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Original Article

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Association of Vitamin D status with Visceral Adiposity Index and Lipid Accumulation Product Index among a Group of Iranian People

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ABSTRACT

There is a growing body of evidence linking vitamin D and its antiadipogenic activity with body composition. The aim of this study was to investigate the association between vitamin D levels, visceral adiposity index (VAI), and lipid accumulation product index among a group of Iranian people. This cross-sectional study was conducted with 270 Iranian adults. Body composition was measured via bio-impedance analysis. The 25-hydroxyvitamin D [25(OH)D] was also measured using the enzyme-linked immunosorbent assay method. The VAI and lipid accumulation product index were calculated. Multiple linear and logistic regression after controlling for confounder was used to report the results. Multiple linear regression showed that serum 25(OH)D levels were positively correlated with age (crude: β ± standard error [SE] = 0.23 ± 0.06, p ≤ 0.001; model I: β ± SE = 0.18 ± 0.05, p = 0.002) and percent body fat (crude: β ± SE = 0.10 ± 0.04, p = 0.02). Binary logistic regression analysis showed a higher chance of greater percent body fat and lipid accumulation product index in the crude model (odds ratio [OR], 2.05; 95% confidence interval [CI], 1.13–3.72 for percent body fat and OR, 2.07; 95% CI, 1.14–3.76 for lipid accumulation product index), which disappeared after adjusting for covariates. Adults with higher vitamin D levels had higher scores of percent body fat and lipid accumulation product index. More longitudinal studies are needed to confirm these results.

Keywords: Vitamin D; 25(OH)D; Adiposity; Adults; Lipid accumulation product

INTRODUCTION

Obesity is an excessive fat accumulation [1] is a global epidemic that has affected more than half of the world's adult population [2,3]. Obesity strongly increases morbidity and mortality from chronic disease, namely cardiovascular disease (CVD), insulin resistance and diabetes mellitus, hypertension, and a certain type of cancers [4]. In addition, obesity has been reported to alter the absorption, distribution, metabolism, and excretion of micronutrients [5,6]. Vitamin D deficiency has been also known as a risk factor for several abovementioned diseases. In obese people, serum levels of 25-hydroxyvitamin D3 [25(OH)D3] are low [7,8].

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Conflict of Interest
The authors declared that they have no competing interests.

The confiscation of vitamin D in visceral adipose tissue in obese people may reduce the release of vitamin D into the bloodstream [9].

The traditional role of vitamin D as an essential nutrient is controlling musculoskeletal system and maintaining bone metabolism [10]. Also, the serum levels of vitamin D are key importance in several non-communicable diseases, including insulin resistance, diabetes, cardiovascular disease, obesity, and anthropometric traits especially body fat particularly visceral adiposity [11,12]. Based on cellular [13], animal [14], and epidemiological [15] studies vitamin D through the deterrence of adipogenesis inhibits the beginning of obesity, also vitamin D improves the metabolic function of adipose tissue by increasing lipid consumption in adipocytes [16]. In this regard, the findings of a previous study showed a positive association between 25(OH)D concentrations and visceral fat area (VFA) [17]. The results of a meta-analysis also showed a significant association between vitamin D levels and fat mass (FM) or percentages fat mass (PFM) [18]. In addition, a negative significant association between body mass index (BMI), percentage body fat (PBF) [19], and lipid accumulation product (LAP) with serum vitamin D levels has been reported [20]. In contrast, some studies show no link between vitamin D deficiency or status and some indicators of fat accumulation such as and PFM and LAP [21,22].

The purpose of this study was to examine the association between serum levels of 25(OH)D and fat accumulation index in Iranian adults.

MATERIALS AND METHODS

Study design

This cross-sectional study was conducted among 271 adults aged 18–70 years, recruited by way of convenience sampling. Recruitment took six months from April to September 2018. Participants were chosen based on the following criteria: 1) age range of 18–70 years, 2) no alcohol or drug abuse, 3) no history of heart failure, hepatic or renal diseases, not being pregnant or lactating. All participants were informed completely about the study protocol and signed a written consent in advance to engage in the study procedure. The study was approved by the local Ethics Committee of Tehran University of Medical Sciences (ethic number: IR.TUMS.VCR.REC.1396.4085). This study was conducted according to the guidelines laid down in the Declaration of Helsinki.

Biochemical assessment

Blood samples were collected between 8:30–10:30 a.m. after 10 to 12 hours of fasting at the Nutrition Laboratory of Tehran University of Medical Science. Plasma samples were stored and kept frozen at −80°C until analysis. Serum 25-dihydroxyvitamin D [25(OH)2D] was measured using a 25(OH)D kit (Monobind kit, Monobind Inc., Lake Forest, CA, USA) by the enzyme-linked immunosorbent assay method. Enzymatic methods were used for assessing fasting serum glucose (FSG). Serum total cholesterol (TC) and high-density lipoprotein-cholesterol (HDL-C) were measured using a cholesterol oxidase phenol amino antipyrine method, and triglyceride (TG) was measured using a glycerol-3 phosphate oxidase phenol amino antipyrine enzymatic method. All these tests were done by commercial kits (all from Pars Azmoon, Tehran, Iran) using an auto-analyzer system (Selectra E, Vitalab, Holliston, The Netherlands).

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Anthropometric measurements and body composition

Digital scales were used to measure the weight with minimal clothing and no shoes. Height was measured using a tape measure while subjects were standing without shoes and their head, shoulders, hip, and heels touch the wall. BMI was calculated by dividing weight (kg) by height in meters squared (m^2). Waist and hip circumference were measured using a non-elastic tape meter without any pressure to the body surface. Lean body mass (LBM), total body fat, visceral fat mass, abdominal fat mass, FM, and PBF were measured by multi-frequency bio-impedance analysis (BIA) (InBody 720, BioSpace, Tokyo, Japan). Participants were asked to avoid food ingestion for at least 4 hours, taking more than 2 L water the day before, physical activity for at least 8 hours, taking coffee or alcohol for at least 12 hours, or any diuretic for at least 24 hours. It was advised patients empty their bladder immediately before the BIA test [23].

Definition of visceral adiposity index (VAI) and LAP

The VAI [24] and LAP [25] are both calculated according to formulas that have been previously validated:

$$\text{Men VAI} = \left(\frac{WC}{39 \cdot 68 + (1 \cdot 88 \times BMI)}\right) \times \left(\frac{TG}{1 \cdot 03}\right) \times \left(\frac{1 \cdot 31}{HDL - C}\right)$$

$$\text{Women VAI} = \left(\frac{WC}{36 \cdot 58 + (1 \cdot 89 \times BMI)}\right) \times \left(\frac{TG}{0 \cdot 81}\right) \times \left(\frac{1 \cdot 52}{HDL - C}\right)$$

$$\text{Men LAP} = \text{TG}(mmol/L) \times [WC(cm) - 65)]$$

$$\text{Women LAP} = \text{TG}(mmol/L) \times [WC(cm) - 58)]$$

Assessment of other variables

Data on age, smoking (nonsmoker, smoker) and physical activity (low, moderate, high), education (under diploma, diploma, educated), occupation (employee, housekeeper, retired, unemployed), marital status (single, married), and lifestyle (alone, with someone) was obtained using a pre-tested questionnaire. A validated International Physical Activity Questionnaire short form (IPAQ-SF) [26] was used to assess the level of physical activity for any participant and then classified into three levels; i.e. low, moderate, and high physical activity accordance with calculated metabolic equivalents (METs) over the past week low (600–3,000 MET-minutes/week), and moderate and high (> 3,000 MET-minutes/week) [27]. We asked the participants to think about the intense and moderate activities that they engaged in during the past 7 days, considering the time spent on these activities, before completing the questionnaire.

Statistical analysis

Participants were categorized according to tertiles of 25(OH)D. One-way analysis of variance for continuous variables and χ^2 analysis for categorical variables were used to compare participants' general characteristics across tertiles of vitamin D. To determine any association between vitamin D and age, BMI, waist circumference (WC), LAP, VAI, and TG/HDL-C, multiple linear regression analysis was performed in different models. The first model unadjusted for any variable. In the second model, we further adjusted for age, sex, BMI, WC, and smoking. The binary logistic regression model was also used to find the relationship between vitamin D with the odds ratio (OR) of higher fat free mass (FFM), PBF, visceral fat level (VFL), LAP, and VAI. First, the variables were taken as the median, and 2 upper and lower groups were created for each variable. We controlled for the confounding impact of age, BMI, WC, and smoking.

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In this analysis, the first tertile of vitamin D level was considered the reference category. All statistical analysis was performed using the Statistical Package for Social Sciences (version 24; SPSS Inc, Chicago, IL, USA). The $p < 0.05$ was considered statistically significant.

RESULTS

Table 1 presents summary data for general and sociodemographic characteristics of the participants across tertiles of vitamin D levels. Participants were grouped based on tertiles of vitamin D levels. The total number of participants was 270, with 90 participants in each tertile. The mean age of individuals was 36.8 ± 13.1 and 55.8% were women. The distribution of participants was different in terms of sex ($p = 0.02$), occupation ($p < 0.001$) and marital status ($p = 0.02$). There was a significant difference in the mean age ($p < 0.001$) across tertiles of vitamin D levels. Furthermore, participants in the highest tertile of vitamin D levels had significantly higher BMI ($p = 0.01$), PBF ($p = 0.04$), and VFL ($p = 0.04$) than those in the lowest tertile. There was no significant difference in the mean LAP index and VAI across tertiles of serum vitamin D.

Multiple linear regression models in **Table 2** showed a significant and positive association between 25(OH)D status with age in both models ($p < 0.001$ for crude model and $p = 0.002$ for model I) and PBF ($p = 0.02$) in the crude model. In contrast, TG/HDL-C ($p = 0.5$) and FFM ($p = 0.08$) were inversely related to 25(OH)D concentrations, however, the associations were not statistically significant.

Table 3 reports multivariate-adjusted ORs for the adiposity measures across the tertile's vitamin D levels. The only statistically significant correlation was related to PBF and LAP index. In the crude model, individuals at the top tertile of vitamin D level had higher PBF (OR, 2.05; 95% confidence interval [CI], 1.13–3.72; $p = 0.01$) and LAP index (OR, 2.07; 95% CI, 1.14–3.76; $p = 0.01$) compared with those in the lowest tertile. After control for confounders, the significant associations were disappeared.

DISCUSSION

This is the first study to examine the relationship between vitamin D with some adiposity indicators including VFL, LAP, and VAI. In this cross-sectional study, we found that in a higher level of serum vitamin D, mean age, BMI, PBF, and VFL were higher. A positive significant association was observed between 25(OH)D statuses with age and PBF. Also, a significant relationship was observed between serum vitamin D and odds of PBF and LAP; however, after controlling the confounders, only a significant correlation remained for age.

Vitamin D deficiency is a global problem with several consequences for chronic diseases including obesity, cardiovascular disease, and type 2 diabetes mellitus [28]. In recent years, many studies have examined the link between vitamin D and obesity, including various observational studies [29-32] that demonstrated the relationship between vitamin D with body composition components. Among the various studies, a meta-analysis study reported that vitamin D levels were inversely related to FM and PFM [18]. Findings from two other review studies also showed the same results [33,34]. In obese people, compared to non-obese people, FM as the main source of vitamin D, leads to reduced access to vitamin D in

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Table 1. General characteristics of Iranian adults according to tertiles of vitamin D levels

Characteristics	Tertiles of vitamin D			p value*
	T1	T2	T3	
No. of participants	90	90	90	
Age (yr)	33.3 ± 11.2	36.8 ± 13.3	40.3 ± 14.0	< 0.001
Weight (kg)	70.5 ± 17.6	74.8 ± 16.3	72.9 ± 13.8	0.19
Height (cm)	169 ± 10.1	169 ± 10.1	165 ± 9.39	0.04
BMI (kg/m^2)	24.4 ± 4.37	25.9 ± 4.72	26.4 ± 4.72	0.01
WC (cm)	87.3 ± 13.2	91.0 ± 12.5	90.6 ± 11.6	0.10
WHR	0.89 ± 0.06	0.91 ± 0.06	0.90 ± 0.06	0.16
FBG (mg/dL)	97.3 ± 10.4	95.7 ± 9.35	102 ± 29.0	0.06
TG (mg/dL)	113 ± 65.6	127 ± 80.6	117 ± 60.3	0.36
HDL-C (mg/dL)	49.9 ± 10.2	47.9 ± 10.4	51.4 ± 10.9	0.08
TC (mg/dL)	185 ± 40.8	186 ± 35.6	191 ± 38.5	0.48
SBP (mmHg)	112 ± 11.4	114 ± 13.4	113 ± 14.7	0.36
DBP (mmHg)	70.1 ± 7.97	72.4 ± 9.84	70.8 ± 9.63	0.25
FFM (kg)	49.8 ± 13.9	52.1 ± 12.2	48.8 ± 10.4	0.17
PBF (%)	29.2 ± 8.89	29.8 ± 9.14	32.5 ± 9.76	0.04
VFL	9.00 ± 4.20	9.90 ± 4.59	10.6 ± 4.68	0.04
LAP index	37.6 ± 39.6	43.4 ± 33.6	41.2 ± 27.6	0.51
VAI	1.76 ± 1.29	2.05 ± 1.68	1.83 ± 1.16	0.37
Sex (%)				0.02
Male	43.8	54.4	34.4	
Female	56.2	45.6	65.6	
Smoking (%)				0.05
Not smoking	84.1	87.8	87.8	
Quit smoking	3.4	7.8	4.4	
Physical activity (%)				0.77
Low	37.5	35.6	42.2	
Moderate	38.6	44.4	40.0	
High	23.9	20.0	17.8	
Education (%)				
Under diploma	5.7	6.7	10.0	
Diploma	15.9	23.3	16.7	
Educated	77.3	70.0	73.3	
Occupation (%)				< 0.001
Employee	55.7	62.2	42.2	
Housekeeper	9.1	12.2	27.8	
Retired	3.4	7.8	13.3	
Unemployed	31.8	17.8	16.7	
Marriage (%)				0.02
Single	53.4	41.1	33.3	
Married	43.2	52.2	64.4	
Lifestyle (%)				0.87
Alone	9.1	7.8	10.0	
With someone	90.9	92.2	90.0	

Values are means ± standard deviation unless indicated.
BMI, body mass index; WC, waist circumference; WHR, waist to hip ratio; FBG, fasting blood glucose; TG, triacylglycerol; HDL-C, high-density lipoprotein cholesterol; TC, total cholesterol; SBP, systolic blood pressure; DBP, diastolic blood pressure; FFM, fat free mass; PBF, percent body fat; VFL, visceral fat level; LAP, lipid accumulation product; VAI, visceral adiposity index.
*Obtained using one-way analysis of variance for continuous variables and χ^2 test for categorical variable.

metabolic functions [35]. However, the following study showed that the pattern of vitamin D accumulation was similar in obese with normal individuals. Since obese people have bigger FM and body size, most oral and synthesized vitamin D enters the FM, which reduces the amount of vitamin D available to become in its active form [36].

The Framingham Heart Study [37] examined the link between vitamin D and cardiometabolic risk factors, reported that in those with high subcutaneous adipose tissue (SAT) and high

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Table 2. Multiple linear regression models on vitamin D levels among Iranian adults

Variables	Vitamin D		p value
	β ± SE	95% CI	
Age (yr)			
Crude	0.23 ± 0.06	0.10, 0.35	< 0.001
Model I*	0.18 ± 0.05	0.06, 0.29	0.002
BMI (kg/m²)			
Crude	0.03 ± 0.02	−0.006, 0.083	0.08
Model I	0.01 ± 0.009	−0.007, 0.02	0.24
WC (cm)			
Crude	0.02 ± 0.06	−0.09, 0.15	0.63
Model I	−0.02 ± 0.02	−0.07, 0.02	0.28
TG/HDL-C			
Crude	−0.006 ± 0.01	−0.02, 0.01	0.53
Model I	−0.005 ± 0.01	−0.02, 0.01	0.59
FFM (kg)			
Crude	−0.10 ± 0.06	−0.22, 0.01	0.08
Model I	−0.003 ± 0.03	−0.06, 0.5	0.91
PBF (%)			
Crude	0.10 ± 0.04	0.01, 0.19	0.02
Model I	−0.009 ± 0.02	−0.05, 0.03	0.66
VFL			
Crude	0.04 ± 0.02	−0.004, 0.083	0.07
Model I	−0.002 ± 0.008	−0.01, 0.01	0.78
LAP index			
Crude	0.02 ± 0.16	−0.30, 0.34	0.89
Model I	−0.09 ± 0.13	−0.34, 0.16	0.47
VAI			
Crude	0.00 ± 0.007	−0.01, 0.01	0.97
Model I	−0.003 ± 0.007	−0.01, 0.01	0.66

BMI, body mass index; WC, waist circumference; TG, triglyceride; HDL-C, high-density lipoprotein cholesterol; FFM, fat free mass; PBF, percent body fat; VFL, visceral fat level; LAP, lipid accumulation product; VAI, visceral adiposity index.
*Model I: adjusted for age, sex, BMI, WC, and smoking.

Table 3. Multivariable-adjusted ORs and 95% CIs of FFM, PBF, VFL, LAP index, and VAI according to tertiles of vitamin D levels among Iranian adults

Variables	Vitamin D			p trend
	T1	T2	T3	
	OR (95% CI)	OR (95% CI)	OR (95% CI)	
FFM*				
Crude	1	1.49 (0.83–2.69)	0.87 (0.48–1.57)	0.65
Model I†	1	1.43 (0.69–2.94)	0.83 (0.39–1.77)	0.64
PBF*				
Crude	1	1.04 (0.58–1.88)	2.05 (1.13–3.72)	0.01
Model I	1	0.65 (0.32–1.31)	1.33 (0.66–2.69)	0.41
VFL*				
Crude	1	1.15 (0.63–2.09)	1.64 (0.91–2.98)	0.09
Model I	1	0.60 (0.26–1.37)	1.02 (0.45–2.32)	0.94
LAP index*				
Crude	1	1.65 (0.91–2.99)	2.07 (1.14–3.76)	0.01
Model I	1	1.04 (0.46–2.33)	1.47 (0.65–3.33)	0.35
VAI*				
Crude	1	1.25 (0.69–2.25)	1.19 (0.66–2.15)	0.54
Model I	1	1.02 (0.54–1.94)	0.98 (0.51–1.89)	0.96

OR, odds ratio; CI, confidence interval; FFM, fat free mass; PBF, percent body fat; VFL, visceral fat level; LAP, lipid accumulation product; VAI, visceral adiposity index.
*The median was considered as cut-off; †Model I: adjusted for age, BMI, WC, and smoking.

visceral adipose tissue (VAT) compared to those with low SAT and VAT, deficiency of vitamin D (25[OH]D < 20 ng/mL) was higher. In this regard, some other studies showed that higher

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levels of vitamin D are inversely related to adiposity, especially VAT [38,39]. Framingham's study showed that SAT and VAT, as a source of vitamin D storage, were associated with vitamin D status [37], although they are very connected to each other they appeared independently linked with 25(OH)D [40]. VAT is associated with different BMI categories, even in low-weight individuals. However, the association of SAT with vitamin D weakened in the lowest subgroup. Because SAT is so closely related to BMI, the link between SAT and vitamin D may be attributed to changes in body size caused by BMI [37]. In another meta-analysis on 21 prospective studies, Vimaleswaran et al. [41] reported that vitamin D decreases by 1.15% per 1 kg/m^2 increased in BMI. Although Drincic et al. [36] demonstrated that BMI is not a good predictor of 25(OH)D level compared with body weight and both weight and FM.

However, the results of our study are different from previous studies. Surprisingly, higher levels of vitamin D, age, and BMI were also higher. This might be due to the fact that older people (mean age, 60.6 years) can affect the outcome. With increasing age, changes in body composition occur as an increase in FM and a decrease in FFM [42]. But the average age of the participants in our study was not high, they were healthy young to middle-aged adults with no comorbidities and no medication use. On the other side, the study by Vatandost et al. [43] in Iran showed that the lowest prevalence rate of vitamin D deficiency is in Tehran. Where the samples we studied were selected. Likewise, it is important to note that BMI is a general indicator of body fat mass, which is also affected by other compounds such as bone mass and muscle.

There are no similar results among clinical trials that examined the effect of vitamin D supplementation on body composition. In a study on 40 obese and overweight adults, supplementation with 2,000 IU/day of vitamin D for 6 months had no effect on BMI and PBF [44]. Similar results were observed in another study [45]. Nevertheless, a study by Salehpour et al. [46] on 85 women with BMI ≥ 25 kg/m^2 showed that vitamin D supplementation for 12 weeks resulted in a significant reduction in BFM and an increase in FFM. While it did not affect body weight, BMI, and PBF. In contrast, Sun et al.'s study [47] found that after a year of supplementation with vitamin D, LBM increased significantly, but other components of the body (BMI, WC, PBF, and VFA) did not change. Moreover, Forouhi et al. [48] in a cohort study, over a 4.5- or 10-year period did not find any association between vitamin D status and WC. These inconsistent findings may be attributed to the different measures of body composition and baseline characteristics of participants.

The only study that looked at the LAP index was Bardini et al.'s study [20]. The results of their study showed that LAP index is significantly associated with low vitamin D levels in both type 2 diabetes and obese non-diabetic persons. These results were in contrast to our findings that a significant association an increase in LAP index with the increase in serum vitamin D.

Overall, most studies have agreed on the inverse relationship between vitamin D and total body fat or regional fat. But the cause and effect mechanism has not been accurately identified. Several mechanisms are associated with vitamin D deficiency related to adipocytes. First, some believe that obesity is associated with reduced activity such as being outdoors and less exposed to sunlight [37]. Experimental studies showed that exposure to sunlight is not sufficient to calculate the difference in vitamin D concentrations in obese and non-obese individuals [9]. Thus, confounding by differences in sunlight exposure is highly unlikely as an explanation for poorer vitamin D status with greater adiposity [37]. Second, because vitamin D is fat-soluble, many researchers believe that vitamin D metabolites in different parts of fat reduce access to these metabolites in obese people compared to non-

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obese people [9]. Given this hypothesis, the change in SAT, which is the largest source of fat storage in the body, should be accompanied by a change in the storage form of vitamin D (25[OH]D). However, in Cheng et al.'s study [37] there was a strong association between 25(OH)D and VAT. The third mechanism is that vitamin D deficiency promotes the secretion of parathyroid hormone, which increases lipogenesis by enhancing the entry of calcium into adipocytes [49].

This study has some strengths and limitations. The main strength is that this is the first study which, in addition to examining the relationship between vitamin D and the factors related to adiposity studied in previous studies, also investigates the link between new indicators (VFL, VAI, and LAP index). One of the limitations of our study is that we did not consider the impact of gender in our analysis. Previous studies, however, showed that vitamin D deficiency is higher in women because their FM is higher compared to men. Another limitation is that due to the cross-sectional nature of the study, the longitudinal relationship between vitamin D and body composition could not be established.

In this study, we did not find any association between serum vitamin D with WC, FFM, PBF, VFL, VAI, and LAP index in a representative sample of Iranian adults. Although the results of our study were inconsistent with previous observational studies, a definitive conclusion about vitamin D with various indicators of obesity requires further study, especially clinical trials.

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