristic of the study participants. Additionally, the differences in the cut-off point for determining vitamin deficiency (30 ng/mL vs. 20 ng/mL) and small sample size of this study may contribute to the null results of our study.

The present study hypothesized that the levels of IL-17 and ICAM-1, which are both inflammatory and progressive factors for atherosclerosis [26], were probably higher in people with vitamin D deficiency. However, we did not observe any association between the vitamin D status with IL-17 and ICAM-1. It has been suggested that vitamin D deficiency can increase pro-inflammatory cytokines, including IL-17, as well as adhesion molecules such as ICAM-1 and decrease anti-inflammatory cytokines [27,28]. In confirmation of this hypothesis, Gurses et al. [10] reported that people with vitamin D deficiency (mean = 10.6 ng/mL) had higher levels of IL-17. In another study, Sokol et al. [26] also observed that people with vitamin D deficiency had higher ICAM levels. In contrast, in large studies such as Framingham, there was no definite link between vitamin D status and these 2 inflammatory factors [26]. This discrepancy could be explained by the role of vitamin D in the regulation of immune response. In fact, the enzyme engaged in the final hydroxylation step in the synthesis of $1,25(OH)_2$ D3 is expressed by activated macrophages, making them able to synthesize and secret $1,25(OH)_2$ D3 in a regulated mode. Unlike the renal version of the enzyme, the macrophage version is mainly under the regulation of immune signal such as interferon-γ

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[29]. Since CHD is associated with an inflammatory response by activating the immune system and exacerbate the chronic systemic inflammation, the higher level of vitamin D in patients with higher levels of IL-17 and ICAM-1 might be related to the increased activity of the 25(OH)D3-1α-hydroxylase enzyme in activated macrophages [4]. Additionally, due to the small sample size of this study, discern a definite opinion in this regard is difficult.

Vitamin D deficiency can affect the risk of heart attacks in several ways, including compensatory increased in parathyroid hormone levels, blood calcium levels, plaque formation], impaired immune function [10], increased Inflammatory cytokines such as IL-17, stimulation of the nuclear factor kappa B pathway, further expression of adhesion molecules such as ICAM, increased leukocytes and macrophages adhesion to the vascular endothelium and eventually the development of vascular sclerosis [7,10,15,30]. In confirmation of this, it has been suggested that if other risk factors are controlled, vitamin D deficiency increases the risk of heart attacks twice as much, especially in men [9]. Studies of people with myocardial infarction have also shown that vitamin D deficiency increases the risk of having a second attack [12]. In connection with strokes, the most prominent available mechanism is an increase in parathyroid hormone levels, which increases arterial pressure and ultimately increases the risk of ischemic and hemorrhagic strokes. A study of women with stroke found that they had lower levels of vitamin D than their healthy peers. In addition, epidemiological studies have shown that the incidence of strokes in winter and higher latitudes are higher, which is a risk factor for vitamin D deficiency [7]. Canpolat et al. [11], comparing 48 people with a history of intermittent atrial fibrillation (common arrhythmia in the atrium) and healthy individuals, concluded that people with a history of atrial arrhythmia had lower levels of vitamin D. Yarjanli et al. [18], in a study with a follow-up period of 5.7 years, reported that the incidence of these events in people with vitamin D levels lower than 10 ng/mL compared with people with normal levels of vitamins (above 30 ng/mL) is 3.21 times higher. Heidari et al. [12] followed up 2,607 people with diabetes for 8.5 years and concluded that the level of vitamin D is inversely related to the incidence of the above-mentioned events. However, in the study of Mahdavi et al. [9], as the present study, there was no relationship between vitamin D deficiency and the incidence of cardiovascular complications. It seems that factors including high sample size, long-term follow-up, and the presence of underlying diseases have been effective in the results of Yarjanli et al. [18] and Heidari et al. [12]'s studies. One of the limitations of the present study was the time constraint for long-term follow-up of patients after surgery. However, the present study had some strengths, such as inclusion of patients of both sexes and taken into account the patient's lifestyle and their pharmaceutical profile. In addition, verified examiners following standardized protocols, performed all examinations and laboratory measurements. Finally conducting multivariate analysis to control the confounder variables is another strength of this study.

CONCLUSION

Considering the inverse association observed between serum vitamin D with EF and body weight, vitamin D may play a vital role in modulating of these indices. Since all the participants in the current study had metabolic syndrome (waist circumference > 102 cm, FBG > 100 mg/dL, and HDL < 40 mg/dL) and the body weight of patients with higher vitamin levels was significantly lower; it seems that in addition to normal vitamin D levels, having a lifestyle that helps improve the components of metabolic syndrome can reduce the number of CABG surgeries.

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REFERENCES

1. Hedman A, Larsson PT, Alam M, Wallen NH, Nordlander R, et al. CRP, IL-6 and endothelin-1 levels in patients undergoing coronary artery bypass grafting. Do preoperative inflammatory parameters predict early graft occlusion and late cardiovascular events? Int J Cardiol 2007;120:108-14. PUBMED | CROSSREF
2. Winterhalter M, Brandl K, Rahe-Meyer N, Osthaus A, Hecker H, et al. Endocrine stress response and inflammatory activation during CABG surgery. A randomized trial comparing remifentanil infusion to intermittent fentanyl. Eur J Anaesthesiol 2008;25:326-35. PUBMED | CROSSREF
3. Moseley TA, Haudenschild DR, Rose L, Reddi AH. Interleukin-17 family and IL-17 receptors. Cytokine Growth Factor Rev 2003;14:155-74. PUBMED | CROSSREF
4. Arnson Y, Itzhaky D, Mosseri M, Barak V, Tzur B, et al. Vitamin D inflammatory cytokines and coronary events: a comprehensive review. Clin Rev Allergy Immunol 2013;45:236-47. PUBMED | CROSSREF
5. Richter V, Rassoul F, Purschwitz K, Hentschel B, Reuter W, et al. Circulating vascular cell adhesion molecules VCAM-1, ICAM-1, and E-selectin in dependence on aging. Gerontology 2003;49:293-300. PUBMED | CROSSREF
6. Mohammadi Z, Abdollahzad H, Rezaeian S, Sabzi F, Tafteh N. The association of dietary total antioxidant capacity with inflammatory biomarkers and anthropometric indices in patients who candidate for coronary artery bypass graft surgery: a cross-sectional study. Clin Nutr Res 2021;10:353-63. PUBMED | CROSSREF
7. Lee JH, O'Keefe JH, Bell D, Hensrud DD, Holick MF. Vitamin D deficiency an important, common, and easily treatable cardiovascular risk factor? J Am Coll Cardiol 2008;52:1949-56. PUBMED | CROSSREF
8. Moradzadeh K, Larijani B, Keshtkar AA, Hossein-Nezhad A, Rajabian R, et al. Normative values of vitamin D among Iranian population: a population based study. Int J Osteoporos Metab Disord 2008;1:8-15. CROSSREF
9. Mahdavi K, Amirajam Z, Yazdankhah S, Majidi S, Adel MH, et al. The prevalence and prognostic role of vitamin D deficiency in patients with acute coronary syndrome: a single centre study in South-West of Iran. Heart Lung Circ 2013;22:346-51. PUBMED | CROSSREF
10. Gurses KM, Tokgozoglu L, Yalcin MU, Kocyigit D, Dural M, et al. Markers of subclinical atherosclerosis in premenopausal women with vitamin D deficiency and effect of vitamin D replacement. Atherosclerosis 2014;237:784-9. PUBMED | CROSSREF
11. Canpolat U, Aytemir K, Hazirolan T, Özer N, Oto A. Relationship between vitamin D level and left atrial fibrosis in patients with lone paroxysmal atrial fibrillation undergoing cryoballoon-based catheter ablation. J Cardiol 2017;69:16-23. PUBMED | CROSSREF
12. Heidari B, Nargesi AA, Hafezi-Nejad N, Sheikhbahaei S, Pajouhi A, et al. Assessment of serum 25-hydroxy vitamin D improves coronary heart disease risk stratification in patients with type 2 diabetes. Am Heart J 2015;170:573-579.e5. PUBMED | CROSSREF
13. Lee CH, Shieh YS, Tsai CS, Hung YJ, Tsai YT, et al. Plasma concentrations predict aortic expression of growth-arrest-specific protein 6 in patients undergoing coronary artery bypass grafting. PLoS One 2013;8:e79452. PUBMED | CROSSREF
14. Separham A, Sohrabi B, Pourafkari L, Sepasi N, Ghaffari S, et al. Vitamin D is a predictor of ST segment resolution and infarct size following thrombolysis in patients with acute ST elevation myocardial infarction. Turk Kardiyol Dern Ars 2017;45:324-32. PUBMED | CROSSREF
15. Bonakdaran S, Varasteh A, Khaajeh-Dalouie M. Serum 25 hydroxy vitamin D3 and laboratory risk markers of cardiovascular diseases in type 2 diabetic patients. Iranian J Endocrinol Metab 2010;11:504-9.
16. Ziaee A, Hashemipoor S, Karimzadeh T, Jalalpoor A, Javadi A. Relation of vitamin D3 level with metabolic syndrome indices among patients with diabetes and non-diabetic individuals. J Ardabil Univ Med Sci 2012;12:149-56.
17. Alhamad HK, Nadukkandiyil N, El-Menyar A, Abdel Wahab L, Sankaranarayanan A, et al. Vitamin D deficiency among the elderly: insights from Qatar. Curr Med Res Opin 2014;30:1189-96. PUBMED | CROSSREF
18. Yarjanli M, Hosseinpanah F, Sheikholeslami F, Azizi F. Association between vitamin D deficiency and cardiovascular disease. Iranian J Endocrinol Metab 2011;12:520-8.

https://doi.org/10.7762/cnr.2024.13.3.165

19. Fall T, Shiue I, Bergeå af Geijerstam P, Sundström J, Ärnlöv J, et al. Relations of circulating vitamin D concentrations with left ventricular geometry and function. Eur J Heart Fail 2012;14:985-91. PUBMED | CROSSREF
20. Stürmer M, Šebeková K, Fazeli G, Bahner U, Stäb F, et al. 25-Hydroxyvitamin D and advanced glycation endproducts in healthy and hypertensive subjects: are there interactions?. J Ren Nutr 2015;25:209-16. PUBMED | CROSSREF
21. Yang L, Zhao H, Liu K, Wang Y, Liu Q, et al. Smoking behavior and circulating vitamin D levels in adults: a meta-analysis. Food Sci Nutr 2021;9:5820-32. PUBMED | CROSSREF
22. Gepner AD, Ramamurthy R, Krueger DC, Korcarz CE, Binkley N, et al. A prospective randomized controlled trial of the effects of vitamin D supplementation on cardiovascular disease risk. PLoS One 2012;7:e36617. PUBMED | CROSSREF
23. McCarty MF, Thomas CA. PTH excess may promote weight gain by impeding catecholamine-induced lipolysis-implications for the impact of calcium, vitamin D, and alcohol on body weight. Med Hypotheses 2003;61:535-42. PUBMED | CROSSREF
24. Oh J, Weng S, Felton SK, Bhandare S, Riek A, et al. 1,25(OH)$_2$ vitamin D inhibits foam cell formation and suppresses macrophage cholesterol uptake in patients with type 2 diabetes mellitus. Circulation 2009;120:687-98. PUBMED | CROSSREF
25. Mead JR, Irvine SA, Ramji DP. Lipoprotein lipase: structure, function, regulation, and role in disease. J Mol Med (Berl) 2002;80:753-69. PUBMED | CROSSREF
26. Sokol SI, Srinivas V, Crandall JP, Kim M, Tellides G, et al. The effects of vitamin D repletion on endothelial function and inflammation in patients with coronary artery disease. Vasc Med 2012;17:394-404. PUBMED | CROSSREF
27. Colotta F, Jansson B, Bonelli F. Modulation of inflammatory and immune responses by vitamin D. J Autoimmun 2017;85:78-97. PUBMED | CROSSREF
28. Thompson D, Walhin JP, Batterham AM, Stokes KA, Cooper AR, et al. Effect of diet or diet plus physical activity versus usual care on inflammatory markers in patients with newly diagnosed type 2 diabetes: the Early ACTivity in Diabetes (ACTID) randomized, controlled trial. J Am Heart Assoc 2014;3:e000828. PUBMED | CROSSREF
29. Overbergh L, Decallonne B, Valckx D, Verstuyf A, Depovere J, et al. Identification and immune regulation of 25-hydroxyvitamin D-1-alpha-hydroxylase in murine macrophages. Clin Exp Immunol 2000;120:139-46. PUBMED | CROSSREF
30. Luc G, Arveiler D, Evans A, Amouyel P, Ferrieres J, et al. Circulating soluble adhesion molecules ICAM-1 and VCAM-1 and incident coronary heart disease: the PRIME study. Atherosclerosis 2003;170:169-76. PUBMED | CROSSREF